REVIEW ARTICLE

Value of ST-segment change in lead aVR in diagnosing left main disease in Non-ST-elevation acute coronary syndrome—A meta-analysis

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Abstract

Background: Previous researches proved that the ST-segment elevation (STE) in lead aVR had great significance on the prediction of severe left main lesion or serious multivessel lesions. The current research is to summarize the published data and evaluate the overall association of STE in lead aVR and left main coronary artery disease (LMD) in Non-ST-elevation acute coronary syndrome.

Methods: Literature searching was performed in the online database, and a systematic review was conducted based on the searched results. Meaningful STE in lead aVR was summarized and analyzed for odds ratio (OR) and 95% confidence intervals (95% CI).

Results: Twenty-seven articles were included for final data analysis. Compared with STE < 0.05, STE ≥ 0.05 mV was associated with a higher incidence rate of LMD (OR = 6.64, 95% CI: 4.80 ~ 9.17), and the degree of STE in lead aVR was significantly associated with LMD. Myocardial infarction was more likely to occur in patients with STE ≥ 0.05 mV than in patients with STE < 0.05 mV (OR = 3.12, 95% CI: 1.73 ~ 5.62).

Conclusions: The STE in lead aVR and the degree of STE are independent predictors in diagnosing LMD or myocardial infarction.

KEYWORDS

aVR lead, left main, myocardial infarction, ST-segment elevation

1 | INTRODUCTION

Non-ST-elevation acute coronary syndrome (NSTEMI/ACS) includes unstable angina pectoris and non-ST-elevation myocardial infarction. The patient with NSTEMI/ACS has a variable severity and prognosis. Early stratification of the patient is very important in reducing the incidence of sudden death and adverse events. The electrocardiogram (ECG) is a rapid and noninvasive diagnostic method, which exerts a critical role in the assessment of early risk stratification. Left main coronary artery (LMCA) is one of the major factors that affect the patient's prognosis. Atie found that most patients with LMCA lesions would appear to have ST-segment elevation (STE) in lead V1

and aVR and ST-segment depression in lead V3, V4, and V5 (especially in lead V4) when chest pain occurs (Atie et al., 1991).

Lead aVR is often ignored in clinical practice. However, a number of studies have shown that the STE in lead aVR had a great significance on the prediction of vascular anticipation and clinical prognosis in patients with acute myocardial infarction (Nair & Glancy, 2002; Yamaji et al., 2001). As the research advanced, researchers commonly thought that STE in lead aVR suggested severe left main lesion or serious multivessel lesions (Li et al., 2009). But the results were not consistent among different studies (Chen, Lu, & Wang, 2005; Morris & Body, 2016). For example, Morris reviewed a total of 12 best evidence articles selected from

FIGURE 1 Study selection flow diagram. ECG indicates electrocardiograph

141 articles and he found that “In patient with acute coronary syndrome, STE in lead aVR can accurately identify acute myocardial infarction, cause by LMCA lesion” and found that it has only a little diagnostic value for identifying patients with stenosis of the LMCA. (Morris & Body, 2016) Therefore, we performed a meta-analysis to summarize the prediction of lead aVR on left main coronary artery disease (LMD) defined as $\geq 50\%$ diameter stenosis in a patient vessel in NSTEMI ACS.

2 | MATERIALS AND METHODS

2.1 | Literature search

Several online databases, such as Pub Med, Web of Science, Cochrane Library, MEDLINE, and China National Knowledge Infrastructure (CNKI), were used for the literature search. Potentially relevant articles published up to October 22, 2018 were searched using the following terms: “aVR” or “aVR lead”; “ST” or “non-ST-segment elevation”; “myocardial infarction” or “left main”. To identify other potentially relevant publications, the reference lists of all retrieved articles were manually searched. In addition, cited review articles were retrieved and perused for the mention of any additional relevant articles. Only published studies with full-text articles were included in the meta-analysis.

2.2 | Data extraction

Two independent investigators assessed the selected articles for eligibility following the predefined procedure as shown in Figure 1. Exclusion criteria: duplication or overlapping reports; reviews; only ECG analysis; case reports; only prediction of clinical prognosis;

no LMCA; LMCA total occlusion; studies with insufficient data. Discrepancy about including an article or not was resolved by discussion, and another author was consulted where necessary. The following information, though some studies did not contain all of them, was then extracted from each included study: the first author, date of publication, sample size, demographic data of the subjects, and the distribution data of the left main lesion.

