Received: 2 July 2020 | Revised: 26 August 2020 | Accepted: 14 September 2020

DOI: 10.1111/anec.12811

REVIEW ARTICLE

WILEY

Prognostic implications of ST-segment elevation in lead aVR in patients with acute coronary syndrome: A meta-analysis

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Funding information
This work was supported by the National Natural Science Foundation of China (81770300, 81860059, 81460072); CAS "Light of West China" Program; International Joint Research Program of Gansu Province (18YF1WA046); Innovation and Entrepreneurship Program of Lanzhou City (2018-RC-78); and the Science Foundation of Gansu Provincial Hospital (18GSSY5-4).

Abstract

Background: ST-segment elevation (STE) in lead aVR is a useful tool in recognizing patients with left main or left anterior descending coronary obstruction during acute coronary syndrome (ACS). The prognostic implication of STE in lead aVR on outcomes has not been established.

Methods: We performed a systematic search for clinical studies about STE in lead aVR in four databases including PubMed, EMBASE, Cochrane Library, and Web of Science. Primary outcome was in-hospital mortality. Secondary outcomes included in-hospital (re)infarction, in-hospital heart failure, and 90-day mortality.

Results: We included 7 studies with a total of 7,700 patients. The all-cause in-hospital mortality of patients with STE in lead aVR during ACS was significantly higher than that of patients without STE (OR: 4.37, 95% CI 1.63 to 11.68, $p = .003$). Patients with greater STE (>0.1 mV) in lead aVR had a higher in-hospital mortality when compared to lower STE (0.05–0.1 mV) (OR: 2.00, 95% CI 1.11–3.60, $p = .02$), However, STE in aVR was not independently associated with in-hospital mortality in ACS patients (OR: 2.72, 95% CI 0.85–8.63, $p = .09$). The incidence of in-hospital myocardial (re)infarction (OR: 2.77, 95% CI 1.30–5.94, $p = .009$), in-hospital heart failure (OR: 2.62, 95% CI 1.06–6.50, $p = .04$), and 90-day mortality (OR: 10.19, 95% CI 5.27–19.71, $p < .00001$) was also noted to be higher in patients STE in lead aVR.

Conclusions: This contemporary meta-analysis shows STE in lead aVR is a poor prognostic marker in patients with ACS with higher in-hospital mortality, reinfarction, heart failure and 90-day mortality. Greater magnitude of STE portends worse prognosis. Further studies are needed to establish an independent predictive role of STE in aVR for these adverse outcomes.

KEYWORDS

acute coronary syndrome, lead aVR, meta-analysis, prognosis, ST-segment elevation

Aqian Wang and Vikas Singh authors contributed equally.

1 | INTRODUCTION

Acute coronary syndrome (ACS) is characterized by erosion or rupture of plaques in the coronary arteries. It can lead to many complications including heart failure, malignant arrhythmias, pulmonary edema, and even death (Derumeaux and Ternacle, 2018). Electrocardiogram (ECG) is a useful tool for diagnosis, risk stratification, and monitoring treatment response in coronary heart disease in clinical practice. Lead aVR is unipolar facing the cardiac apex to the outflow tract of the right ventricle under normal condition. (Wong et al., 2012). Once overlooked, changes in lead aVR are now utilized to diagnose pericarditis and localize coronary artery disease (Ducas et al., 2013; Rathi et al., 2016) especially in the setting of exercise stress test (Kosuge et al., 2011; Nough et al., 2012; Ozmen et al., 2010). ST-segment elevation (STE) in lead aVR is a useful tool in recognizing patients with left main (LM) or left anterior descending (LAD) coronary obstruction during acute coronary syndrome (ACS) (Yan et al., 2007). Also, STE in aVR is a poor prognostic marker in pulmonary embolism and tricyclic antidepressant toxicity; however, the studies evaluating prognostic significance of STE in aVR during ACS including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris have yielded conflicting results(Aygul et al., 2008; Barrabes et al., 2003; Kosuge et al., 2001, 2006; Misumida et al., 2016; Nabati et al., 2016; Yan et al., 2007). We performed this contemporary systematic review and meta-analysis to determine prognostic significance of STE in aVR in patients with ACS.

2 | METHODS

We systematically searched four databases; PubMed, EMBASE, Cochrane Library, and Web of Science with no language limitations, using a detailed search strategy (See Supplementary Material). Two reviewers (WAQ and SX) independently performed the literature search. Two blinded authors (SX and DYC) performed data extraction while two authors (SHL and CYS) checked the data for accuracy. STE of 0.5 mm or more in lead aVR was considered significant.

Inclusion criteria for the studies included: (a) retrospective or prospective cohort studies; (b) studies compared the outcomes of STE in aVR versus no STE in aVR in patients with ACS; (c) aVR STE defined as ST elevation 0.5 mm or more above the isoelectric line on ECG, no aVR STE is defined as 0–0.5 mm or −0.5–0.5 mm; (d) endpoint events (in-hospital death, 90-day death, in-hospital infarction, in-hospital heart failure,) were described clearly; (e) studies with full text; and (f) studies in English. Based on the above criteria, two reviewers evaluated and screened all the articles, while any disagreements were settled by a third reviewer.

Exclusion criteria: (a) Studies did not compare outcomes of STE in aVR and no STE in aVR (b) studies with abstract only; and (c) missing data to calculate OR.

We used Newcastle–Ottawa Quality Assessment Scale (NOS) to evaluate quality of the studies eventually included. The NOS ranges from zero to nine points. A study with > 8 points is considered good quality and 5–7 points for fair and < 5 points for poor study. Studies with points equal to or more than 6 were included in this analysis (Meng et al., 2017).

We analyzed the ORs with 95% confidence interval (CI) for each included study. Random-effects model was used for the heterogeneity evaluation. We used the chi-square test ($p \leq .05$ was considered statistically significant for heterogeneity) and I^2 statistics ($I^2 > 50\%$ was considered a measure of severe heterogeneity). We used RevMan 5.3 for data analysis.

