

ST segment elevation in lead aVR and coronary artery lesions in patients with acute coronary syndrome

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Abstract

Introduction: Recently, the prognostic value of ST segment elevation in lead aVR in acute coronary syndrome (ACS) and its relationship with significant stenosis of the left main coronary artery (LMCAS) and three-vessel disease have been highlighted.

Aim: Analysis of the relationship between ST segment elevation observed in aVR lead and angiographic severity of coronary artery disease in patients with ACS.

Methods: The study involved 134 patients with ACS, including 54 subjects with ST elevation in aVR (group A) and 80 patients without elevation of ST in the same lead (group B), aged 33-78 years, mean 59.9±9.7 years. The severity of coronary artery disease was compared between the two groups. The logistic regression model was used for the analysis of factors affecting ST segment in aVR, as well as LMCAS and three-vessel disease probability.

Results: In patients with ST elevation in aVR, three-vessel disease prevalence was two times higher (61.1% vs 35.0%; $p < 0.01$), and LMCAS – three times higher (55.6% vs 17.5%; $p < 0.000001$) than in those without ST elevation in aVR. Factors independently associated with ST elevation in aVR were LMCAS (OR 6.1; 95% CI 2.62-14.23; $p < 0.00005$), ST segment elevation in V_1 (OR 3.03; 95% CI 1.34-6.86; $p < 0.01$) and diabetes (OR 2.89; 95% CI 1.17-7.15; $p < 0.05$). The predictors of LMCAS were three-vessel disease and ST elevation in aVR, while the predictors of three-vessel disease were: LMCAS, diabetes, male gender and history of myocardial infarction.

Conclusions: Elevation of the ST segment in aVR in the setting of acute coronary syndrome identifies patients with severe coronary artery disease. Only left main coronary artery disease, however, remains independently associated with ST segment elevation in aVR. Three-vessel disease and the left main coronary artery stenosis equivalent are not independent predictors of ST segment elevation in aVR of standard electrocardiograms recorded in patients with acute coronary syndrome.

Key words: acute coronary syndrome, left main coronary artery stenosis, three-vessel disease, ECG, aVR lead

Kardiologia Polska 2006; 64: 8-14

Introduction

In the developed countries coronary artery disease (CAD) is the major cause of mortality, including sudden cardiac death, both in females and males [1]. Despite the enormous development of non-invasive diagnostic methods, especially imaging techniques, electrocardiography remains one of the most valuable diagnostic and prognostic tools that may be used by clinicians for the evaluation of patients with angina at rest [2, 3]. Precordial leads and limb leads I, II, III, aVF and aVL have undeniable clinical value, but the electrocardiographic changes in lead aVR and their interpretation in the

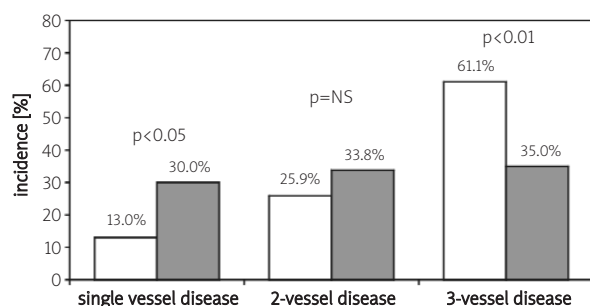
setting of acute coronary syndrome (ACS) have not been conclusively investigated and are currently the subject of many clinical studies [4-8].

Lead aVR of standard electrocardiographic recording, commonly underestimated in clinical practice, enables the recording of electrical potentials from the right superior part of the heart [7, 9]. Although it has been assumed that ECG abnormalities in aVR reflect only changes in the left ventricular lateral wall, i.e. in leads II, aVL, V_5 and V_6 , the results of clinical trials, as well as our observations, seem to contradict such a theory [4-10].