2.3 | Statistical analyses

Statistical analyses were performed using the Review Manager for Windows (version 5.1; the Cochrane Collaboration) and STATA software programs (version 12.0; STATA Corporation). The association strength between STE in lead aVR and LMD in NSTEMI ACS was determined by calculating the respective odds ratio (OR) and 95% confidence intervals (CI). The significance of the pooled OR was determined by the Z-test, and the p -value of $< .05$ was considered significant. It is considered to have clinical significance if the ST-segment in lead aVR deviates from the baseline more than 0.05 mV (Barrabes, Figueras, Moure, Cortadellas, & Soler-Soler, 2003). Two meta-analysis models for dichotomous outcomes were used: the random-effects model (using DerSimonian and Laird's method) and the fixed-effects model (using Mantel-Haenszel's method). Heterogeneity of included studies was estimated by both Cochran's Q statistic (p -value $< .10$ was considered as statistically significant heterogeneity) and the I^2 statistic (values of 25%, 50%, and 75% represent low, medium, and high heterogeneity, respectively) (Higgins, Thompson, Deeks, & Altman, 2003). For the Cochran's Q statistic, the results were pooled by using the random-effect model when $p < .10$, otherwise the fixed-effect model was used. Metaregression and subgroup analysis were conducted to explore potential sources

TABLE 1 Characteristics of left main coronary artery lesions distributions in two groups in studies included in the meta-analysis

Author publi- cation year	Study design	Duration of study	No. of case and grouping	Age	Male/Female	NOS	STE ^a < 0.05 mV			STE ^a ≥ 0.05 mV		
							LMD ^b	Non-LMD ^c	Total	LMD ^b	Non-LMD ^c	Total
Barrabes et al. (2003)	Retrospective	15 years	AMI (n = 775)			6	11	514	525	30	220	250
			525 STE < 0.05 mV	60 ± 11	423/102							
			250 STE ≥ 0.05 mV	64 ± 10	169/81							
Xin et al, 2004	Retrospective	5 years	ACS (n = 571)	Unclear		6	94	283	377	103	91	194
			377 STE < 0.055 mV									
			86 STE ≥ 0.05 < 0.1 mV									
			108 STE ≥ 0.1 mV									
Chen et al, 2005	Retrospective	7.3 years	NSTEMI (n = 78)	62 ± 13.	59/19	5	1	37	38	7	33	40
			38 STE < 0.055 mV									
			18 STE ≥ 0.05 < 0.1 mV									
			22 STE ≥ 0.1 mV									
Hirano et al. (2006)	Retrospective	16 years	AMI (n = 140)			8	7	97	104	28	8	36
			35 LMT	68 ± 11	23/12							
			35 LAD	66 ± 8	23/12							
			35 LCX	64 ± 12	9/26							
			35 RCA	62 ± 10	11/24							
Kosuge et al. (2006)	Prospective	3 years	NSTE ACS (n = 333)			5	1	242	243	11	79	90
			243 STE < 0.05 mV	66 ± 16	171/72							
			90 STE ≥ 0.05 mV	69 ± 11	59/31							
Rostoff & Piwowarska (2006)	Retrospective	Unclear	ACS (n = 134)	59.9 ± 10	92/42	6	14	66	80	30	24	54
			80 STE < 0.05 mV	59.5 ± 10	58/22							
			54 STE ≥ 0.05 mV	60.9 ± 10	34/20							
			NSTE ACS (n = 5,064)			7	115	2,137	2,252	17	147	164
Yan et al. (2007)	Prospective	4.8 years	4,696 STE < 0.05 mV	66	2996/1700							
			292 STE ≥ 0.05 < 0.1 mV	69	160/132							
			76 STE ≥ 0.1 mV	70	43/33							
			NSTEMI (n = 426)			6	47	234	281	68	77	145
Wu et al, 2008	Retrospective	Unclear	281 STE < 0.05 mV	57 ± 11	200/81							
			68 STE ≥ 0.05 < 0.1 mV	60 ± 13	46/22							
			77 STE ≥ 0.1 mV	65 ± 13	46/31							

(Continues)