3 | RESULTS

We identified 5,762 records of which 23 were potentially eligible. Finally, 7 studies met all criteria to be included in this meta-analysis (Figure 1) (Aygul et al., 2008; Barrabes et al., 2003; Kosuge et al., 2001, 2006; Misumida et al., 2016; Nabati et al., 2016; Yan et al., 2007). The total number of patients was 7,700:1,035 individuals with STE in lead aVR and 6,665 individuals with no STE in lead aVR. The baseline characteristics of the 7 included studies are listed in Tables 1–3.

3.1 | Primary endpoint

As shown in Figure 2a, three studies (Aygul et al., 2008; Barrabes et al., 2003; Yan et al., 2007) demonstrated that STE in aVR is associated with higher in-hospital mortality in patients with ACS compared with no STE while one study did not (Misumida et al., 2016). The pooled analysis of all 4 studies showed a significantly higher in-hospital mortality in patients with STE in lead aVR compared with those without STE (OR: 4.37, 95% CI 1.63–11.68, $p = .003$), and the heterogeneity was high ($I^2 = 86\%$, $p < 0.0001$). Also, the subgroup analysis (Figure 2b) showed that the patients with greater STE (>0.1 mV) in lead aVR had a higher in-hospital mortality when compared with lower STE (0.05–0.1 mV) (OR: 2.00, 95% CI 1.11–3.60, $p = .02$), and the heterogeneity was low ($I^2 = 12\%$, $p = .29$). Of note, STE in aVR was not independently associated with in-hospital mortality in ACS patients as shown in Figure 2c (OR: 2.72, 95% CI 0.85 to 8.63, $p = .09$), and the heterogeneity was high ($I^2 = 88\%$, $p = .0003$) (Table S1).

3.2 | Secondary endpoints

3.2.1 | In-hospital (re)infarction

As shown in Figure 3, the pooled analysis of 2 studies (Barrabes et al., 2003; Misumida et al., 2016) demonstrated higher in-hospital (re) infarction in ACS patients with STE in aVR versus those

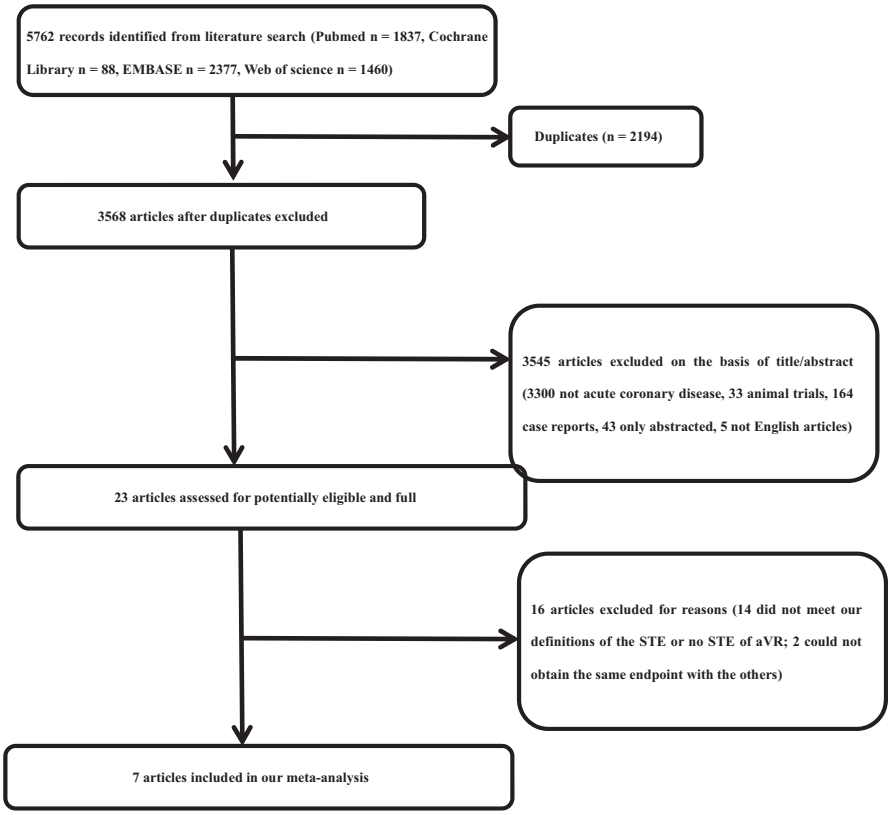

FIGURE 1 Flow chart of selection of studies

without STE (OR: 2.77, 95% CI 1.30–5.94, $p = .009$), and the heterogeneity was low ($I^2 = 0\%$, $p = .50$). There are not enough data to analyze independent association of STE in aVR with in-hospital (re)infarction.

3.2.2 | In-hospital heart failure

As shown in Figure 4a, the pooled analysis of 4 studies showed that the incidence of heart failure during hospitalization in patients with STE in aVR was significantly higher than those with no STE (OR: 2.62, 95% CI 1.06–6.50, $p = .04$), and the heterogeneity was high ($I^2 = 87\%$, $p < .0001$). The subgroup analysis showed higher in-hospital heart failure in ACS patients with greater STE (>0.1 mV) in aVR compared with lower STE (0.05–0.1 mV) in Figure 4b (OR: 2.65, 95% CI 1.37–5.11, $p = .004$), and the heterogeneity was low ($I^2 = 53\%$, $p = .15$). There are not enough data to analyze independent association of STE in aVR with in-hospital heart failure.

3.2.3 | 90-day death

As shown in Figure 5, the pooled analysis of 2 studies showed that the ACS patients with STE in aVR had a higher 90-day mortality compared with patients with no STE in aVR (OR: 10.19, 95% CI 5.27–19.71, $p < 0.00001$), and the heterogeneity was low ($I^2 = 0\%$, $p = .96$). There are not enough data to analyze independent association of STE in aVR with 90-day death.

4 | DISCUSSION

This meta-analysis shows that ACS patients with ST-segment elevation in lead aVR have higher in-hospital mortality, reinfarction, heart failure, and 90-day death when compared with those without STE. Greater STE portends higher in-hospital mortality and heart failure. Further studies are needed to establish an independent association of STE in lead aVR with adverse outcomes in patients with ACS.

