

Impact of reperfusion therapy and infarct localization on frequency of premature ventricular beats in acute myocardial infarction

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ABSTRACT

Aim To determine the impact of infarct localization and types of reperfusion therapy on the frequency of ventricular premature beats (VPBs) in patients with acute myocardial infarction (AMI) and reduced left ventricular ejection fraction (LVEF).

Methods A total of 705 patients with acute ST elevation myocardial infarction (STEMI) were divided according to the infarct localization (anteroseptal, anterolateral, inferior and posterior) and reperfusion therapy (fibrinolysis or percutaneous coronary intervention with stenting) into two groups: LVEF<45% was an experimental group and LVEF≥45% was a control group. The occurrence of VPBs<10 per hour was defined as a non-significant, and the occurrence of VPBs≥10 per hour defined as a significant.

Results In patients with fibrinolysis therapy and LVEF<45% significant number of VPBs were in anteroseptal (p=0.017), anterolateral (p<0.001) and posterior AMI (p<0.001), but in patients with percutaneous coronary intervention (PCI) and LVEF<45% significant number of VPBs were only in anteroseptal AMI (p=0.001) localization.

Conclusion In patients with reduced ejection fraction in AMI, treatment with PCI method has a better antiarrhythmic effect compared to fibrinolysis treatment.

Key words: fibrinolysis, percutaneous coronary intervention, ventricular arrhythmias

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INTRODUCTION

Ventricular premature beats (VPB) represent a premature ventricular contraction (1). The association between VPBs and poor patient prognosis has been well documented (2). Ventricular premature beats in the early phase of an acute myocardial infarction (AMI) are not considered in the high mortality rate (3,4). However, after the first 48 hours, VPBs are a problem with long-term prognostic significance (5).

The background might be an unsynchronized myocardial repolarization on the grounds of ischemia, lesion or myocardial necrosis (6). Patients with frequent premature ventricular contractions or certain patterns of premature ventricular contractions may be at increased risk of developing heart rhythm problems (arrhythmias) or weakening of the heart muscle (cardiomyopathy) (7-9). The difference in conduction velocity between injured and uninjured tissue can trigger re-entry or a feedback loop that is believed to be the cause of many lethal arrhythmias (10). The most serious of arrhythmias is ventricular fibrillation, an extremely fast and chaotic heart rhythm that is the leading cause of sudden cardiac death. Another life-threatening arrhythmia is ventricular tachycardia, which can cause sudden cardiac death. Rarely, when accompanied by underlying heart disease, frequent premature contractions can lead to chaotic, dangerous heart rhythms and possibly sudden cardiac death (11,12). Post-AMI VPBs, particularly if frequent (more than 10 per hour) or complex (repetitive forms, primarily nonsustained ventricular tachycardia), appear to be associated with a worse prognosis in patients with a prior AMI (10).

The relationship among reduced left ventricular ejection fraction (LVEF) and the size of affected myocardial area might be also important (13). Therefore, reperfusion therapy as a percutaneous coronary intervention (PCI) or fibrinolytic therapy should be attempted as soon as possible (14).

The impact of AMI localization on VPBs is also unclear. In general, large studies analyzed the occurrence of VPBs in the post infarction period by *anterior* or *inferior* localization but, the results are contradictory. Bluzite had more VPBs in *inferior* (15), while Stone concluded that VPBs are more frequent in *anterior* AMI (16) localization.

Our aim was to determine the impact of AMI loca-

lization and type of reperfusion therapy on the frequency of VPBs in patients with reduced LVEF.

PATIENTS AND METHODS

Patients

This retrospective research was conducted from the 2000 to 2012. Among the total of 705 patients with acute ST elevation myocardial infarction (STEMI) (the average age 62.5 years), 484 (68.7%) were males and 221 (31.3%) were females. They were hospitalized in the Coronary Unit of the General Hospital in Karlovac, Croatia.