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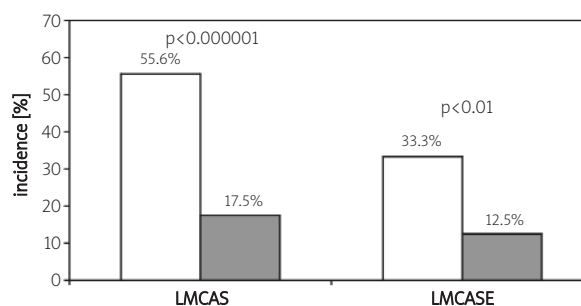
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Received: 10 May 2005. **Accepted:** 22 August 2005.



White bars – patients with ST segment elevation in lead aVR;
Grey bars – patients without ST segment elevation in lead aVR

Figure 1. Angiographic assessment of coronary artery disease severity in the study population



White bars and grey bars – as in Figure 1

Figure 2. Comparison of the incidence of left main coronary artery stenosis (LMCAS) and its equivalent (LMCASE) in the study population

Elevation of the ST segment in aVR, which may be accompanied by ST segment depression in leads I, II, and V₄-V₆, indicates the possibility of significant left main coronary artery stenosis (LMCAS) or, as reported in the literature, three-vessel disease [4, 6, 10]. Despite the fact that several studies have proven the association between electrocardiographic changes in aVR and the risk of LMCAS and three-vessel disease, the clinical relevance of ST segment elevation in aVR as an independent predictor of LMCAS, left main coronary artery stenosis equivalent (LMCASE) and three-vessel disease in patients with ACS remains unknown.

The aim of this study was to evaluate the predictive value of ST segment elevation in lead aVR on resting ECG, recorded in patients with anginal pain in the diagnosis of significant LMCAS, LMCASE and three-vessel disease in the setting of ACS.

Methods

Patients

The study involved 134 consecutive patients with ACS, including 42 (31.3%) females and 92 (68.7%) males, aged 33-78 years, mean 59.9±9.7 years. Thirty-six (26.9%) patients were diagnosed with acute myocardial infarction (AMI), and the remainder with unstable angina (UA). Patients were divided into two groups, based on ECG findings recorded when suffering anginal pain: with ST segment elevation in aVR or without ST elevation in this lead. In accordance with published data [8], ST segment elevation was assumed significant if >0.05 mV above the isoelectric line measured 20 ms after the J point. Clinical and demographic characteristics of patients participating in the study are shown in Table I. The two study groups did not differ significantly, except for considerably higher prevalence of diabetes and overweight in patients with

ST segment elevation in aVR and obesity in patients without ST segment elevation in aVR. Patients with cardiac pacemakers and intraventricular conduction disorders were excluded.

Definitions

The ACS diagnosis was established according to the current standards of the European Society of Cardiology [11,

Table I. Characteristics of studied patients

Parameter	Patients with ST segment elevation in lead aVR	Patients without ST segment elevation in lead aVR	p
Number of patients	54	80	–
Mean age ±SD [years]	60.6±9.5	59.5±9.9	NS
Gender: females	20 (37.0%)	22 (27.5%)	NS
males	34 (63.0%)	58 (72.5%)	
Acute myocardial infarction	13 (24.1%)	23 (28.8%)	NS
Unstable angina pectoris	41 (75.9%)	57 (71.2%)	NS
Arterial hypertension	47 (87.0%)	64 (80.0%)	NS
including: JNC 7 class 1	1 (2.1%)	1 (1.6%)	NS
JNC 7 class 2	46 (97.9%)	63 (98.4%)	NS
Diabetes mellitus type 2	20 (37.0%)	14 (17.5%)	<0.05
Hypercholesterolemia	43 (79.6%)	62 (77.5%)	NS
Hypertriglyceridemia	26 (48.1%)	29 (36.3%)	NS
Smoking	7 (13.0%)	17 (21.3%)	NS
BMI [kg/m ²]	26.9±3.3	28.0±4.7	NS
Overweight	25 (46.3%)	22 (27.5%)	<0.05
Obesity	9 (16.7%)	28 (35.0%)	<0.05
Past myocardial infarction	28 (51.9%)	43 (53.8%)	NS
Past stroke	1 (1.9%)	3 (3.8%)	NS

Table II. Severity of coronary artery disease and its treatment in study patients