TABLE 1 (Continued)

Author publi- cation year	Study design	Duration of study	No. of case and grouping	Age	Male/Female	NOS	STE ^a < 0.05 mV			STE ^a ≥ 0.05 mV		
							LMD ^b	Non-LMD ^c	Total	LMD ^b	Non-LMD ^c	Total
Pei et al, 2008	Retrospective	1 year	STEMI (n = 140)			5	3	108	111	8	21	29
			111 STE < 0.05 mV	64.5 ± 11	92/19							
			29 STE ≥ 0.05 mV	67.4 ± 10	23/6							
Tang, et al, 2008	Retrospective	4.5 years	AMI (n = 56)			7	1	29	30	6	20	26
			30 STE < 0.05 mV	65 ± 11	17/13							
			26 STE ≥ 0.05 mV	67 ± 11	169/81							
Chen et al, 2008	Retrospective	3.25 years	NSTEMI (n = 160)	60 ± 12	82/38	6	0	76	76	4	40	44
			76 STE < 0.05 mV									
			18 STE ≥ 0.05 < 0.1 mV									
			26 STE ≥ 0.1 mV									
Tuna et al. (2008)	Prospective	6 years	ETT ^d (+) (n = 104)			6	2	37	39	26	39	65
			39 STE < 0.05 mV	60 ± 9	27/12							
			65 STE ≥ 0.05 mV	61 ± 8	52/13							
			NSTE ACS (n = 367)	67 ± 10	252/115	6	3	272	275	13	79	92
Kosuge et al. (2008)	Retrospective	unclear	275 STE < 0.05 mV	66 ± 11	192/83							
			92STE ≥ 0.05 mV									
			Resolution ^e (+) 50	69 ± 8	37/13							
			Resolution ^e (-) 42	72 ± 10	23/19							
Aygul et al. (2008)	Prospective	6 years	STEMI (n = 950)	59 ± 12	742/208	6	1	794	795	4	151	155
			792 STE < 0.05 mV	59 ± 11	636/159							
			155 STE ≥ 0.05 mV	60 ± 12	106/49							
Li et al, 2009	Retrospective	1 year	NSTE ACS (n = 245)	67 ± 10	174/71	5	6	156	162	10	73	83
			162 STE < 0.05 mV	66 ± 10	110/52							
			83 STE ≥ 0.05 mV	68 ± 11	58/25							
Kosuge et al. (2009)	Prospective	unclear	NSTE ACS (n = 501)	66 ± 11	348/153	8	23	347	370	73	58	131
Geng et al, 2010	Retrospective	1 year	NSTE ACS (n = 255)	67 ± 10	174/71	5	1	185	186	8	61	69
			186 STE < 0.05 mV	66 ± 9	130/56							
			69 STE ≥ 0.05 mV	68 ± 11	45/24							

(Continues)

TABLE 1 (Continued)

