

# The prognostic value of ST-segment elevation in the lead aVR in patients with acute pulmonary embolism

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## Abstract

**Background:** Electrocardiogram (ECG) in patients with acute pulmonary embolism (APE) presents many abnormalities. There are no data concerning prognostic significance of ST-elevation (STE) in lead aVR in patients with APE.

**Aim:** To assess the prevalence of STE in aVR in patients with APE and its correlation with clinical course as well as other ECG parameters recorded at admission.

**Methods:** The retrospective analysis of 293 patients with APE diagnosed according to the ESC guidelines (182 females, 111 males, mean age  $65.4 \pm 15.5$  years).

**Results:** The STE in lead aVR was observed in 133 (45.3%) patients. In comparison with patients without STE, patients with STE in lead aVR (STaVR[+]) had significantly more often systolic blood pressure  $< 90$  mm Hg on admission (27% vs 10%,  $p < 0.001$ ) and positive troponin level (64.8% vs 27.9%,  $p < 0.001$ ). Thrombolytic therapy (14.3% vs 5.6%,  $p = 0.009$ ) and catecholamines (29.3% vs 7.5%,  $p < 0.001$ ) were more frequently used in patients with STaVR(+). The overall mortality (16.5% vs 6.9%,  $p = 0.009$ ) and complication rates during hospitalisation (38.3% vs 12.5%,  $p < 0.001$ ) were significantly higher in patients with STaVR(+). The STaVR(+) was significantly more frequent in patients with negative T-waves in inferior leads (59.4% vs 39.4%,  $p < 0.001$ ), STE in lead III (24% vs 5.6%,  $p < 0.001$ ), STE in lead V<sub>1</sub> (46.6% vs 7.5%,  $p < 0.001$ ), ST depression in lead V<sub>4</sub>–V<sub>6</sub> (48.9% vs 7.5%,  $p < 0.001$ ), right bundle branch block (15.8% vs 8.1%,  $p = 0.04$ ), QR sign in lead V<sub>1</sub> (18% vs 6.2%,  $p < 0.001$ ) and SI-QIII-TIII (46.6% vs 21.2%,  $p < 0.001$ ).

**Conclusions:** The presence of STE in lead aVR in patients with APE is associated with poor prognosis. The presence of STE in lead aVR could be an easily obtainable and noninvasive ECG parameter, helpful in risk stratification of patients with APE.

**Key words:** acute pulmonary embolism, lead aVR, ECG, mortality

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## INTRODUCTION

Until recently, ST-segment changes in lead aVR have rarely been included in the electrocardiogram (ECG) analysis. There was even a common belief that ECG consists of 11 leads and that lead aVR is only a scarcely usable "addition" [1, 2]. However, over the last years it has been demonstrated that ST changes in lead aVR occur in acute coronary syndromes and that they are clinically and prognostically relevant. The ST-segment elevation in lead aVR can also be useful in differentiation of supraventricular arrhythmias, wide QRS complex tachycardias and in risk stratification in patients with Brugada syndrome [3–5].

Recently published studies showed that the presence of ST-segment elevation in lead aVR is related to the clinical course of non-ST-elevation myocardial infarction (NSTEMI) [6, 7]. The usefulness of the assessment of ST-segment elevation in lead aVR in patients with 3-vessel disease or left main disease was confirmed [8, 9].

The ST-segment changes in lead aVR can be useful in the identification of infarct-related artery in STEMI patients [10–12]. Japanese investigators demonstrated that the extent of ST-segment depression in lead aVR in the course of inferior wall STEMI correlates with impaired reperfusion despite primary intervention [13]. Similarly, it has been demonstrated that ST-depression in lead aVR in patients with NSTEMI of the anterior wall undergoing primary intervention, was more frequently related to in-hospital heart failure and greater extent of left ventricular dysfunction despite successful reperfusion [14].

In patients with acute pulmonary embolism (APE), multiple ECG abnormalities can be found [15], however, little is known on the prognostic value of ST-elevation in lead aVR.