Acute coronary syndrome (ACS) is a life-threatening disease (Nikus et al., 2012), with up to 40% mortality at 5 years after experiencing an event (Makki et al., 2015). STE in lead aVR is observed in 7.3% to 32.3% of the patients presenting with ACS (Nabati et al., 2016). Studies have shown the value of STE in lead aVR in identifying culprit vessels during ACS. In 2001, Yamaji et al. studied the electrocardiographic characteristics of patients with LM occlusion and concluded that STE in lead aVR with a lower degree of STE in lead V1 is predictive of LM disease while STE in lead aVR is a predictor of adverse outcomes (Yamaji et al., 2001). In a meta-analysis regarding the value of culprit vessel identification with STE in aVR during acute STEMI, pooled data showed that STE in aVR has a sensitivity of 76% (95% CI 73–80%), a specificity of 83% (95% CI 76–88%) for recognizing LM coronary artery disease and a sensitivity 58% (95% CI 37–77%), a specificity 93% (95% CI 81–97%) for

TABLE 1 Characteristics of seven studies included in the meta-analysis

Study (year)	Country	Type of study	Study design	Number of patients Included	Study population	ST-segment shift measurement	Time between admission and cardiac catheterization	Endpoint	Quality score
Kosuge et al. (2006)	Japan	SC	RS	333	NSTEACS	20 ms after the J point	a median of 3 days	The composite of death, myocardial infarction, urgent revascularization at 90 days.	8
Nabati et al. (2016)	Iran	SC	RS	129	ACS	20 ms after the J point	2–3 days	In-hospital/ three-month outcome	7
Barrabes et al. (2003)	Spain	SC	RS	775	NSTEAMI	20 ms after the J point	within 6 months (*N* = 437)	In-hospital adverse events (death, (re) infarction, angina, heart failure)	8
Yan et al. (2007)	Canada	MC	PS	5,064	NSTEACS	80 ms after the J point	*N/A*	In-hospital/ three-month death	7
Aygul et al. (2008)	Turkey	SC	PS	950	STEMI	60 ms after the J point	within the first 6 hr (*N* = 693); 1–7 days (*N* = 238); 8–12 days after admission (*N* = 19)	In-hospital death	7
Misumida et al. (2016)	America	SC	RS	379	NSTEMI	J point	within 5 day	the prevalence of LM/3VD, in-hospital mortality, recurrent MI, heart failure, cardiogenic shock, length of hospital stays	8
Kosuge et al. (2001)	Japan	SC	RS	70	AMI	nearest 0.5 mm, 20 milliseconds after the end of the QRS complex	14 days	Intra-aortic balloon pump during Hospitalization; Congestive heart failure during hospitalization	7

Abbreviations: MC, multicenter study; NA, not available; PS, prospective study; RS, retrospective study; SC, single center study; STE, ST-segment elevation

TABLE 2 Characteristics of seven studies included in the meta-analysis

	Kosuge et al. (2006)	Nabati et al. (2016)	Barrabés et al. (2003)	Yan et al. (2007)	Aygul et al. (2008)	Misumida et al. (2016)	Kosuge et al., (2001)
Total patients, *n*	333	129	775	5,064	950	379	70
Male/female, *n*	230/103	65/64	592/183	3199/1865	742/208	226/153	63/7
Age (years)	66.8	58.4	61.3	66.2	59.2	64.8	57.7
Hypertension, *n* (%)	213 (64.0%)	70 (54.3%)	378 (48.8%)	3,073 (60.7%)	342 (37.8%)	273 (72.0%)	35 (50%)
Diabetes, *n* (%)	115 (34.5%)	38 (29.5%)	182 (23.5%)	1,257 (24.8%)	203 (21.4%)	134 (35.4%)	17 (24.3%)
Smoking, *n* (%)	N/A	28 (21.7%)	321 (41.4%)	2,882 (56.9%)	505 (53.2%)	96 (25.3%)	46 (65.7%)
Hyperlipidemia, *n* (%)	N/A	50 (38.8%)	309 (39.9%)	2,497 (49.3%)	N/A	215 (56.7%)	N/A
Killip's class ≥ 2, *n* (%)	24 (7.2%)	N/A	104 (13.4%)	860 (17.0%)	234 (24.6%)	43 (11.3%)	NA
Previous MI, *n* (%)	78 (23.4%)	26 (20.2%)	N/A	1689 (33.4%)	50 (5.3%)	50 (13.2%)	NA
Previous PCI, *n* (%)	66 (19.8%)	N/A	N/A	939 (18.6%)	N/A	109 (28.8%)	NA
Previous CABG, *n* (%)	21 (6.3%)	5 (3.9%)	N/A	690 (13.6%)	N/A	N/A	NA
STD in leads other than aVR, *n* (%)	233 (70.0%)	69 (53.5%)	N/A	2,267 (44.8%)	N/A	N/A	NA
0 narrowed coronary arteries, *n* (%)	58 (17.4%)	15 (11.6%)	22 (5%) (N = 437)	N/A	N/A	N/A	NA
1 narrowed coronary artery, *n* (%)	141 (42.3%)	19 (14.7%)	153 (35.0%)	N/A	547 (57.6%)	N/A	NA
2 narrowed coronary arteries, *n* (%)	74 (22.2%)	41(31.8%)	111 (25.4%)	N/A	284 (29.9%)	N/A	NA
3 narrowed coronary arteries, *n* (%)	60 (18.0%)	N/A	118 (27.0%)	N/A	119 (12.5%)	N/A	NA
LM coronary artery disease, *n* (%)	12 (3.6%)	N/A	33 (7.6%)	N/A	5 (0.5%)	14 (3.7%)	NA
LM and/or 3V coronary disease, *n* (%)	62 (18.6%)	2 (1.6%)	N/A	652 (27%) (N = 2,416)	N/A	88 (23.2%)	NA
Peripheral vascular disease, *n* (%)	N/A	N/A	118 (15.2%)	493 (9.7%)	N/A	N/A	NA
PCI in hospital, *n* (%)	181(54.4%)[b]	N/A	110 (14.2%)	1,443 (28.5%)	514 (54.1%)	203 (53.6%)	NA
CABG in hospital, *n* (%)	47 (14.1%)	N/A	76 (9.8%)	228 (4.5%)	43 (4.5%)	37 (9.8%)	NA
STE ≥ 0.1mv in V1, *n* (%)	N/A	37 (28.7%)	58 (7.5%)	N/A	N/A	N/A	NA
Anterior STD, *n* (%)	N/A	65 (50.4%)	223 (28.8%)	N/A	N/A	56 (14.8%)	NA