Author publi- cation year	Study design	Duration of study	No. of case and grouping	Age	Male/Female	NOS	STE ^a < 0.05 mV			STE ^a ≥ 0.05 mV		
							LMD ^b	Non-LMD ^c	Total	LMD ^b	Non-LMD ^c	Total
Ozmen et al. (2010)	Cross-sec- tional	–	61 ETT ^f (+)			6	3	37	40	16	5	21
			40 STE < 0.05 mV	49.1 ± 18	27/13							
			21 STE ≥ 0.05 mV	45.5 ± 20	15/6							
Nough et al. (2012)	Prospective	1 year	ACS (n = 400)	61.0 ± 12	257/143	6	19	257	276	32	92	124
			276 STE < 0.05 mV									
			81 STE ≥ 0.05 < 0.1 mV									
			43 STE ≥ 0.1 mV									
Guo et al, 2014	Retrospective	5.3 years	NSTE ACS (n = 625)			5	28	509	537	10	78	88
			537 STE < 0.05 mV	56 ± 8	349/188							
			58 STE ≥ 0.05 < 0.1 mV	63 ± 7	32/26							
			30 STE ≥ 0.1 mV	66 ± 8	17/13							
Zhang et al, 2015	Retrospective	4 years	ACS (n = 446)	62.1 ± 12	335/91	6	11	243	254	31	161	192
			254 STE < 0.05 mV	60.6 ± 11	208/46							
			192 STE ≥ 0.05 mV	63.9 ± 10	147/45							
Yan, & Wei, 2015	Retrospective	3 years	NSTE ACS (n = 195)			5	8	133	141	9	45	54
			54 STE ≥ 0.05 mV	65.5 ± 10	32/22							
			141STE < 0.05 mV	62.0 ± 12	80/61							
Misumida et al. (2016)	Retrospective	1.5 years	NSTE ACS (n = 379)			5	6	276	282	8	89	97
			282STE < 0.05 mV	64	174/108							
			97 STE ≥ 0.05 mV	67	52/45							
Nabati et al. (2016)	Prospective	1 year	NSTE ACS (n = 129)			8	0	77	77	2	50	52
			77 STE < 0.05 mV	56.7 ± 11	44/33							
			52 STE ≥ 0.05 mV	60.9 ± 10	21/31							
Wen, 2016	Prospective	1.5 years	ACS (n = 185)			7	13	60	73	48	64	112
			73 STE < 0.05 mV	57.1 ± 15	41/32							
			112 STE ≥ 0.05 mV	60.2 ± 15	72/40							
Ghaffari et al, (2017)	Retrospective	1.25 years	ETT ^f (+) (n = 230)	55.9 ± 10		8	10	115	125	29	76	105
			64 STE < 0.05 mV		42/22							
			106STE ≥ 0.05 < 0.1 mV		75/31							
			66 STE ≥ 0.1 mV		42/18							

(Continues)

TABLE 1 (Continued)

Author publication year	Study design	Duration of study	No. of case and grouping	Age	Male/Female	NOS	STE ^a < 0.05 mV			STE ^a ≥ 0.05 mV		
							LMD ^b	Non-LMD ^c	Total	LMD ^b	Non-LMD ^c	Total
Wu et al, 2016	Retrospective	2.83 years	NSTE ACS (n = 185)	59.2 ± 11	72/40	7	9	48	57	16	8	24
			112 STE ≥ 0.05 mV	60.2 ± 15								
			73 STE < 0.05 mV	57.1 ± 15								

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; LAD, left anterior descending artery; LCX, left circumflex artery; LMD, left main coronary artery disease; LMT, left main trunk; MI, myocardial infarction; Non-MI, Non-myocardial infarction; Non-LMD, Non-left main coronary artery disease; NOS, newcastle-ottawa scale; NSTEMI, non-ST-T elevation myocardial infarction; RCA, right coronary artery; STE, ST-segment elevation in lead aVR.

^aSTE indicates ST-segment elevation in lead aVR.

^bLMD indicates the numbers of patients diagnosed with left main coronary artery disease.

^cNon-LMD indicates the number of patients not diagnosed with LMD.

^dExercise tolerance testing induced ST-segment elevation in lead aVR for detection of left main coronary artery disease.

^e"Resolution+" defined as a reduction > 50% in the degree of ST-segment elevation in lead aVR from admission to 6 hr later.

^fST elevation in the lead aVR during exercise treadmill testing.

of heterogeneity. Publication bias was investigated by the Begg's funnel-plot method, Egger's linear regression method, and Begg's rank correlation method. All *p* values were two sided.

3 | RESULTS

3.1 | Literature searching and data extraction

A total of 676 potentially relevant published articles were identified initially. According to the literature selection criteria, as shown in Figure 1, duplicate articles (*n* = 307) or studies that failed to meet other eligibility criteria (*n* = 342) were excluded. Finally, 27 eligible articles were included in this meta-analysis (Aygul et al., 2008; Barrabes et al., 2003; Chen, Liu, Dong, Shen, & Chen, 2008; Chen et al., 2005; Geng et al., 2010; Ghaffari, Asadzadeh, Tajlil, Mohammadalian, & Pourafkari, 2017; Guo et al., 2014; Hirano et al., 2006; Kosuge et al., 2008, 2009, 2006; Misumida et al., 2016; Nabati, Emadi, Mollaalipour, Bagheri, & Nouraei, 2016; Nough et al., 2012; Ozmen et al., 2010; Rostoff & Piwowarska, 2006; Tang, Sang, & Feng, 2008; Tuna et al., 2008; Wen, 2016; Wu et al., 2008; Wu, Lin, Chen, Han, & Zhao, 2016; Xin & An, 2004; Yan et al., 2007; Yan & Wei, 2015; Zhang, Dong, Ji, & Qin, 2015). Newcastle-Ottawa score was used to assess the quality of studies. Research with 6 points or more believed to have high quality. The characteristics and scores of eligible studies were summarized in Table 1.