The aim of the study was to assess the prevalence of ST-elevation in lead aVR in APE and to evaluate its relationship with clinical presentation and clinical course of APE, myocardial injury markers and other ECG changes.

## METHODS

### Study group

The study group consisted of 293 consecutive patients (182 women, 111 men) aged 17–89 years, hospitalised between 2006 and 2009 with the diagnosis of APE. Mean duration of hospitalisation was 15 days (longest: 46 days, mean  $15.1 \pm 8.7$  days). Demographic and clinical data are presented in Table 1.

### The diagnosis of pulmonary embolism

Acute pulmonary embolism was diagnosed based on the following diagnostic tests: computed tomography 253 (86.3%) patients, echocardiography — 24 (8.2%) patients (including 16 patients with right ventricular overload and shock and 8 patients in whom embolic material was directly visualised in right heart chambers), doppler ultrasound of the proximal

**Table 1.** Demographic and clinical characteristics of the study group

Age [years]	65.4 ± 15.5
Women/men	182/111 (62.1%/37.9%)
Immobilisation	85 (29.1%)
Thrombophlebitis of the lower extremity	136 (46.6%)
Malignancy	22 (7.5%)
HRT/anticonception	8 (2.7%)
Heart failure NYHA class III/IV	36 (12.3%)
Chronic obstructive pulmonary disease	24 (8.2%)
Unexplained fever	36 (12.2%)
High risk group	73 (24.9%)
Chest pain	132 (45.0%)
Syncope	85 (29.0%)

HRT — hormonal replacement therapy; NYHA — New York Heart Association

deep veins of the lower extremity — 9 (3%) patients, scintigraphy — 5 (1.7%) patients and autopsy — 2 (0.7%) patients.

### Electrocardiographic study

In all patients 12-lead ECG was performed at 25 mm/s or 50 mm/s speed and amplitude of 10 mm/mV. First available ECG of each patient performed on admission was analysed in terms of ST-segment elevation in lead aVR. The ST-segment elevation in aVR was diagnosed when the J point was elevated  $\geq 1$  mm above the isoelectric line. The following additional ECG features were analysed: (1) supraventricular arrhythmia occurrence (atrial fibrillation); (2) QRS axis; (3) P-pulmonale, if P wave amplitude was  $> 0.25$  mV in at least one of the inferior limb leads (i.e. leads II, III or aVF); (4) complete right bundle branch block (RBBB); (5) McGinnes-White sign (SI-QIII-TIII); (6) negative T-waves in leads III and aVF; (7) negative T-waves in leads  $V_2-V_4$ ; (8) ST-segment depression in leads  $V_4-V_6$ ; (9) ST-segment elevation in leads III,  $V_1$  and  $V_2-V_4$ ; (10) Q(q)R complex in lead  $V_1$ ; (11) dextrogyria, when amplitude ratio  $R/S \leq 1$  in lead  $V_5$ ; (12) low voltage of the QRS ( $< 5$  mm) in limb leads.

### Acute pulmonary embolism clinical course analysis

In-hospital observation included the rate of the following complications: all cause mortality, cardiac arrest, inotropic drug administration, cardiogenic shock and ventilatory support.

### Statistical analysis

Continuous variables with normal distribution are presented as mean  $\pm$  SD. Categorical variables were analysed with  $\chi^2$  test (for small groups Yates correction was applied). A p-value of  $< 0.05$  (two-tailed) was considered statistically significant.