(Continues)

TABLE 2 (Continued)

	Kosuge et al. (2006)	Nabati et al. (2016)	Barrabés et al. (2003)	Yan et al. (2007)	Aygul et al. (2008)	Misumida et al. (2016)	Kosuge et al., (2001)
Inferior STD, *n* (%)	N/A	12 (9.3%)	84 (10.8%)	N/A	N/A	55 (14.5%)	NA
Lateral STD, *n* (%)	N/A	26 (20.2%)	207 (26.7%)	N/A	N/A	107 (28.2%)	NA
T-wave inversion, *n* (%)	N/A	35(27.1%)[a]	142 (18.3%)	N/A	N/A	95 (25.1%)	NA

Note: Data are shown as mean ± *SD* or percentage.

Abbreviations: 3V, 3-vessel coronary disease; CABG, coronary artery bypass grafting; LM, Left main coronary artery disease; MI, Myocardial infarction; PCI, Percutaneous coronary intervention; STD, ST-segment depression; STE, ST-segment elevation; STE, ST-segment elevation.

[a]Negative T waves without ST-segment depression.

[b]Urgent or in-hospital percutaneous coronary intervention.

proximal LAD lesions (Korniyenko et al., 2010). The diagnostic value of STE in aVR after exercise stress test for LM and LAD lesions has also been shown (Ghaffari et al., 2017; Uthamalingam et al., 2011; Wagener et al., 2017). For its special vector, lead aVR has often been overlooked in the past (Nikus et al., 2012). Some believe that the STE in lead aVR represents reciprocal changes caused by ST-segment depression in the precordial leads instead of being a direct representation of culprit vessel lesion (Sclarovsky et al., 2002). Recent studies have attempted to assess the association between STE in lead aVR and the prognosis of patients with coronary artery diseases; however, the relationship of this finding on ECG and its significance on prognosis of patients with ACS remains to be determined (Cerit, 2017). The current meta-analysis shows that the incidence of in-hospital mortality in patients with ACS and STE in lead aVR is significantly higher when compared with patients without STE in aVR. (OR: 4.37, 95% CI 1.63–11.68, $p < 0.0001$). The magnitude of STE in aVR was also significant where greater STE was associated with higher incidence of in-hospital mortality. The HERO-2 study which included a large population of 15,315 patients with STEMI showed that there is a U-shaped relationship between ST-segment shift in lead aVR and 30-d mortality in anterior wall STEMI (Wong et al., 2012). The prospective Global Registry of Acute Coronary Events (GRACE) study revealed that patients with STE in aVR in non-ST-segment elevation acute coronary syndrome (NSTEACS) have a higher in-hospital mortality (Yan et al., 2007) (OR: 1.597, 95% CI 1.03–2.47). The study in 2008 by Aygul et al. also showed aVR STE ≥ 0.5 mm may be a predictor of all-cause death during hospitalization (OR: 4.34, 95% CI 2.60–7.26) in STEMI. ST depression combined with aVR STE is also thought to be indicative of adverse outcomes in patients with NSTEACS (Kosuge et al., 2005a,b; Nikus et al., 2012; Wong et al., 2010). However, pooled data from multivariable analysis of three trials (Aygul et al., 2008; Barrabes et al., 2003; Yan et al., 2007) did not find an independent association between STE in aVR and increased risk of in-hospital mortality (OR: 2.72, 95% CI 0.85–8.63, $p = .09$); however, there was high heterogeneity ($I^2 = 88\%$, $p = .0003$) and significant differences in variables included in the trials. Therefore, further studies are needed to explore the relationship between STE in lead aVR and in-hospital mortality.

The presence of ST-segment deviation in lead aVR also predicts the success of primary percutaneous coronary intervention (PCI) (Kosuge et al., 2005a,b). The lack of resolution of STE in aVR is associated with adverse events such as death, (re)infarction, or urgent revascularization within 30 days after admission and correlates with the extent and severity of coronary artery disease in patients with NSTEACS (Kosuge et al., 2008). Kosuge et al. showed the high mortality of 90-day mortality reaching 40% in patients with persistent STE in lead aVR in NSTEMI (Kosuge et al., 2008). We also noted a significantly higher 90-day mortality in patients with STE in aVR versus those with no STE in aVR (OR: 10.19, 95% CI 5.27–19.71, $p < 0.00001$). We found significant differences for in-hospital heart failure between two groups (OR: 2.62, 95% CI 1.06–6.50, $p = .04$). Greater magnitude of STE was associated with higher incidence of in-hospital heart failure in ACS patients. These relations between