Parameter	Patients with ST segment elevation in lead aVR	Patients without ST segment elevation in lead aVR	p
Number of patients	54	80	–
Severity: Single-vessel disease	7 (13.0%)	24 (30.0%)	<0.05
2-vessel disease	14 (25.9%)	27 (33.8%)	NS
3-vessel disease	33 (61.1%)	28 (35.0%)	<0.01
Left main coronary artery stenosis	30 (55.6%)	14 (17.5%)	<0.000001
Left main coronary artery stenosis equivalent	18 (33.3%)	10 (12.5%)	<0.01
Left ventricular ejection fraction \pm SD (%)	54.4 \pm 10.3	58.1 \pm 11.7	<0.05 NS
EF<40%	5 (9.3%)	6 (7.5%)	
Interventional treatment of ACS	51 (94.4%)	72 (90.0%)	NS
CABG	31 (57.4%)	26 (32.5%)	<0.01
PTCA	20 (37.0%)	46 (57.5%)	<0.05
Implantation of stent	16 (29.6%)	24 (30.0%)	NS

12]. Acute myocardial infarction was diagnosed if clinical symptoms of acute cardiac ischaemia were accompanied by an increase in troponin I levels [11]. The assessment of severity of CAD (one-, two- or three-vessel disease) was based on the identification of haemodynamically significant stenoses of the coronary arteries, i.e. lumen diameter reduction of more than 70% and LMCAS of over 50%. LMCASE was defined as critical stenoses (>70%) in the proximal left anterior descending (LAD) and circumflex coronary arteries.

In all patients' medical history, non-invasive diagnostics data (resting electrocardiography, echocardiography) as well as coronary angiography and ventriculography findings were analysed. The clinical evaluation of coronary atherosclerosis and its complications included history of MI and strokes.

Statistical analysis

Statistical analysis was performed using the STATISTICA 6.0 PL software package. Quantitative variables were presented as the mean \pm 1 standard deviation. The statistical analysis included: W Shapiro-Wilk test to test normal distribution of quantitative variables, Student's t-test for independent variables, and U Mann-Whitney and χ^2 tests. The logistic regression model was used to search for significant associations between independent variables and the dichotomous dependent variable. The independent variables analysed in the study included: age, gender, body mass index (BMI), the presence of arterial hypertension, diabetes

mellitus, hypercholesterolaemia, hypertriglyceridaemia, smoking, type of acute coronary syndrome (AMI or UA), history of MI and stroke, severity of CAD on angiography, left ventricular ejection fraction (LVEF) and the following resting ECG parameters recorded during angina: heart rate, heart axis deviation, presence of Q waves or QS complexes, negative T waves and depression and/or elevation of the ST segment, including leads aVR and V₁. A p value of less than 0.05 was assumed significant.

Results

The study involved 134 patients with ACS, including 36 (26.9%) subjects with AMI. The incidence of AMI in the group with ST segment elevation in aVR (54 patients) and in the group without ST elevation in aVR (80 patients) was similar, 24.1% and 28.8%, respectively. The most common area affected by MI was the anterior wall in both groups.

Coronary angiography revealed considerable differences in the severity of CAD between the study groups (Table II). In patients with ST segment elevation in aVR the following conditions were significantly more common: LMCAS, LMCASE and three-vessel disease. Single-vessel disease was significantly less frequent. The analysed groups did not differ with respect to the incidence of two-vessel disease.

On ventriculography, patients with ST segment elevation in aVR had more pronounced LV contractility impairment and significantly lower LVEF. Despite this the percentage of patients with LVEF <40% did not differ significantly between the groups (Table II).

Most patients in both groups underwent interventional treatment of ACS; however, significant differences in management techniques were observed (Table II). In ACS patients with ST segment elevation in aVR the most common treatment was coronary artery bypass grafting indicated by the severity of CAD and a high incidence of LMCAS and three-vessel disease, while PCI was most often performed in patients without ST segment elevation in aVR. In 16 (29.6%) subjects from the ST_{aVR} elevation group and 24 (30.0%) from the group without ST segment elevation in aVR, PCI included stent implantation.