**Table 2.** The prevalence of investigated parameters In the whole study group and comparison between patients with or without ST-elevation in aVR

	All; n = 293	STaVR(+); n = 133	STaVR(-); n = 160	P
Chest pain	132 (45%)	53 (39.9%)	79 (49.4%)	NS
Syncope	85 (29%)	40 (30%)	45 (28.1%)	NS
SBP < 90 mmHg	52 (17.8%)	36 (27%)	16 (10%)	< 0.001
RV ECHO > 30 mm	183 (62.4%)	79 (59.4%)	104 (65%)	NS
cTnT(+)*	102/227*	68/105 (64.8%)	34/122 (27.9%)	< 0.001
Thrombolysis	28 (9.5%)	19 (14.3%)	9 (5.6%)	0.009
Cardiac arrest	35 (12%)	23 (17.3%)	12 (7.5%)	0.01
Inotropic drugs	51 (17.4%)	39 (29.3%)	12 (7.5%)	< 0.001
Death	33 (11.2%)	22 (16.5%)	11 (6.9%)	0.009
Complications	71 (24.2%)	51 (38.3%)	20 (12.5%)	< 0.001
High risk group	73 (24.9%)	53 (39.8%)	20 (12.5%)	< 0.001

STaVR(+) — ST-elevation in lead aVR; STaVR(-) — no ST-elevation in lead aVR; SBP < 90 mm Hg — systolic blood pressure on admission < 90 mm Hg, RV ECHO — right ventricular dimension on echocardiography; cTnT(+) — elevated troponin concentration\*, only patients in whom troponin was measured were included (n = 227)

**Table 3.** Electrocardiographic changes — prevalence in the whole study group and comparison between patients with or without ST-elevation in aVR

	All patients	STaVR(+)	STaVR(-)	P
Atrial fibrillation	62 (21.1%)	34 (25.6%)	28 (17.5%)	NS
Left axis deviation	140 (47.8%)	60 (45.1%)	80 (50%)	NS
Negative T-wave inferior	142 (48.5%)	79 (59.4%)	63 (39.4%)	< 0.001
Negative T-wave anterior	117 (39.9%)	62 (46.6%)	55 (34.8%)	NS
ST-elevation III	41 (13.9%)	32 (24%)	9 (5.6%)	< 0.001
ST-elevation V <sub>1</sub>	74 (25.6%)	62 (46.6%)	12 (7.5%)	< 0.001
ST-depression V <sub>4</sub> -V <sub>6</sub>	77 (26.3%)	65 (48.9%)	12 (7.5%)	< 0.001
Right bundle branch block	34 (11.6%)	21 (15.8%)	13 (8.1%)	0.04
QR sign V <sub>1</sub>	34 (11.6%)	24 (18%)	10 (6.2%)	< 0.001
SI-QIII-TIII sign	96 (32.8%)	62 (46.6%)	34 (21.2%)	< 0.001
Dextrogyria	181 (61.8%)	89 (66.9%)	92 (57.5%)	NS
P pulmonale	43 (14.7%)	24 (18%)	19 (11.9%)	NS
Low voltage QRS	24 (8.2%)	13 (9.8%)	11 (6.9%)	NS

Abbreviations as in Table 2

Statistical calculations were performed with STATISTICA 6.1 PL (StatSoft Inc.).