TABLE 3 Outcomes of seven studies included in the meta-analysis

		Kosuge et al. (2006)	Nabati et al. (2016)	Barrabés et al. (2003)	Yan et al. (2007)	Aygul et al. (2008)	Misumida et al. (2016)	Kosuge et al. (2001)
Patients with STE in lead aVR, *n* (%)		90 (27.0%)	52 (40.3%)	250 (32.3%)	368 (7.3%)	155 (16.3%)	97 (25.6%)	NA
In-hospital death in group with STE in lead aVR, *n* (*N*)	STE 0.05–0.1 mV	N/A	N/A	10 (116)	18 (292)	29 (155)	2 (97)	NA
	STE > 0.1 mV			26 (134)	6 (76)			
In-hospital death in group with no STE in lead aVR, *n* (*N*)		N/A	N/A	7 (525)	197 (4,696)	41 (795)	1 (282)	NA
In-hospital heart (re) infarction in group with STE in lead aVR, *n* (*N*)		N/A	N/A	15 (250)	41 (368)	N/A	0 (97)	NA
In-hospital heart (re) infarction in group with no STE in lead aVR, *n* (*N*)		N/A	N/A	11 (525)	423 (4,696)	N/A	1 (282)	NA
In-hospital heart failure in group with STE in lead aVR, *n* (*N*)	STE 0.05–0.1 mV	N/A	N/A	12 (116)	53 (292)	N/A	13 (97)	1 (23)
	STE > 0.1 mV			41 (134)	23 (76)			
In-hospital heart failure in group with no STE in lead aVR, *n* (*N*)		N/A	N/A	17 (525)	540 (4,696)	N/A	33 (282)	1 (47)
90-day death in group with STE in lead aVR, *n* (*N*)		2 (90)	3 (52)	N/A	N/A	N/A	N/A	NA
90-day death in group with no STE in lead aVR, *n* (*N*)		0 (243)	0 (77)	N/A	N/A	N/A	N/A	NA

Note: Data are shown as mean ± *SD* or percentage.

Abbreviation: STE, ST-segment elevation.

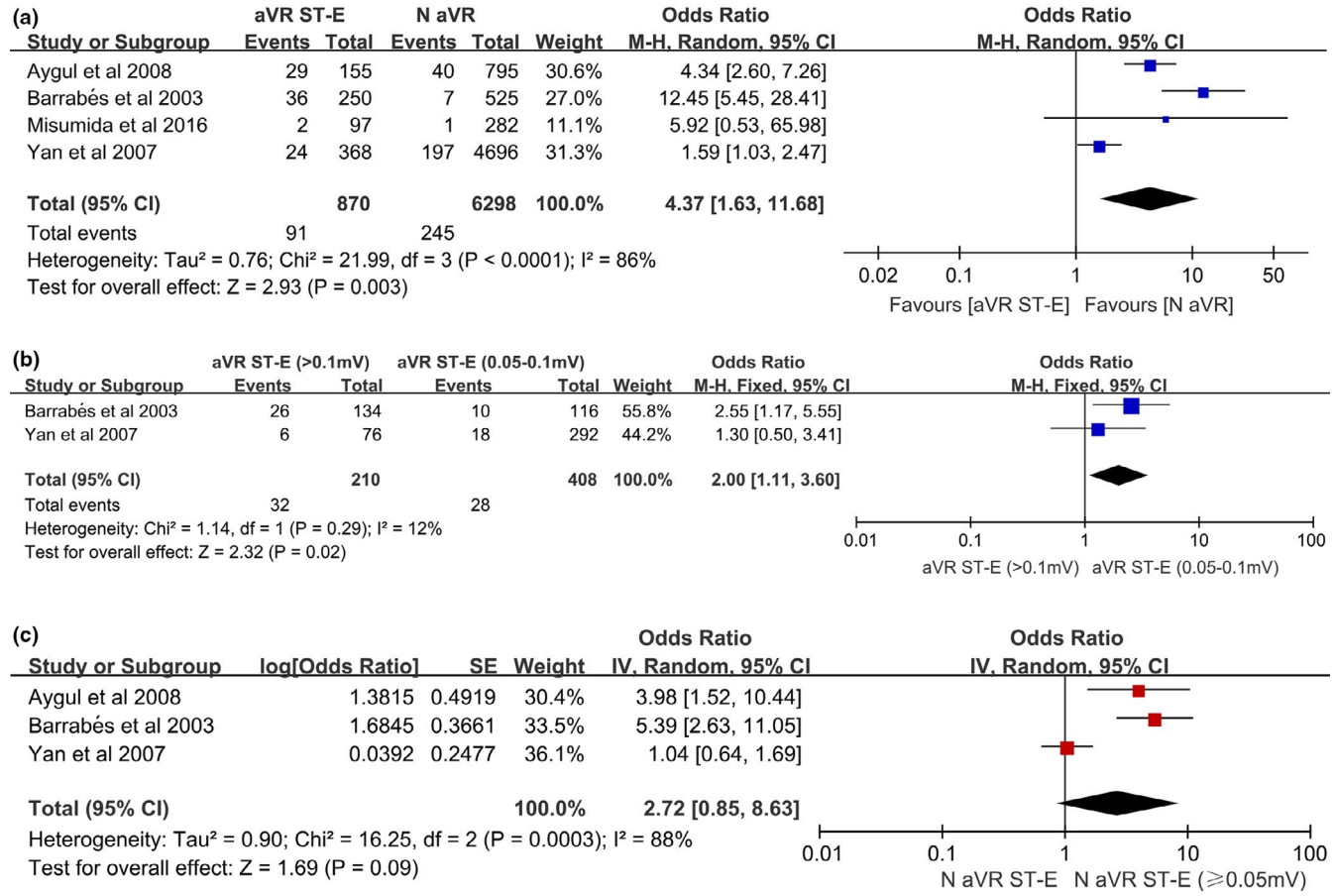

FIGURE 2 ST-segment elevation in lead aVR and in-hospital mortality. (a) Forest plot demonstrating the association between ST-segment deviation in aVR and the in-hospital mortality in the patients with ACS. (b) Forest plot demonstrating the association between magnitude of ST-segment elevation in aVR and the in-hospital mortality in the patients with ACS. (c) Forest plot demonstrating the independent association between ST-segment elevation in aVR and the in-hospital mortality in the patients with ACS