The majority of current studies suggested that STE in lead aVR was related to LMD in acute coronary syndrome. Table 1 shows the data extracted from the articles dealing with STE in lead aVR and LMD. Twenty-seven articles, involving 7,870 cases with STE < 0.05 mV and 2,582 cases with STE ≥ 0.05 mV (according to different studies, ST-T segment shift was measured from baseline around 20–80 ms after the J point), reported the association between STE in lead aVR and LMD. Nine of the twenty-seven studies deeply investigated the association between STE in lead aVR and LMD, including 4,426 cases with STE < 0.05 mV, 681 cases with 0.05 ≤ STE < 0.1 mV and, 534 cases with STE ≥ 0.1 mV (Table 2). STE in lead aVR was also found to be related with myocardial infarction. As shown in Table 2, nine articles examined the association between STE and myocardial infarction, including 6,455 cases with STE < 0.05 mV and 1,069 cases with STE ≥ 0.05 mV.

3.2 | Publication bias of included studies

As recommended, it was not necessary to evaluate publication bias when <10 articles were involved (Sterne et al., 2011). Therefore, publication bias was evaluated among articles dealing with LMD by the Begg's funnel-plot interpretation. Significant publication bias was found among those articles with LMD in Begg's test (*p* = .011) and in Egger's test (*p* = .012). To know the influence of publication bias, the consistency of the results was analyzed before and after using the trim-and-fill method. After filling the studies, the results of both fixed-effect and random-effect models were the same.

Sensitivity analysis was conducted to evaluate the stability of the result. In this meta-analysis, after removing one study at a time, we

TABLE 2 Characteristics of left main coronary artery lesions distributions in three groups and myocardial infarction in two groups is studied and included in the meta-analysis

Author publica- tion year	Left main coronary artery lesions						Myocardial infarction											
	STE ^a < 0.05 mV			0.05 ≤ STE ^a <0.1 mV			STE ^a ≥ 0.1 mV			STE ^a < 0.05 mV			STE ^a ≥ 0.05 mV					
	LMD ^b		Total	LMD ^b		Total	LMD ^b		Total	LMD ^b		Total	Non-MI ^e		Total	MI ^d		Total
	Non-LMD ^c	Total1		LMD ^b	Non-LMD ^c		LMD ^b	Non-LMD ^c		LMD ^b	Non-LMD ^c		Non-MI ^e	MI ^d		Non-MI ^e	MI ^d	
Barrabes et al. (2003)	11	514	525	9	107	116	21	113	134	Kosuge et al. (2006)	2	241	243	11	79	90		
X'in, & An, 2004	94	283	377	38	48	86	65	43	108	Rostoff & Piowarska (2006)	23	57	80	13	41	54		
Chen et al, 2005	1	37	38	2	16	18	5	17	22	Yan et al. (2007)	423	4,273	4,696	41	327	368		
Yan et al. (2007)	115	2,137	2,252	12	118	130	5	29	34	Wu et al, 2008	9	272	281	10	135	145		
Wu et al, 2008	47	234	281	25	43	68	43	34	77	Chen et al, 2008	4	72	76	18	26	44		
Chen et al, 2008	0	76	76	1	17	18	3	23	26	Li et al, 2009	10	152	162	14	69	83		
Nough et al. (2012)	19	257	276	14	67	81	18	25	43	Kosuge et al. (2009)	87	390	477	9	15	24		
Guo et al, 2014	28	509	537	5	53	58	5	25	30	Geng et al, 2010	1	185	186	8	61	69		
Ghaffari et al, 2017	0	64	64	14	92	106	25	35	60	Zhang et al, 2015	24	230	254	45	147	192		

Abbreviations: LMD, left main coronary artery disease; MI, myocardial infarction; No LMD, Non-left main coronary artery disease; Non-MI, Non- myocardial infarction; STE, ST-segment elevation in lead aVR.
^aSTE indicates ST-segment elevation in lead aVR.
^bLMD indicates the numbers of patients diagnosed with left main coronary artery disease.
^cNon-LMD indicates the number of patients not diagnosed with LMD.
^dMI indicates the numbers of patients diagnosed with myocardial infarction.
^eNon-MI indicates the number of patients not diagnosed with myocardial infarction.

found that the pooled OR changed just a little, the overall result was not influenced by single study, with ORs and 95% CIs ranging from 4.91 (4.19–5.75) to 6.03 (5.10–7.11).