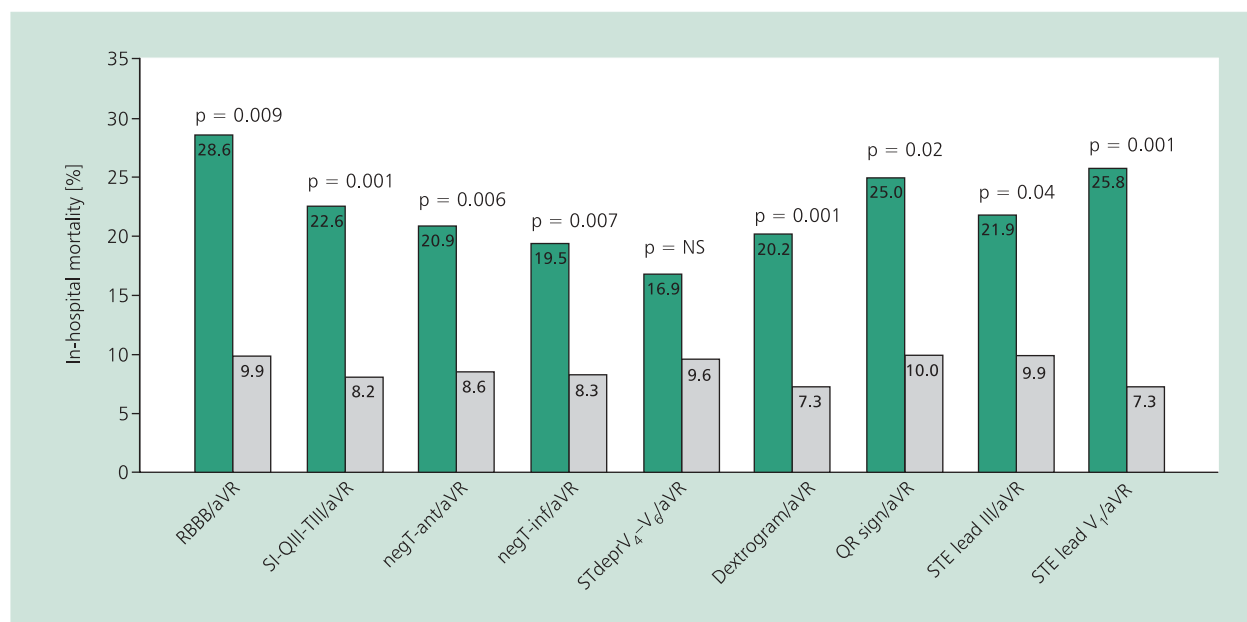
## RESULTS

The ST-segment elevation in lead aVR was observed in 133 (45.3%) patients. In these patients, systolic blood pressure (SBP) < 90 mm Hg on admission and elevated troponin concentrations were significantly more frequent than in the remaining patients. Moreover, fibrinolysis and positive inotropic agents were significantly more frequently used in these patients. In high risk APE patients, the ST-elevation in lead aVR was found significantly more frequently than in patients with non-high risk APE. Overall in-hospital mortality and the number of pre-discharge complications were significantly hi-

gher in patients with ST-elevation in lead aVR than in the remaining patients (Table 2).

The sensitivity and specificity of the ST-elevation in lead aVR as a predictor of mortality were 66.7% and 57.3%, respectively. The respective positive and negative predictive values were 16.6% and 93.1%. In non-high risk patients, sensitivity and specificity for the prediction of mortality were 44% and 64%, respectively, whereas the positive and negative predictive values (PPV, NPV) were 5% and 96.4%.

The ST-segment elevation in lead aVR was more frequently seen in patients with inferior leads T-wave inversion, with lead III ST-elevation, V<sub>1</sub> ST-elevation, ST-depression in leads V<sub>4</sub>-V<sub>6</sub>, RBBB, the QR sign in lead V<sub>1</sub> and in patients with SI-QIII-TIII sign (Table 3).



**Figure 1.** Comparison of in-hospital mortality rates in patients with ST-segment elevation in lead aVR in combination with other ECG parameters (green bars) and in patients without these ECG abnormalities (gray bars); RBBB — right bundle branch block, negT-ant — negative T-wave in leads V<sub>2</sub>-V<sub>4</sub>; negT-inf — negative T-wave in leads III and aVF, ST depV<sub>4</sub>-V<sub>6</sub> — ST-depression in leads V<sub>4</sub>-V<sub>6</sub>; STE lead III/V<sub>1</sub> — ST-elevation in lead III/V<sub>1</sub>

In patients with ST-elevation in lead aVR who also had such ECG findings as RBBB, QR in lead V<sub>1</sub>, negative T-waves in leads III and aVF, ST-elevation in leads III and V<sub>1</sub> or SI-QIII-TIII sign, the overall in-hospital mortality was significantly higher than in the remaining patients (Fig. 1).

## DISCUSSION

The diagnosis of APE is still difficult and its clinical course frequently insidious [15]. The ECG is one of the first diagnostic tests performed in patients with chest pain or dyspnea on admission. It should be emphasised, that there are no sensitive or specific ECG signs of APE. The ECG can not be used for APE diagnosis, but it can be helpful in differential diagnosis of other acute cardiovascular conditions.