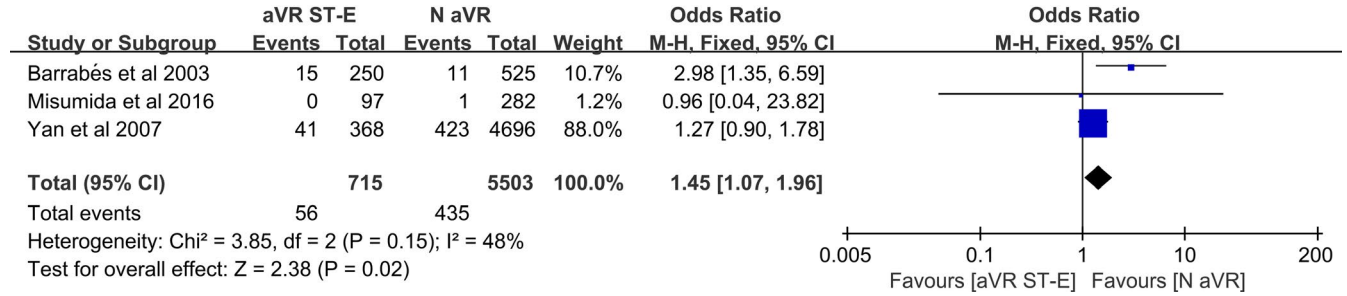

FIGURE 3 Forest plot demonstrating the association between ST-segment deviation in aVR and the in-hospital (re) infarction in the patients with ACS

STE in aVR and increased risk of adverse outcomes could be explained by the association of STE in aVR with severe underlying coronary disease such as LM disease or three vessels disease. It should also be noted that STE in aVR can be observed in many other clinical diseases such as acute pulmonary embolism (Pourafkari et al., 2017), myocardial hypertrophy, and acute aortic dissection (Kosuge et al., 2016).

4.1 | Limitations of the study

Firstly, there are some heterogeneity (Meng et al., 2017); therefore, we used the random-effects model to estimate all pooled effects. Secondly, the definition of no deviation of ST segment in lead aVR was not consistent in the studies, including ST-segment shift ranging from 0–0.5 or −0.5–0.5 mm, which may be a potential confounding

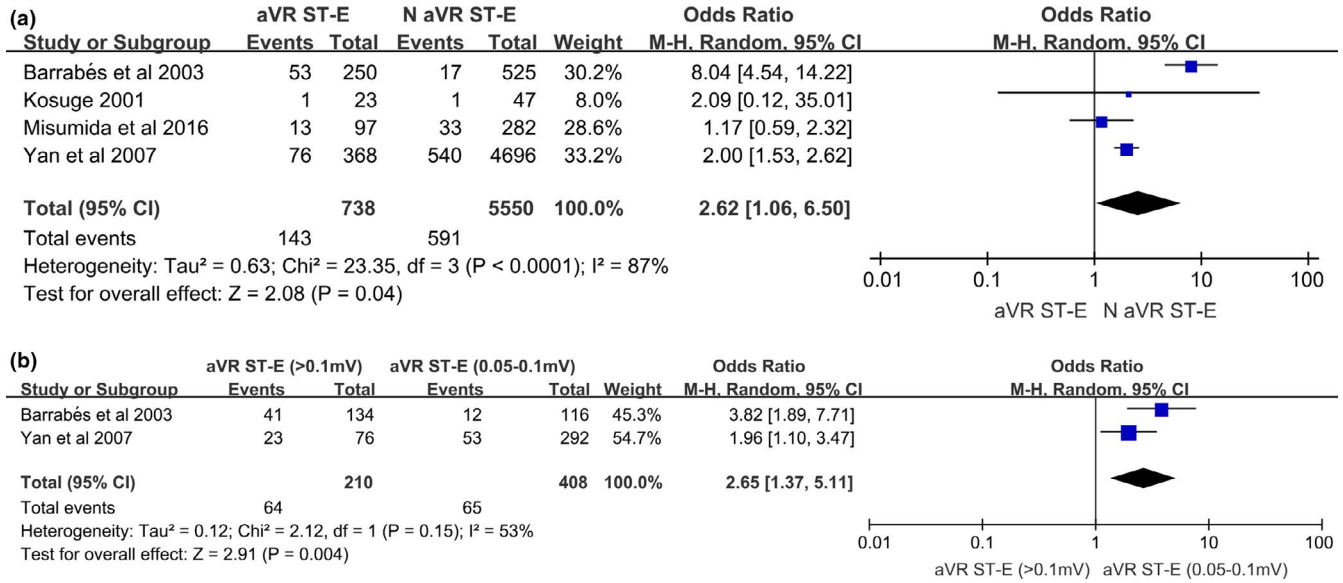

FIGURE 4 ST-segment elevation in lead aVR and in-hospital heart failure. (a) Forest plot demonstrating the association between ST-segment deviation in aVR and the in-hospital heart failure in the patients with ACS. (b) Forest plot demonstrating the association between magnitude of ST-segment elevation in aVR and the in-hospital heart failure in the patients with ACS

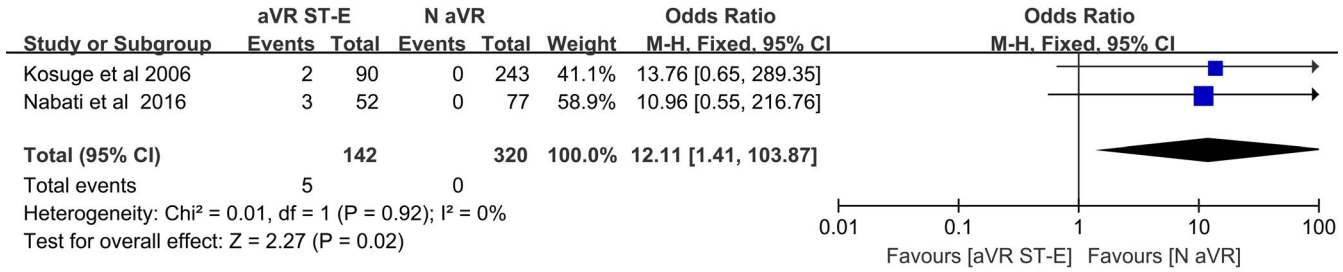

FIGURE 5 Forest plot demonstrating the association between ST-segment deviation in aVR and the 90-day mortality in the patients with ACS

factor in this study. Despite the limitations, the study has several strengths including the large number of patients included.