In ECG performed during anginal pain, patients with ACS and ST segment elevation in aVR were more often found to have depressions of the ST segments in the remaining leads (Table III).

Multivariable analysis showed that only LMCAS, diabetes mellitus type 2 and ST segment elevation in lead V₁ were independent factors associated with ST segment elevation in aVR (Table IV). The presence of LMCAS increased the risk of ST segment elevation in aVR by over 6 times, whereas it was increased by the presence of diabetes mellitus and ST segment elevation

Table III. Evaluation of 12-lead ECG performed in patients during resting anginal pain

Parameter	Patients with ST segment elevation in lead aVR	Patients without ST segment elevation in lead aVR	p
Number of patients	54	80	–
Sinus rhythm	54 (100%)	80 (100%)	NS
Heart rate	77.15±14.23	72.68±12.81	NS
PQ [ms]	159±29	160±26	NS
Heart axis deviation	17 (31.5%)	29 (36.3%)	NS
Left	15 (27.8%)	28 (35.0%)	NS
Left pathological	1 (1.9%)	1 (1.3%)	NS
Right	1 (1.9%)	0	NS
Pathological Q wave or QS complex	22 (40.7%)	37 (46.3%)	NS
Negative T wave	35 (64.8%)	52 (65.0%)	NS
ST segment depression	24 (44.4%)	18 (22.5%)	<0.01
ST segment elevation	12 (22.2%)	21 (26.3%)	NS

Table IV. Factors influencing ST segment elevation in the lead aVR of resting ECG

ST segment elevation in the lead aVR	OR	95% CI	p
LMCAS	6.1	2.62-14.23	<0.00005
ST segment elevation in the lead V ₁	3.03	1.34-6.86	<0.01
Diabetes mellitus type 2	2.89	1.17-7.15	<0.05
p for model			<0.000001

OR – odds ratio; CI – confidence interval; LMCAS – left main coronary artery stenosis

Table V. Factor influencing the probability of significant stenosis of the left main coronary artery (LMCAS)

LMCAS	OR	95% CI	p
3-vessel CAD	6.67	2.74-16.25	<0.0001
ST segment elevation in the lead aVR	4.8	2.02-11.41	<0.0005
p for model			<0.000001

OR – odds ratio; CI – confidence interval

in lead V₁ by 2.89 and 3.03 times, respectively. At the same time it was not shown that three-vessel disease or LMCASE were independent factors associated with ST segment elevation in aVR in patients with ACS.

The significance of the studied variables, including electrocardiographic parameters, as predictors of LMCAS and three-vessel disease was also analysed. It has been

Table VI. Factor influencing the probability of three-vessel disease

Three-vessel disease	OR	95% CI	p
LMCAS	12.85	4.66-35.41	<0.00001
Diabetes mellitus type 2	7.31	2.36-22.70	<0.001
Males	4.25	1.48-12.16	<0.01
Past myocardial infarction	2.69	1.37-5.31	<0.005
p for model			<0.000001

OR – odds ratio; CI – confidence interval

Table VII. Comparison of ST segment elevation value in the lead aVR of resting ECG in the diagnosis of significant left main coronary artery stenosis (LMCAS), left main coronary artery stenosis equivalent (LMCASE) and 3-vessel disease

ST segment elevation in the lead aVR	LMCAS	LMCASE	3-vessel disease
Sensitivity	68.2%	64.3%	54.1%
Specificity	73.3%	66.0%	71.2%
Positive predictive value	55.6%	33.3%	61.1%
Negative predictive value	82.5%	87.5%	65.0%
Diagnosis precision	71.6%	65.7%	63.4%

proven that only three-vessel disease and ST segment elevation in aVR in resting ECG are independent predictors of LMCAS (Table V). As it stems from the analysis, among the potential factors predicting the probability of three-vessel disease, the following were of considerable significance: LMCAS, diabetes mellitus, male gender and history of MI. None of the analysed ECG parameters was an independent predictor of three-vessel disease (Table VI).

