

Assessment of heart rate and QT variability's after revascularization in patients with acute coronary syndrome *

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Abstract

Background and aim: Depressed heart rate variability and increased QT variability that occurred after acute coronary syndromes are associated with poor long-term prognosis. But a few data is available about the influence of revascularization on these parameters. The aim of this study was to investigate heart rate and QT variabilities in the early phase of acute coronary syndromes and also to evaluate possible changes after revascularization.

Study design and methods: Heart rate and QT variabilities were recorded prospectively within 2 hours after ischemic attack and repeated after revascularization by using short-time ECG recordings.

Results: Twenty three patients with acute coronary syndrome with the mean age of 56.8 ± 10.5 years were included. Of patients, 12 had non-ST elevation myocardial infarction (MI), while 11 had unstable angina pectoris (USAP). In patients with non-ST elevation MI, significant increases were determined in SDNN ($p=.012$) and RMSSD ($p=.034$) values after revascularization. Mentioned parameters were also found to be increased in patients with USAP, but without statistically significant degree. In both of the groups, no significant change was found in QT parameters after revascularization.

Conclusion: The present study indicate that time domain parameters of patients with acute coronary syndromes could increase after revascularization, and this increase could be observed more significantly in patients with MI.

Key words: electrocardiography, myocardial infarction, heart rate variability, QT variability.

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Introduction

Unstable angina pectoris (USAP) and acute myocardial infarction (AMI), as defined as acute coronary syndromes, have potentially high morbidity and mortality. A low heart rate variability (HRV) has been shown to be a powerful predictor of cardiac events in patients surviving AMI and USAP.¹⁻⁴ In the same way, myocardial ischemia seen during acute coronary syndromes has been shown to increase repolarization variability. QT variability has been accepted as a good marker for the regional inhomogeneity of ventricular

repolarization.⁵ As a result, both of increased QT interval variability and reduced HRV have been shown to be associated with vulnerability to malignant ventricular tachyarrhythmias and sudden cardiac deaths in patients with AMI.^{6,7}

It is well known that successful revascularization after acute coronary syndromes improve the prognosis.⁸ This effect may be related to both an improvement in electrical heart stability, as elucidated by electrophysiologic study, and a favorable action on the cardiac sympathovagal balance.⁹ It has been shown that depressed HRV at early period (first 48 hours) after AMI is associated with poor long-term prognosis.¹⁰ Heart rate variability studies on this subject are very few¹⁰⁻¹² and the majority of them refer to the survivors of AMI and to the long term prognostic value of HRV assessed at the time of discharge.¹³ But HRV at very early period (first 2 hour) after AMI is not clear yet. Furthermore, no data exist for the changes in QT dynamics beyond the first 24 hours after AMI and during the early period of revascularization. The aim of this study was to investigate heart rate and QT

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variabilities in the early phase of acute coronary syndromes and possible changes after revascularization.

Materials and Methods

Study population

Twenty three patients admitted to the emergency department of a university hospital with a diagnosis of acute coronary syndrome (11 patients with USAP and 12 patients with acute MI) were enrolled in the study. This prospective study included patients admitted to the emergency department during the weekday daytime with a diagnosis of USAP or non-ST elevation MI, in whom angioplasty and/or stent implantation procedures were then performed. Informed consent was obtained from each subject.

Unstable angina pectoris diagnosis was made by the presence of resting prolonged (15-30 minute) new onset angina or resting angina occurring in patients with either a history of myocardial infarction or a previous chronic stable angina. Non-ST elevation MI diagnosis was made by the presence of prolonged chest pain (>30 minutes) without ST-elevation in ECG accompanied by an increase in cardiac enzyme levels to at least twice the upper normal limit of the laboratory. The following characteristics were also recorded for each patient: age, gender, history of previous MI, diabetes, smoking habit, hypertension (systolic blood pressure >140 mmHg, and/or diastolic blood pressure >90 mmHg and/or treatment with antihypertensive drugs), and family history of coronary heart disease. Troponin I values were evaluated for all patients.