5 | CONCLUSION

This contemporary meta-analysis shows STE in lead aVR is a poor prognostic marker in patients with ACS with higher in-hospital mortality, reinfarction, heart failure, and 90-day mortality. Greater magnitude of STE portends worse prognosis. Further studies are needed to establish an independent predictive role of STE in aVR for these adverse outcomes.

CONFLICT OF INTEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

WAQ and SV drafted the manuscript. SX and DYC performed data extraction while SHL and WR checked the data. ZM and CYS made the design of the disagreement and gave final approval.

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REFERENCES

Derumeaux, G., & Ternacle, J. (2018). Layer-specific strain in acute coronary syndrome: back to the future!. *European Heart Journal – Cardiovascular Imaging*, *19*(12), 1325–1326.

Aygul, N., Ozdemir, K., Tokac, M., Aygul, M. U., Duzenli, M. A., Abaci, A., Bacaksiz, A., Yazici, H., & Bodur, S. (2008). Value of lead aVR in predicting acute occlusion of proximal left anterior descending coronary artery and in-hospital outcome in ST-elevation myocardial infarction: An electrocardiographic predictor of poor prognosis. *Journal of Electrocardiology*, *41*(4), 335–341. https://doi.org/10.1016/j.jelectrocard.2008.02.025

Barrabes, J. A., Figueras, J., Moure, C., Cortadellas, J., & Soler-Soler, J. (2003). Prognostic value of lead aVR in patients with a first non-ST-segment elevation acute myocardial infarction. *Circulation*, *108*(7), 814–819. https://doi.org/10.1161/01.CIR.0000084553.92734.83

Cerit, L. (2017). Chicken or the egg: ST elevation in lead aVR or SYNTAX score. *Cardiovascular Journal of Africa*, *28*(2), 100–103. https://doi.org/10.5830/CVJA-2016-062

Ducas, R., Ariyarajah, V., Philipp, R., Ducas, J., Elliott, J., Jassal, D., Tam, J., Garber, P., Shaikh, N., & Hussain, F. (2013). The presence

of ST-elevation in lead aVR predicts significant left main coronary artery stenosis in cardiogenic shock resulting from myocardial infarction: The Manitoba cardiogenic shock registry. *International Journal of Cardiology*, *166*(2), 465–468. https://doi.org/10.1016/j.ijcard.2011.11.003

Ghaffari, S., Asadzadeh, R., Tajlil, A., Mohammadalian, A., & Pourafkari, L. (2017). Predictive value of exercise stress test-induced ST-segment changes in leads V-1 and avR in determining angiographic coronary involvement. *Annals of Noninvasive Electrocardiology*, *22*(1), e12370.

Korniyenko, A., Cordova, J. P., Berrios, R. S., Nadkarni, G., Alviar, C., & Herzog, E. (2010). Utility of ST segment changes in lead aVR to identify the culprit lesion in acute myocardial infarction: An updated meta-analysis on sensitivity and specificity. *Journal of the American College of Cardiology*, *56*(13), B105.

Kosuge, M., Ebina, T., Hibi, K., Endo, M., Komura, N., Hashiba, K., Kiyokuni, M., Nakayama, N., Umemura, S., & Kimura, K. (2008). ST-segment elevation resolution in lead aVR a strong predictor of adverse outcomes in patients with non-ST-segment elevation acute coronary syndrome. *Circulation Journal*, *72*(7), 1047–1053. https://doi.org/10.1253/circj.72.1047

Kosuge, M., Ebina, T., Hibi, K., Morita, S., Endo, M., Maejima, N., Iwahashi, N., Okada, K., Ishikawa, T., Umemura, S., & Kimura, K. (2011). An early and simple predictor of severe left main and/or three-vessel disease in patients with nonst-segment elevation acute coronary syndrome. *American Journal of Cardiology*, *107*(4), 495–500. https://doi.org/10.1016/j.amjcard.2010.10.005

Kosuge, M., Kimura, K., Ishikawa, T., Ebina, T., Hibi, K., Toda, N., & Umemura, S. (2005). ST-segment depression in lead aVR – A useful predictor of impaired myocardial reperfusion in patients with inferior acute myocardial infarction. *Chest*, *128*(2), 780–786. https://doi.org/10.1378/chest.128.2.780

Kosuge, M., Kimura, K., Ishikawa, T., Ebina, T., Hibi, K., Tsukahara, K., Kanna, M., Iwahashi, N., Okuda, J., Nozawa, N., Ozaki, H., Yano, H., Kusama, I., & Umemura, S. (2006). Combined prognostic utility of ST segment in lead aVR and troponin T on admission in non-ST-segment elevation acute coronary syndromes. *American Journal of Cardiology*, *97*(3), 334–339. https://doi.org/10.1016/j.amjcard.2005.08.049

Kosuge, M., Kimura, K., Ishikawa, T., Endo, T., Hongo, Y., Shigemasa, T., Iwasawa, Y., Tochikubo, O., & Umemura, S. (2001). ST-segment depression in lead aVR predicts predischarge left ventricular dysfunction in patients with reperfused anterior acute myocardial infarction with anterolateral ST-segment elevation. *American Heart Journal*, *142*(1), 51–57. https://doi.org/10.1067/mhj.2001.116073

Kosuge, M., Uchida, K., Karube, N., Ebina, T., Hibi, K., Iwahashi, N., Maejima, N., Matsuzawa, Y., Masuda, M., & Kimura, K. (2016). ST-segment elevation in lead aVR strongly predicts in-hospital mortality in patients with type a acute aortic dissection. *Circulation*, *134*.

Kosuge, U., Kimura, K., Ishikawa, T., Ebina, T., Hibi, K., Toda, N., & Umemura, S. (2005). A usST-segment depression in lead aVR:Eful predictor of impaired myocardial reperfusion in patients with inferior acute myocardial infarction. *Chest*, *128*(2), 780–786. https://doi.org/10.1378/chest.128.2.780

Makki, N., Brennan, T. M., & Girotra, S. (2015). Acute coronary syndrome. *Journal of Intensive Care Medicine*, *30*(4), 186–200. https://doi.org/10.1177/0885066613503294

Meng, L., Letsas, K. P., Baranchuk, A., Shao, Q., Tse, G., Zhang, N., Zhang, Z., Hu, D., Li, G., & Liu, T. (2017). Meta-analysis of fragmented QRS as an electrocardiographic predictor for arrhythmic events in patients with Brugada syndrome. *Frontiers in Physiology*, *8*, 678.