The value of ST segment elevation in aVR was compared with the diagnosis of LMCAS, LMCASE and three-vessel disease in patients with ACS (Table VII). The results support the particular usefulness of electrocardiographic evaluation including aVR analysis in non-invasive evaluation aimed at diagnosing significant LMCAS.

Discussion

According to available data the mechanism of ST segment elevation in aVR in ACS patients is not entirely clear. Currently it is assumed that it reflects transmural ischaemia of the basal segment of the interventricular septum, where the current is directed towards the right shoulder [6].

The clinical analyses showed that electrocardiographic changes in aVR were common in patients with ACS. First

observations indicating the association between ST segment elevation in aVR in ACS patients and the severity of coronary artery atherosclerosis, LMCAS and three-vessel disease were reported by Gorgels et al. [4, 7]. They found that elevation of the ST segment in lead aVL with concomitant ST segment depression in leads I, II, and V₄-V₆ in patients with UA was typical of LMCAS, and for three-vessel disease [4]. In the study of Gorgels et al. the above-mentioned electrocardiographic abnormalities, called *left main electrocardiogram* by the authors, indicated the presence of LMCAS and three-vessel disease with sensitivity of 90% and 50%, respectively. To compare, the rate of such ECG changes in one-vessel disease was significantly lower and was merely 21%. Nevertheless, the specificity and the predictive values of *left main electrocardiogram* for the diagnosis of LMCAS were relatively low; according to the authors, this resulted from the fact that both two-vessel and three-vessel disease, and even a single vessel lesion if affecting the circumflex coronary artery, may produce ischaemia within the same region of the left ventricular myocardium and produce similar electrocardiographic changes [4].

The analysis of ST segment changes in aVR in AMI patients, particularly in the setting of anterior wall infarction, is clinically relevant. According to the studies of Engelen et al., ST segment elevation in aVR was observed in resting ECG recordings in patients with LAD as the infarct-related artery that was occluded proximal to the main septal branch (5). Yamaji et al. convincingly documented that ST segment elevation in aVR and concomitant lower ST segment elevation in V₁ in resting ECG was indicative of acute occlusion of LM [6]. In this study, ST segment elevation in aVR was observed in 88% of patients with LM occlusion, in 43% with LAD occlusion and only in 8% of patients with occlusion of the right coronary artery. Interestingly, the authors observed a significant correlation between ST segment elevation in aVR and mortality of their patients. AMI survivors had significantly lower ST segment elevation in aVR than individuals with a fatal outcome (0.09 mV±0.09 mV vs 0.23 mV±0.14 mV; p <0.05). Such a prognostic value has not been shown for lead V₁ [6].

Barrabes et al., who analysed the prognostic value of electrocardiographic abnormalities in aVR in patients with first non-ST segment elevation MI, demonstrated that ST segment elevation of 0.05-0.1 mV in aVR increased the risk of in-hospital death by over four times, whereas ST segment elevation in aVR of above 0.1 mV was an independent risk factor that increased the risk of death by almost seven times [8]. They also noted a significantly greater incidence of LMCAS and three-vessel disease in patients with MI without ST segment elevation in aVR [8].

Only a few papers deal with a separate evaluation of the association between ST segment elevation in aVR in

ACS patients and the incidence of LMCAS and three-vessel disease. Our own studies involving 134 patients with ACS have documented that only LMCAS, ST segment elevation in V₁ and diabetes mellitus are independent predictors of ST segment elevation in aVR in resting ECG recorded during anginal pain. Statistical analysis using the logistic regression model failed to prove that three-vessel disease or LMCASE were factors associated with ST segment elevation in aVR. Additionally, it has not been observed that any of the analysed electrocardiographic parameters had a statistically significant independent predictive value for three-vessel disease. This study is the continuation of and is also consistent with our previous report on the great importance of electrocardiographic abnormalities in lead aVR of standard ECG in the diagnosis of significant LMCAS [10]. Although three-vessel disease has been associated with LMCAS in many cases, our results have not indicated that three-vessel disease was associated with ST segment elevation in aVR. This finding adds to our understanding of the clinical value of aVR electrocardiogram analysis in patients with ACS and may influence the indications for coronary angiography [4, 6, 8].