Methods

All patients were divided according to the reperfusion therapy to patients with fibrinolysis and the PCI. According to the AMI localization, the patients were divided into four groups (*anteroseptal*, *anterolateral*, *inferior* and *posterior* localization). Because LVEF<50% represents a reduced value of LVEF, we established the experimental group of patients with LVEF<45% and the control group with better LVEF (≥45%). According to the number of VPBs, we established the group with less VPBs (<10 per hour) and the group with more VPBs (≥10 per hour).

The exclusion criteria were cardiomyopathy, left ventricular hypertrophy, hyperkalemia, hyperthyroidism, mitral valve prolapse, digitalis therapy, history of VPBs, and previous myocardial infarctions.

The AMI diagnostic criteria were chest pain (the first six hours). The ECG diagnosis of the ST segment elevation type of acute myocardial infarction require at least 1 mm (0.1 mV). These elevations must be present in anatomically contiguous leads (I, aVL, V3-V6 correspond to the *anterolateral* wall; V1-V4 correspond to the *anteroseptal* wall; II, III, aVF correspond to the *inferior* wall and ST-denivelation in V3-4 or R-wave enlargement in V1-V3 leads for *posterior* AMI). The cardiac enzyme troponin I was >1.00 ug/L.

Streptokinase was used as a fibrinolytic agent, and the dose was 1.5 million international units. Each patient was treated with beta-blockers, acetylsalicylic acid (ASA), angiotensin converting enzyme inhibitor, statin and in the PCI method with clopidogrel. The PCI treatment had to be with stenting.

A coronary angiogram in the PCI treatment had the criteria of post angioplasty blood flow of the TIMI grade III (17). Ventricular premature beats had been verified between the sixth and tenth day of hospitalization with a 24 hour Holter ECG monitoring. Left ventricular ejection fraction was assessed with the heart ultrasound and the Simpson biplane technique in the apical projection.

RESULTS

The study evaluated a total of 705 patients. The patients' average age was 62.4 years, 484 (68.7%) were males and 221 (31.3%) were females.

A significant number of VPBs were identified in 194 (27.4%) patients. A total of 155 (22.0%) patients had the LVEF<45%. A total of 166 (23.5%) patients had *anteroseptal*, 106 (15.0%) *anterolateral*, 159 (22.6%) *inferior* and 274 (38.9%) *posterior* infarct localization (Table 1).

Table 1. Distribution of myocardial infarction localization

Localization	N (%) of patients
<i>Anteroseptal</i>	166 (23.5)
<i>Anterolateral</i>	106 (15.0)
<i>Inferior</i>	159 (22.6)
<i>Posterior</i>	274 (38.9)
Total	705 (100)

There were 522 patients with fibrinolysis and 183 patients with PCI treatments (Table 2).

Table 2. Distribution of reperfusion therapy

Reperfusion therapy	N (%) of patients
Fibrinolysis	522 (74)
Percutaneous coronary intervention	183 (26)
Total	705 (100)

In the fibrinolysis and LVEF<45% group, a significant number of VPBs were in *anteroseptal* (p=0.017), *anterolateral* (p<0.001) and *posterior* localization (p<0.001) (Table 3).

Table 3. Myocardial infarction and ventricular premature beats in fibrinolysis

Localization of myocardial infarction	Ventricular premature beat/h	No (%) of patients with left ventricular ejection fraction		95% CI	p
		<45%	>45%		
<i>Anteroseptal</i>	<10	28 (5.4)	72 (13.8)	50.57-54.91	
	>10	18 (3.4)	18 (3.4)	44.44-52.62	0.017
<i>Anterolateral</i>	<10	14 (2.7)	52 (10.0)	48.28-52.78	
	>10	16 (3.1)	8 (1.5)	38.56-47.27	<0.001
<i>Inferior</i>	<10	12 (2.3)	88 (16.9)	56.38-59.94	
	>10	8 (1.5)	22 (4.2)	49.64-57.89	0.080
<i>Posterior</i>	<10	10 (1.9)	120 (23.0)	54.63-57.66	
	>10	14 (2.7)	22 (4.2)	45.76-51.80	<0.001

In the PCI treatment significant number of VPBs were in *anteroseptal* localization (p=0.001) (Table 4).