Currently, ECG is not taken into account in the APE risk stratification. Toosi et al. [16] developed a 21-point ECG evaluation score and demonstrated that score  $\geq 3$  allows for prediction of complicated clinical course and all-cause mortality with a sensitivity of 58% and 59%, specificity of 60% and 58% and with NPV of 89 and 95%, respectively. The ECG score of  $\geq 3$  allowed for prediction of right ventricular dysfunction (RVD) with 76% sensitivity, 82% specificity and PPV and NPV of 76% and 86%, respectively [16].

Punukollu et al. [17] found that ECG can be helpful in RVD prediction. In their study, McGinne-White sign (SI-QIII-TIII) and negative T-waves in leads V<sub>1</sub>-V<sub>3</sub> were observed significantly more frequently in APE patients with RVD than in patients with preserved RV function [17]. The ECG score was then used for predic-

tion of perfusion defects. Iles et al. [18] demonstrated that ECG score of  $\geq 3$  predicted  $> 50\%$  perfusion defect on scintigraphy with a sensitivity of 70% and a specificity of 59%. In a study of Kostrubiec et al. [19], the ECG score of  $\geq 3$  had 92% sensitivity and NPV of 97% in the prediction of RVD. Also, the score of  $\geq 3$  had sensitivity and NPV of 75% and 92%, respectively, in the prediction of complicated clinical course. Hence, it seems that ECG evaluation conveys relevant information and can add to risk stratification in APE patients.

There is one abstract available in the literature regarding the prognostic significance of ST-segment elevation in lead aVR in APE [20]. Hoechtel et al. [20] reported ST-segment elevation in lead aVR in 35% of 396 APE patients. In our study, ST-segment elevation in lead aVR was observed in 133 (45%) patients. In the study by Hoechtel et al. [20], ST-segment elevation in lead aVR was related to more unfavourable clinical outcome of APE. These patients significantly more frequently presented with syncope, tachycardia of  $> 100$  bpm, SBP  $< 90$  mm Hg on admission, signs of RVD on echocardiography and higher troponin concentrations.

In our study, 27% of the patients with ST-elevation in lead aVR were haemodynamically unstable on admission (SBP  $< 90$  mm Hg), and 64.8% of these patients had elevated troponins. In the study by Hoechtel et al. [20], patients with ST-segment elevation in lead aVR significantly more frequently received thrombolysis (29% patients). Similarly, in our study patients with ST-segment elevation in lead aVR significantly more frequently required intensified therapy, as more

of these patients received thrombolysis (14.3% vs 5.6%) and inotropic drugs (29.3% vs 7.5%)

Hoehchl et al. [20] observed a somewhat higher mortality (albeit non-significant) in patients with ST-segment elevation in lead aVR than in the remaining patients (10.3% vs 5.4%). In our study, clinical outcomes were worse: mortality (16.5% vs 6.9%) and in-hospital complication rates (38.3% vs 12.5%) were significantly higher in patients with ST-segment elevation in lead aVR compared to patients without such ECG finding. In patients with high risk of death, ST-segment elevation in lead aVR was significantly more frequent (39.8% vs 12.5%).

The ST-segment elevation in lead aVR in the setting of APE can be related to acute right ventricular overload, transient hypoxaemia resulting from impaired coronary blood flow and increased oxygen demand [21].

In our study, the in-hospital mortality rate was doubled in patients with ST-segment elevation in lead aVR when it was combined with RBBB, QR in lead V<sub>1</sub>, negative T-waves in leads V<sub>2</sub>-V<sub>4</sub> or III and aVF, ST-elevation in III and V<sub>1</sub>, SI-QIII-TIII sign or dextrogyria, in comparison to patients without the combination of such ECG findings.