The results of our studies and published data show that the evaluation of underestimated lead aVR tracings is an important element of complete clinical workup in patients with ACS.

Conclusions

1. Significant stenosis of the left main coronary artery is an independent factor associated with ST segment elevation in lead aVR in patients with acute coronary syndromes.
2. Three-vessel disease and the left main coronary artery stenosis equivalent are not independent factors responsible for ST segment elevation in lead aVR of standard ECG recorded in patients with acute coronary syndromes.
3. ST segment elevation in lead aVR of resting ECG in patients with acute coronary syndrome identifies patients with severe coronary artery disease on angiography.
4. The analysis of electrocardiographic abnormalities in lead aVR of widely available standard ECGs is of importance in the global assessment of patients with acute coronary syndrome.

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Uniesienie odcinka ST w aVR w ostrym zespole wieńcowym a zmiany w tętnicach wieńcowych

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Streszczenie

Wstęp: Ostatnio zwrócono uwagę na znaczenie rokownicze uniesienia odcinka ST w odprowadzeniu aVR w ostrym zespole wieńcowym (ACS) i jego związek z istotnym zwężeniem pnia lewej tętnicy wieńcowej (LMCAS) lub chorobą trzech naczyń.

Cel: Analiza zależności pomiędzy uniesieniem odcinka ST w odprowadzeniu aVR a angiograficznym zaawansowaniem choroby wieńcowej u pacjentów z ACS.

Metodyka: Badaniem objęto 134 chorych z ACS, w tym 54 z uniesieniem ST_{aVR} (grupa A) i 80 bez uniesienia ST_{aVR} (grupa B), w wieku 33–78 lat, średnio 59,9±9,7 lat. Porównano zaawansowanie choroby wieńcowej w obu grupach. Za pomocą modelu regresji logistycznej analizowano czynniki wpływające na uniesienie odcinka ST_{aVR}, prawdopodobieństwo LMCAS i choroby 3-naczyniowej.

Wyniki: U chorych z uniesieniem ST_{aVR} choroba trzech naczyń występowała prawie dwukrotnie częściej (61.1% vs 35.0%; $p < 0.01$), zaś LMCAS trzykrotnie częściej (55.6% vs 17.5%; $p < 0.000001$) niż w grupie bez uniesienia ST_{aVR}. Niezależnymi czynnikami wpływającymi na uniesienie odcinka ST_{aVR} okazały się obecność LMCAS (OR 6.1; 95%CI 2,62–14,23; $p < 0.00005$), uniesienie odcinka ST_{V1} (OR 3,03; 95%CI 1,34–6,86; $p < 0,01$) i cukrzyca (OR 2,89; 95%CI 1,17–7,15; $p < 0.05$). Predyktorami LMCAS były choroba 3 naczyń i uniesienie ST_{aVR}, natomiast choroby 3-naczyniowej: LMCAS, cukrzyca, płeć męska i wywiad zawału serca.

Wnioski: Uniesienie odcinka ST_{aVR} w ostrym zespole wieńcowym identyfikuje chorych z zaawansowaną chorobą wieńcową, jednak tylko choroba pnia lewej tętnicy wieńcowej jest niezależnym czynnikiem wpływającym na uniesienie odcinka ST_{aVR}. Choroba trzech naczyń i ekwiwalent choroby pnia lewej tętnicy wieńcowej nie są niezależnymi czynnikami odpowiadającymi za uniesienie odcinka ST w odprowadzeniu aVR standardowego elektrokardiogramu u chorych z ostrymi zespołami wieńcowymi.

Słowa kluczowe: ostry zespół wieńcowy, zwężenie pnia lewej tętnicy wieńcowej, 3-naczyniowa choroba wieńcowa, EKG, odprowadzenie aVR

Kardiologia Pol 2006; 64: 8-14

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Praca wpłynęła: 10.05.2005. Zaakceptowana do druku: 22.08.2005.