All patients were monitored in the coronary unit and treated with standard medical therapy with aspirin, parenteral nitrate, and heparin infusion. None of the patient in the study group received thrombolytic therapy. Coronary angiography was performed in all cases within the first 24 hours. First ECG analysis was performed in the emergency department within 30 minutes of hospital admission. And second ECG analysis was performed after revascularization, within 48 hours but before discharge from the hospital.

Catheterization

Coronary angiography and angioplasty were performed by percutaneous femoral approach. Heparin (5000 u) was administered after arterial access. After left and right coronary artery clearly visualized, percutaneous transluminal coronary angioplasty (PTCA) and/or stent implantation was performed.

Heart rate and QT variability analysis

Heart rate and beat to beat QT variabilities were measured in supine position by using short-term (200 beats) resting high-resolution ECG recordings (PC-ECG 1200 software program, Kiryat Bialik, Israel). All QRS labelling was

manually edited by an experienced observer (O.H.). Ventricular ectopies and artifacts were removed manually. Heart rate variability was performed according to time and frequency domain parameters.

The following frequency-domain measures were assessed for both of the HRV and QT variabilities:

VLF (0.003-0.04 Hz), LF (0.04 to 0.15 Hz), HF (0.15 to 0.40 Hz), and low/high frequency (LF/HF) ratio as an index of symphatovagal balance.

Time-domain measures were derived from short time ECG recordings:

SDNN: Variability in the RR interval was expressed as the standard deviation of all sinus beat RR intervals.

RMSSD: Square root of the mean sum of squares of the differences between the adjacent RR intervals.

SDQT: Variability in the QT interval was expressed as the standard deviation of all QT intervals.

RMSQT: Square root of the mean sum of squares of the differences between the adjacent QT intervals.

Statistical Analysis

All data was shown as mean \pm SD. Paired t test was used to compare variables before and after revascularization. All statistical calculations were performed with commercially available computer software (SPSS 11.0), and $p < .05$ was considered significant.

Results

Twenty three patients with acute coronary syndrome with the mean age of 56.8 ± 10.5 (range: 42-76) years were included in this study. Of patients, 12 had non-ST elevation myocardial infarction, while 11 had unstable angina pectoris. Especially, hypertension and the family history of coronary diseases were found to be high among subjects. Cardiovascular risk factors of the patients are listed in table 1.

After revascularization, time domain parameters were found to be increased for all study patients, but SDNN and RMSSD values of time domain HRV parameters were found to be increased significantly only in patients with non-ST elevation MI. Mentioned parameters were also found to be increased in patients with USAP, but without statistically significant degree.

The evaluation of whole records obtained from all patients revealed that only HF value among frequency domain parameters increased slightly (36.4 ± 7.6 versus 86.4 ± 18.0 , $p = .012$). But after grouping subjects into non-ST elevation MI patients and USAP patients, no difference was found in frequency domain parameters after revascularization. All examined HRV parameters are listed in Table 2. For all patients, no significant difference was detected in QT parameters between before and after revascularization (Table 3).

Discussion

The aim of this study was to investigate HRV and QT variability in the early phase of acute coronary syndromes and possible changes after revascularization. Although, the long term prognostic value of HRV in patients surviving AMI and USAP has been investigated extensively¹³, there is only little information about HRV changes after revascularization.¹⁰⁻¹² In very few studies, it has been suggested that revascularization might increase HRV.^{10,11} Pedretti et al.⁹ demonstrated that thrombolytic therapy in AMI improves HRV parameters. In the present study, the values of SDNN and RMSSD were significantly increased after revascularization in AMI patients. It is well known that, increased LF power is in correlation with high sympathetic activity and increased HF power indicates an increase in vagal tone of the heart. Our findings showed that only HF value, among frequency domain parameters, increased slightly but significantly after revascularization. But after grouping subjects into non-ST elevation MI patients and USAP patients, no difference was found in frequency domain parameters after revascularization. It is well known that HRV parameters initially are depressed and recover to some degree within the first year after infarction.¹² Furthermore, Balanescu et al.¹⁴ compared the conventional therapy with reperfusion therapy in patients after the first year of AMI. They showed that the patients received reperfusion therapy had better recovery in HRV parameters and also good prognosis.