It seems that ECG in APE patients can be of value in risk stratification. The ECG analysis and application of several proposed ECG scoring systems conveys significant information. However, from practical point of view, it can be time-consuming, hence the use of those scoring systems in everyday clinical practice is limited. On the other hand, the analysis of the ECG in terms of ST-segment elevation in lead aVR provides relevant information. The ST-segment elevation in lead aVR has limited sensitivity and specificity, but high NPV for mortality (93%). Hence, the lack of ST-segment elevation in lead aVR is related to good prognosis. Our study shows that ST-segment elevation in lead aVR predicts unfavourable outcome: increased all-cause mortality and higher in-hospital complication rates.

## CONCLUSIONS

1. The ST-segment elevation in lead aVR in patients with APE is related to unfavourable outcome.
2. The ST-segment elevation in lead aVR in patients with APE can be a valuable, non-invasive and easily obtainable marker, helpful in risk stratification of patients with APE.

**Conflict of interest:** none declared

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# Znaczenie prognostyczne uniesienia odcinka ST w odprowadzeniu aVR u chorych z ostrą zatorowością płucną

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## Streszczenie

**Wstęp:** W EKG chorych z ostrym zatorom tętnicy płucnej można stwierdzić wiele różnych nieprawidłowości. Brakuje doniesień dotyczących znaczenia rokowniczego uniesienia odcinka ST w odprowadzeniu aVR.

**Cel:** Celem pracy była ocena częstości występowania uniesienia odcinka ST w odprowadzeniu aVR w ostrym zatorze tętnicy płucnej oraz związku tego zjawiska z prezentacją kliniczną tej choroby w chwili przyjęcia do szpitala, przebiegiem klinicznym, obecnością markerów uszkodzenia mięśnia sercowego i występowaniem innych zmian w EKG.

**Metody:** Do badania włączono 293 chorych (182 kobiety, 111 mężczyzn) w wieku 17–89 lat (średni wiek 65,4 ± 15,5 roku).

**Wyniki:** Uniesienie odcinka ST w odprowadzeniu aVR stwierdzono u 133 (45,3%) chorych. U pacjentów z uniesieniem odcinka ST w odprowadzeniu aVR [STaVR(+)] w porównaniu z osobami bez uniesienia odcinka ST znamienne częściej obserwowano skurczowe ciśnienie tętnicze < 90 mm Hg przy przyjęciu (27% v. 10%; p < 0,001), podwyższone stężenie troponiny (64,8% v. 27,9%; p < 0,001). U terapii chorych z STaVR(+) znamienne częściej stosowano fibrynolizę (14,3% v. 5,6%; p = 0,009) i aminy katecholowe (29,3% v. 7,5%; p < 0,001). Śmiertelność całkowita (16,5% v. 6,9%; p = 0,009) i liczba powikłań w trakcie hospitalizacji (38,3% v. 12,5%; p < 0,001) była znamienne większa u pacjentów z STaVR(+). STaVR(+) znamienne częściej obserwowano u chorych z ujemnymi załamkami T w odprowadzeniach znad ściany dolnej (59,4% v. 39,4%; p < 0,001), uniesieniem odcinka ST w odprowadzeniu III (24% v. 5,6%; p < 0,001), uniesieniem odcinka ST w odprowadzeniu V1 (46,6% v. 7,5%; p < 0,001), obniżeniem odcinka ST w odprowadzeniach V4–V6 (48,9% v. 7,5%; p < 0,001), blokiem prawej odnogi pęczka Hisa (15,8% v. 8,1%; p = 0,04), objawem QR w odprowadzeniu V1 (18% v. 6,2%; p < 0,001) oraz objawem SI-QIII-TIII (46,6% v. 21,2%; p < 0,001).

**Wnioski:** Obecność STaVR(+) u chorych z ostrym zatorom tętnicy płucnej wiąże się z niekorzystnym rokowaniem i może być nieinwazyjnym oraz łatwo dostępnym markerem pomocnym w stratyfikacji ryzyka chorych z ostrym zatorom tętnicy płucnej.

**Słowa kluczowe:** zator tętnicy płucnej, odprowadzenie aVR, EKG, śmiertelność

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