Misumida, N., Kobayashi, A., Fox, J. T., Hanon, S., Schweitzer, P., & Kanei, Y. (2016). Predictive value of ST-segment elevation in lead aVR for left main and/or three-vessel disease in non-ST-segment elevation myocardial infarction. *Annals of Noninvasive Electrocardiology*, *21*(1), 91–97. https://doi.org/10.1111/anec.12272

Nabati, M., Emadi, M., Mollaalipour, M., Bagheri, B., & Nouraei, M. (2016). ST-segment elevation in lead aVR in the setting of acute coronary syndrome. *Acta Cardiologica*, *71*(1), 47–54. https://doi.org/10.1080/AC.71.1.3132097

Nikus, K. C., Sclarovsky, S., Huhtala, H., Niemela, K., Karhunen, P., & Eskola, M. J. (2012). Electrocardiographic presentation of global ischemia in acute coronary syndrome predicts poor outcome. *Annals of Medicine*, *44*(5), 494–502. https://doi.org/10.3109/07853890.2011.585345

Nough, H., Jorat, M. V., Varasteravan, H. R., Ahmadieh, M. H., Tavakkolian, N., & Sheikhvatan, M. (2012). The value of ST-segment elevation in lead aVR for predicting left main coronary artery lesion in patients suspected of acute coronary syndrome. *Romanian Journal of Internal Medicine = Revue Roumaine De Médecine Interne*, *50*(2), 159–164.

Ozmen, N., Yiginer, O., Uz, O., Kardesoglu, E., Aparci, M., Isilak, Z., Cingozbay, B. Y., Cebeci, B. S., & Kocum, H. T. (2010). ST elevation in the lead aVR during exercise treadmill testing may indicate left main coronary artery disease. *Kardiologia Polska*, *68*(10), 1107–1110.

Pourafkari, L., Ghaffari, S., Tajlil, A., Akbarzadeh, F., Jamali, F., & Nader, N. D. (2017). Clinical significance of ST elevation in lead aVR in acute pulmonary embolism. *Annals of Noninvasive Electrocardiology*, *22*(2), e12368. https://doi.org/10.1111/anec.12368

Rathi, N., Baloch, M. Z., Sachdewani, R. K., & Memon, F. (2016). Frequency of left main artery/three vessel disease predicted through ECG changes in patients presenting with non-ST segment acute coronary syndrome. *Journal of the Liaquat University of Medical and Health Sciences*, *15*(2), 93–97.

Sclarovsky, S., Nikus, K. C., & Birnbaum, Y. (2002). Manifestation of left main coronary artery stenosis is diffuse ST depression in inferior and precordial leads on ECG. *Journal of the American College of Cardiology*, *40*(3), 575–576. author reply 576–577.

Uthamalingam, S., Zheng, H., Leavitt, M., Pomerantsev, E., Ahmado, I., Gurm, G. S., & Gewirtz, H. (2011). Exercise-induced ST-segment elevation in ECG lead aVR is a useful indicator of significant left main or ostial LAD coronary artery stenosis. *Jacc-Cardiovascular Imaging*, *4*(2), 176–186. https://doi.org/10.1016/j.jcmg.2010.11.014

Wagener, M., Abacherli, R., Honegger, U., Schaerli, N., Pretre, G., Twerenbold, R., Puelacher, C., Sunier, G., Reddiess, P., Gimenez, M. R., Wildi, K., Boeddinghaus, J., Nestelberger, T., Badertscher, P., Sabti, Z., Schmid, R., Leber, R., Widmer, D. F., Shrestha, S., … Reichlin, T. (2017). Diagnostic and prognostic value of lead aVR during exercise testing in patients suspected of having myocardial ischemia. *American Journal of Cardiology*, *119*(7), 959–966. https://doi.org/10.1016/j.amjcard.2016.11.056

Wong, C.-K., Gao, W., Stewart, R. A. H., Benatar, J., French, J. K., Aylward, P. E. G., White, H. D., & Investigators, H. (2010). aVR ST elevation: An important but neglected sign in ST elevation acute myocardial infarction. *European Heart Journal*, *31*(15), 1845–1853. https://doi.org/10.1093/eurheartj/ehq161

Wong, C. K., Gao, W., Stewart, R. A., French, J. K., Aylward, P. E., & White, H. D. (2012). The prognostic meaning of the full spectrum of aVR ST-segment changes in acute myocardial infarction. *European Heart Journal*, *33*(3), 384–392. https://doi.org/10.1093/eurheartj/ehr301

Yamaji, H., Iwasaki, K., Kusachi, S., Murakami, T., Hirami, R., Hamamoto, H., Hina, K., Kita, T., Sakakibara, N., & Tsuji, T. (2001). Prediction of acute left main coronary artery obstruction by 12-lead electrocardiography: ST segment elevation in lead aVR with less ST segment elevation in lead V1. *Journal of the American College of Cardiology*, *38*(5), 1348–1354. https://doi.org/10.1016/S0735-1097(01)01563-7

Yan, A. T., Yan, R. T., Kennelly, B. M., Anderson, F. A. Jr, Budaj, A., López-Sendón, J., Brieger, D., Allegrone, J., Steg, G., & Goodman, S. G. (2007). Relationship of ST elevation in lead aVR with angiographic findings and outcome in non-ST elevation acute coronary syndromes.

American Heart Journal, *154*(1), 71–78. https://doi.org/10.1016/j.ahj.2007.03.037

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Wang A, Singh V, Duan Y, et al. Prognostic implications of ST-segment elevation in lead aVR in patients with acute coronary syndrome: A meta-analysis. *Ann Noninvasive Electrocardiol*. 2021;26:e12811. https://doi.org/10.1111/anec.12811