Very few studies have focused on the investigations about recovery time of HRV depression after revascularization. It was suggested that HRV depression, caused by myocardial damage, progressively increase up to normality over a 2-month follow-up.¹⁵ In this study, it was found that HRV time domain parameters were increased in very early period (first 48 hours) after revascularization and no change in LF/HF ratio was detected in patients with AMI. Carpegianni et al.¹⁰ showed that both time and frequency domain parameters of HRV were significantly increased; otherwise LF/HF ratio did not change during hospitalization after AMI. Singh et al.¹⁶ found lower LF/HF ratio to be predictive of death following the first month of AMI. Lanza et al.¹ suggested that a LF/HF ratio was the most useful parameter for predicting cardiac mortality in patients who had undergone thrombolysis. Furthermore; SDNN, LF amplitude and LF/HF ratio were also found to be associated with mortality in patient with USAP.¹⁷ Our results suggested that the recovery time in time domain parameters was shorter than frequency domain parameters. This may be because our second ECG analyzing time, within 48 hours after revascularization, was much

earlier than other studies. An additional improvement in other parameters could also be achieved if long-term follow up evaluations have been performed.

Depressed HRV in AMI at early period (first 48 hours) is associated with poor long-term prognosis.¹⁰ But generally this kind of recordings can be obtained from 24 hours Holter recordings and because of some technical problems or seriously ill patients with unstable vital signs, generally these records can not be obtained in very early period after AMI. It is well known that, long- and short-term data of heart rate variability are in concordance with each other.¹⁸ Also, it was shown that short term heart rate variability was as valuable as long term heart rate variability for the risk stratification after AMI.¹⁹ Bigger and coworkers²⁰ reported that frequency-domain analyses computed from 2- to 15-minute segments were not meaningfully different from those calculated for 24 hours. In the present study, by the advantage of using short time recordings, we were able to obtain ECG recordings in very early period (first 2 hour) after acute coronary syndromes. At the same time, short term HRV procedures compared with long term ones have advantages not only in terms of costs but also in terms of patient comfort.

Myocardial ischemia seen during acute coronary syndromes has been shown to increase repolarization variability besides its negative effects on autonomic functions.⁵ QT variability has been accepted as a good marker for the regional inhomogeneity of ventricular repolarization.⁵ High QT interval variability is a risk factor for arrhythmic events, including sudden cardiac death.⁷ Similar to HRV, the standard deviation of all QT intervals during 24 hours has been investigated, but its predictive value remains unclear.²¹ Bonnemeier et al.²¹ have shown that, reperfusion caused significant decrease in QT interval variability in the majority of patients after one year, but they did not detect any relationship between long term prognosis and QT variability. They investigated only time domain QT parameters in post AMI patients, but in the present study, we investigated both time and frequency domains of QT variability and found no significant difference in QT parameters between before and after revascularization state.

A significant QT variability increase was shown in coronary patients without prior myocardial infarction suggesting that altered ventricular repolarization might be possible in coronary patients.²² Furthermore, automatic QT measurement techniques are less accurate in cardiac patients than in controls.²³ In our study no significant change was determined in QT variabilities that were obtained before and after the revascularization process, this may be because the present study did not have a control group as it was conducted only in patients.

In conclusion, time domain parameters of HRV could increase during the early period after

revascularization in patients with non-ST elevation MI. Mentioned parameters could also be found to be increased without statistically significant degree in patients with USAP. No change could be detected in most of the QT variability parameters.

Study limitations

The study was not performed on consecutive patients because of strict selection criteria for to constitute a homogeneity study group. For similar reasons, this study included a relatively small number of patients. Another study limitation was that only changes in the first 48 hours of acute coronary syndromes were recorded, as there were no data available after this period.