Table 4. Myocardial infarction and ventricular premature beats in percutaneous coronary intervention

Localization of myocardial infarction	Ventricular premature beat/h	No (%) of patients with left ventricular ejection fraction		95% CI	p
		<45%	>45%		
<i>Anteroseptal</i>	<10	2 (1.1)	20 (10.9)	50.90-59.10	
	>10	6 (3.3)	2 (1.1)	31.75-53.00	0.001
<i>Anterolateral</i>	<10	2 (1.1)	8 (4.4)	41.50-56.90	
	>10	4 (2.2)	2 (1.1)	26.95-57.38	0.118
<i>Inferior</i>	<10	4 (2.2)	14 (7.7)	49.22-62.23	
	>10	2 (1.1)	9 (4.9)	51.65-66.17	0.999
<i>Posterior</i>	<10	6 (3.3)	60 (32.8)	53.86-58.47	
	>10	9 (4.9)	33 (18.0)	51.65-57.88	0.071

DISCUSSION

This study established several VPBs in patients with fibrinolysis than PCI treatment in acute STEMI.

In relevant literature sources primary PCI was better than thrombolytic therapy (18). Primary PCI is more effective than thrombolytic therapy for the treatment of acute STEMI because it reduces overall short-term death (7% vs 9%), death excluding the shock (5% vs 7%), non-fatal reinfarction (3% vs 7%), stroke (1% vs 2%) and the combined endpoint of death, non-fatal reinfarction, and stroke (8% vs 14%) (19).

However, there are scarce data about VPBs in patients with fibrinolysis comparing to PCI treatment in acute STEMI. Our results can be compared with a limited number of relevant literature sources. A higher VPBs frequency in *anterior* than *inferior* infarctions (70.2 vs 58.9%) has been described by Stone (16). Breithardt described a higher frequency of tardive ventricular potentials in *anterior* AMI compared to the *inferior* AMI (20). However, Bluzaitė (15) had higher occurrence in the *inferior* than *anterior* infarction. Pascale also found a significantly more VPBs in the *inferior* infarction (21). Future researches with an additional electrophysiological testing would be of interest. Although the cardiac conductive system is mainly in the septum (22), the distal area like His-Purkinje system is also a source of ectopic impulses (23).

An early spontaneous reperfusion in AMI could be a protective factor for VPBs (24,25). The impact of collateral circulation is also important. In case of collateral circulation, the infarction affect-

ted area will be smaller than the area with occluded artery (26).

Our results had the link among the residual LVEF<45% and the significant number of VPBs. These data are in correlation with results of low LVEF and several VPBs (27). Solomon demonstrated the rise in the mortality rate within 30 post-MI days in LVEF<30% (13).

Our analysis verified good results in the PCI treatment. The Croatian PCI network is very important for this process. This is important because the previous large trials such as DANAMI-2 study did not verify less VPBs in the PCI than the fibrinolysis (28).

In conclusion, the AMI cum small LVEF and PCI therapy has less VPBs than the fibrinolysis

therapy. In the fibrinolysis therapy more VPBs were in *anteroseptal*, *anterolateral* and *posterior* localization but in the PCI treatment only in *anteroseptal* localization. In patients with reduced ejection fraction in AMI, treatment with PCI method has a better antiarrhythmic effect compared to fibrinolysis treatment. For this reason, the PCI treatment reduces the possibility of the occurrence of malignant ventricular arrhythmias and sudden death of patients.

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Competing interests: None to declare.