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References

1. Lanza GA, Guido V, Galeazzi MM, Mustilli M, Natali R, Ierardi C, Milici C, Burzotta F, Pasceri V, Tomassini F, Lupi A, Maseri A. Prognostic role of heart rate variability in patients with a recent acute myocardial infarction. *Am J Cardiol* 1998;82:1323-8.
2. Hartikainen JE, Malik M, Staunton A, Poloniecki J, Camm AJ. Distinction between arrhythmic and nonarrhythmic death after acute myocardial infarction based on heart rate variability, signal-averaged electrocardiogram, ventricular arrhythmias and left ventricular ejection fraction. *J Am Coll Cardiol* 1996;28:296-304.
3. Lanza GA, Pedrotti P, Rebuzzi AG, Pasceri V, Quaranta G, Maseri A. Usefulness of the addition of heart rate variability to Holter monitoring in predicting in-hospital cardiac events in patients with unstable angina pectoris. *Am J Cardiol* 1997;80:263-7.
4. Wilcox I, Ben Freedman S, Kelly DT, Harris PJ. Clinical significance of silent ischemia in unstable angina pectoris. *Am J Cardiol* 1990;65:1313-6.
5. Murabayashi T, Fetics B, Kass D, Nevo E, Gramatikov B, Berger RD. Beat-to-beat QT interval variability associated with acute myocardial ischemia. *J Electrocardiol* 2002;35:19-25.
6. Nahshoni E, Strasberg B, Adler E, Imbar S, Sulkes J, Weizman A. Complexity of the dynamic QT variability and RR variability in patients with acute anterior wall myocardial infarction: a novel technique using a non-linear method. *J Electrocardiol* 2004;37:173-9.
7. Chevalier P, Burri H, Adeleine P, Kirkorian G, Lopez M, Leizorovicz A, Andre-Fouet X, Chapon P, Rubel P, Touboul P. QT dynamicity and sudden death after myocardial infarction: results of a long-term follow-up study. *J Cardiovasc Electrophysiol* 2003;14:227-33.
8. Cantor WJ, Goodman SG, Cannon CP, Murphy SA, Charlesworth A, Braunwald E, Langer A. Early cardiac catheterization is associated with lower mortality only among high-risk patients with ST- and non-ST-elevation acute coronary syndromes: observations from the OPUS-TIMI 16 trial. *Am Heart J* 2005;149:275-83.
9. Pedretti RF, Colombo E, Sarzi Braga S, Caru B. Effect of thrombolysis on heart rate variability and life-threatening ventricular arrhythmias in survivors of acute myocardial infarction. *J Am Coll Cardiol* 1994;23:19-26.
10. Carpeggiani C, L'Abbate A, Landi P, Michelassi C, Raciti M, Macerata A, Emdin M. Early assessment of heart rate variability is predictive of in-hospital death and major complications after acute myocardial infarction. *Int J Cardiol* 2004;96:361-8.
11. Casolo GC, Stroder P, Signorini C, Calzolari F, Zucchini M, Balli E, Sulla A, Lazzerini S. Heart rate variability during the acute phase of myocardial infarction. *Circulation* 1992;85:2073-9.
12. Lombardi F, Sandrone G, Spinnler MT, Torzillo D, Lavezzaro GC, Brusca A, Malliani A. Heart rate variability in the early hours of an acute myocardial infarction. *Am J Cardiol* 1996;77:1037-44.
13. Copie X, Hnatkova K, Staunton A, Fei L, Camm AJ, Malik M. Predictive power of increased heart rate versus depressed left ventricular ejection fraction and heart rate variability for risk stratification after myocardial infarction. Results of a two-year follow-up study. *J Am Coll Cardiol* 1996;27:270-6.
14. Balanescu S, Corlan AD, Dorobantu M, Gherasim L. Prognostic value of heart rate variability after acute myocardial infarction. *Med Sci Monit* 2004;10:CR307-15.
15. Fetsch T, Reinhardt L, Makijarvi M, Bocker D, Block M, Borggrete M, Breithardt G. Heart rate variability in time domain after acute myocardial infarction. *Clin Sci (Lond)* 1996;91 Suppl:136-40.
16. Singh N, Mironov D, Armstrong PW, Ross AM, Langer A. Heart rate variability assessment early after acute myocardial infarction. Pathophysiological and prognostic correlates. GUSTO ECG Substudy Investigators. *Global Utilization of Streptokinase and TPA for Occluded Arteries. Circulation* 1996;93:1388-95.
17. Lanza GA, Cianflone D, Rebuzzi AG, Angeloni G, Sestito A, Ciriello G, La Torre G, Crea F, Maseri A. Prognostic value of ventricular arrhythmias and heart rate variability in patients with unstable angina. *Heart* 2005; 30 (in press).
18. Lu F, Malik M: Assessment of short- and long-term heart rate variability for postinfarction risk stratification. p. 329-34. In Malik M, Camm AJ

(eds): Heart rate variability. Armonk, NY: Futura, 1995.