REFERENCES

1. Olgin JE, Zipes DP. Specific Arrhythmias: Diagnosis and Treatment. In: Braunwald, Zipes, Libby, eds. Heart Disease. 7th ed. Philadelphia: Elsevier/Saunders, 2005:838-45.
2. Drögemüller A, Seidl K, Schiele R, Schneider S, Gitt A, Gotwik M. Prognostic value of non-sustained ventricular tachycardias after acute myocardial infarction in the thrombolytic era: importance of combination with frequent ventricular premature beats. *Z Kardiol* 2003; 92:164-72.
3. Timmer JR, Breet N, Svilaas T, Haaksmas J, Van Gelder IC, Zijlstra F. Predictors of ventricular tachyarrhythmia in high-risk myocardial infarction patients treated with primary coronary intervention. *Neth Heart J* 2010; 18:122-8.
4. Volpi A, Cavalli A, Turato R, Barlera S, Santoro E, Negri E. Incidence and short-term prognosis of late sustained ventricular tachycardia after myocardial infarction: results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-3) Data Base. *Am Heart J* 2001; 142:87-92.
5. Newbi KH, Thompson T, Stebbins A, Topol EJ, Califf RM, Natale A. Sustained ventricular arrhythmias in patients receiving thrombolytic therapy: incidence and outcomes. *Circulation* 1998; 98:2567-73.
6. Breithardt G, Borggrefe M, Martinez-Rubio A, Budde T. Pathophysiological mechanisms of ventricular tachyarrhythmias. *Eur Heart J* 1989; 10:9-18.
7. Manolis AS. Ventricular premature beats. <http://www.uptodate.com/home> (16 January 2014).
8. Ventricular premature beats. The Merck Manuals: The Merck Manual for Health Care Professionals. http://www.merckmanuals.com/professional/cardiovascular_disorders/arrhythmias_and_conduction_disorders/ventricular_premature_beats_vp.html (16 January 2014).
9. Cha YM, Lee GK, Klarich KW, Grogan M. Premature ventricular contraction-induced cardiomyopathy. *Circulation: Arrhythmia and Electrophysiology* 2012; 5:229-36.
10. Arrhythmia. National Heart, Lung, and Blood Institute. <http://www.nhlbi.nih.gov/health/health-topics/topics/arr/> (16 January 2014).
11. Eckardt L, Breithardt G. Drug-induced ventricular tachycardia. In: Zipes DP, Jalife J, ed. Cardiac electrophysiology, From Cell to Bedside. 6th ed. Elsevier Saunders, Philadelphia; 2014:1001-8.
12. John RM, Tedrow UB, Koplman BA, Albert CM, Epstein LM, Sweeney MO, Miller AL, Michaud GF, Stevenson WG. Ventricular arrhythmias and sudden cardiac death. *Lancet* 2012; 380:1520-9.
13. Solomon SD, Zelenkofske S, McMurray JJ, Finn PV, Velazquez E, Ertl G. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *N Engl J Med* 2005; 352:2581-8.
14. Terkelsen CJ, Christiansen EH, Sorensen JT, Kristensen SD, Lassen JF, Thuessen L. Primary PCI as the preferred reperfusion therapy in STEMI: it is a matter of time. *Heart* 2009; 95:362-9.
15. Bluazite I, Brazdzionyte J, Bluzhas J, Mickeviciene A. Signal-averaged electrocardiogram peculiarities of the first and recurrent myocardial infarction. *JHong Kong Coll Cardiol* 1997; 5:119-25.
16. Stone PH, Raabe DS, Jaffe AS, Gustafson N, Müller JE, Turi ZG. Prognostic significance of location and type of myocardial infarction: independent adverse outcome associated with anterior location. *J Am Coll Cardiol* 1998; 11:453-63.
17. Gibson CM, Ryan KA, Kelley M, Rizzo MJ, Mesley R, Murphy S. Methodologic drift in the assessment of TIMI grade 3 flow and its implications with respect to the reporting of angiographic trial results. *Am Heart J* 1999; 137:1179-84.
18. Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, Grinfeld L, Gibbons RJ, Ribeiro EE, DeWood MA, Ribichini F. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. *JAMA* 1997; 278:2093-8.

19. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003; 361:13-20.
20. Breithard LG, Schwarzmaier J, Borggrefe M, Haerten K, Seipel L. Prognostic significance of late ventricular potentials after acute myocardial infarction. *Eur Heart J* 1983; 4:487-95.
21. Pascale P, Schlaepfer J, Oddo M, Schaller MD, Pierre Vogt P, Fromer M. Ventricular arrhythmia in coronary artery disease: limits of a risk stratification strategy based on the ejection fraction alone and impact of infarct localization. *Europace* 2009; 11:1639-46.
22. Christoffels VM, Moorman AFM. Why Are Some Regions of the Heart More Arrhythmogenic Than Others? *Circulation: Arrhythmia and Electrophysiology* 2009; 2:195-207.
23. Dave J, Lakhia R, Jha SH. Ventricular Premature Complexes. <http://emedicine.medscape.com/article/158939-overview> (15 September 2014)
24. Baine KR, Fu Y, Wagner GS, Goodman SG, Ross A, Granger CB, Van De Werf F, Armstrong PW. Spontaneous reperfusion in ST-elevation myocardial infarction: comparison of angiographic and electrocardiographic assessments. *Am Heart J* 2008; 156:248-55.
25. Baine KR, Fu Y, Granger CB, Hamm CW, Holmes DR, O'Neil WW. Benefit of angiographic spontaneous reperfusion in STEMI: does it extend to diabetic patients? *Heart* 2009; 95:1331-6.
26. Fujita M, Nakae I, Kihara Y, Hasegawa K, Nohara R, Ueda K. Determinants of collateral development in patients with acute myocardial infarction. *Clin Cardiol* 1999; 22:595-9.
27. Schuster EH, Bulkley BH. Ischemia at a distance after acute myocardial infarction: a cause of early postinfarction angina. *Circulation* 1980; 62:509-15.
28. Hofsten DE, Wachtell K, Lund B, Molgaard H, Egstrup K. Prevalence and prognostic implications of non-sustained ventricular tachycardia in ST-segment elevation myocardial infarction after revascularization with either fibrinolysis or primary angioplasty. *Eur Heart J* 2007; 28:407-14.

Utjecaj reperfuzijske terapije i lokalizacije infarkta na učestalost ventrikulskih ekstrasistola u akutnom infarktu miokarda

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SAŽETAK

Cilj Odrediti utjecaj lokalizacije infarkta i reperfuzijske terapije na učestalost ventrikulskih ekstrasistola (VES) kod pacijenata s akutnim infarktom miokarda (AIM) i reduciranom ejekcijskom frakcijom lijevog ventrikla (EFLV).

Metode Ukupno je 705 bolesnika s akutnim infarktom miokarda i ST elevacijom (STEMI) podijeljeno prema lokalizaciji infarkta (anteroseptalni, anterolateralni, inferiorni i posteriorni) i reperfuzijskoj terapiji (fibrinoliza ili perkutana koronarna intervencija sa stentom) u dvije grupe: EFLV<45% kao ispitivana grupa, te EFLV≥45% kao kontrolna grupa. Pojava VES<10/h bila je nesigifikantna, a pojava VES≥10/h sigifikantna.

Rezultati U pacijenata s fibrinolizom i EFLV<45% značajan broj VES-a bio je u anteroseptalnom (p=0,017), anterolateralnom (p<0,001) i posteriornom AIM-u (p<0,001), a u pacijenata s perkutanom koronarnom intervencijom (PCI) i EFLV<45% značajan broj VES-a bio je samo u anteroseptalnoj AIM (p=0,001) lokalizaciji.

Zaključak U pacijenata sa smanjenom ejekcijskom frakcijom u AIM-u, tretman s PCI metodom imao je bolji antiaritmički efekat u odnosu na fibrinolitički tretman.

Ključne riječi: fibrinoliza, perkutana koronarna intervencija, ventrikulska aritmija