19. Faber TS, Staunton A, Hnatkova K, Camm AJ, Malik M. Stepwise strategy of using short- and long-term heart rate variability for risk stratification after myocardial infarction. *Clin Electrophysiol* 1996;19(11 Pt 2):1845-51.

20. Bigger JT, Fleiss JL, Rolnitzky LM, Steinman RC. The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. *Circulation* 1993;88:927-34.

21. Bonnemeier H, Hartmann F, Wiegand UB, Bode F, Katus HA, Richardt G. Course and prognostic implications of QT interval and QT interval variability after primary coronary angioplasty in acute myocardial infarction. *J Am Coll Cardiol* 2001;37:44-50.

22. Vrtovec B, Starc V, Starc R. Beat-to-beat QT interval variability in coronary patients. *J Electrocardiol* 2000;33:119-25.

23. McLaughlin NB, Campbell RW, Murray A. Accuracy of four automatic QT measurement techniques in cardiac patients and healthy subjects. *Heart* 1996;76:422-6.

Table 3: QT variability differences of the MI and USAP patients between before and after revascularization.

	MI patients (n=12)		
	Before revascularization	After revascularization	P value
QT (ms)	14.7 ± 11	14.2 ± 10	.905
RMSQT (ms)	19.8 ± 14	21.8 ± 15	.756
HRV triangular index	4.0 ± 1.7	4.2 ± 2.4	.862
LF (ms ²)	122 ± 52	99 ± 40	.292
HF-QT (ms ²)	216 ± 49	245 ± 136	.457
VR (SDQT/SDNN)	0.5 ± 0.2	0.5 ± 0.4	.787

Standard deviation of QT intervals, RMSQT: square root of the mean squared differences of successive QT intervals, HF: high frequency, VLF: very low frequency, LF: low frequency, VR: Variability ratio.

Table 1: Cardiovascular risk factors of the patients.

	MI patients (n=12) No (%)	USAP patients (n=11) No (%)
Gender (male)	6 (50)	6 (54.5)
Hypertension	6 (50)	6 (54.5)
Diabetes	3 (25)	3 (27.3)
Smoking habit	5 (41.7)	3 (27.3)
Family history of coronary disease	4 (33.3)	7 (63.6)
Previous MI	6 (50)	4 (36.4)

MI= myocardial infarction

USAP=Unstable angina pectoris

Table 2: Heart rate variability differences of the MI and USAP patients between before and after revascularization.

	MI patients (n=12)			USAP patients (n=11)		
	Before revascularization	After revascularization	P value	Before revascularization	After revascularization	P value
SDNN (ms)	19.1 ± 8.9	36.3 ± 17	.012	18.6 ± 9.4	27.1 ± 15.1	.191
RMSSD (ms)	13.3 ± 5.2	35.5 ± 29	.034	10.5 ± 6.8	27.4 ± 25.6	.073
HRV triangular index	6.3 ± 2.7	7.8 ± 2.9	.078	6.6 ± 2.2	7.9 ± 2.4	.345
LF (ms ²)	214 ± 148	113 ± 61	.054	112 ± 59	150 ± 83	.155
HF (ms ²)	73 ± 36	124 ± 92	.081	66 ± 37	124 ± 83	.094
LF/HF	3.9 ± 3	2.5 ± 3	.394	2.2 ± 1.4	2.1 ± 2.0	.781

SDNN: standard deviation of RR intervals, RMSSD: square root of the mean squared differences of successive RR intervals, HF: high frequency, VLF: very low frequency, LF: low frequency.