3.3 | Meta-analysis results

For LMD, the between-study heterogeneity was significant when all 27 studies were pooled ($I^2 = 68.9\%$, $p < .05$), therefore, the random-effect model was used in subsequent analysis. To know the

robustness of the result, we used both random-effect models and fixed-effect models in other cases.

The pooled results (Figure 2a) showed that STE ≥ 0.05 mV was associated with a higher incidence rate of LMD compared with STE < 0.05 mV (OR = 6.64, 95% CI: 4.80 ~ 9.17). Figure 2b indicated that the degree of STE in lead aVR was significantly associated with LMD. In comparison with STE < 0.05 and $0.05 \leq \text{STE} < 0.1$, STE ≥ 0.1 mV, higher STE was an indicator of higher LMD. The pooled OR from 9 studies was 4.17 (95% CI: 3.04 ~ 5.70). Patients with

FIGURE 2 (a) Forrest plots for association between ST-segment elevation in lead aVR(STE) and LMD. Showed that STE ≥ 0.05 mV compared with STE < 0.05 mV (OR = 6.64, 95% CI: 4.80 ~ 9.17). $I^2 = 68.9\%$, $p = .00$. Patients with STE ≥ 0.05 mV are more likely to occur LMD. The square represents the OR value of each study, and the weight of the square represents the sample size. The diamond represents the merged OR value. The segment represents 95% confidence level of OR. Random: random-effect model; CI: confidence level; weight: the sample weight of each study. (b) The subgroup (STE < 0.05 vs. $0.05 \leq \text{STE} < 0.1$ mV); pooled OR was 2.57 (95% CI: 1.97 ~ 3.36) and the subgroup was (STE < 0.05 vs. STE ≥ 0.1 mV); Pool OR was 6.17 (95% CI: 4.31 ~ 8.84). The overall pooled OR from 9 studies was 4.17 (95% CI: 3.04 ~ 5.70); The degree of ST-segment elevation was significantly associated with LMD. The more STE deviates from the baseline, the incidence rate of LM is higher. (c) Forrest plots for association between ST-segment elevation in lead aVR (STE) and myocardial infarction. Showed that STE ≥ 0.05 mV compared with STE < 0.05 mV (OR = 3.12, 95% CI: 1.73 ~ 5.62); Patients with STE ≥ 0.05 mV are more likely to occur myocardial infarction

FIGURE 2 (Continued)

STE ≥ 0.05 mV were also more likely to occur myocardial infarction than patients with STE < 0.05 mV (OR = 3.12, 95% CI: 1.73 ~ 5.62; Figure 2c).

Metaregression analysis was also performed to investigate the possible effect it has on heterogeneity, such as sample size, average age, sex ratio, number of smokers, and number of patients with hypertension, hyperlipidemia and diabetes mellitus. However, no significance was found among the collected factors. In stratified analysis, there was also no heterogeneity significance in different races.

4 | DISCUSSION

Many recent studies revealed that the role of STE in lead aVR predicted LMD in NSTEMI ACS. The value of lead aVR in clinical cardiology was very helpful in predicting the side of coronary artery occlusion and a number of different clinical disease entities

(Gorgels, Engelen, & Wellens, 2001). However, this must be viewed in other electrocardiographic leads and combined with clinical practice to make a correct differential diagnosis. STE in lead aVR may be seen in the following situation, such as aortic dissection involving left main coronary artery, acute pulmonary embolism, acute pericarditis, critical aortic stenosis, Brugada syndrome in higher-risk patients, tricyclic antidepressants toxicity, takotsubo syndrome, and the total proximal occlusion of the left anterior descending artery (LAD), and it also helpful to evaluate atrioventricular reentry tachycardia, the origin of focal atrial tachycardia, and differentiation of wide QRS complex tachycardia. Furthermore, patients with ACS, STE in lead aVR can aid in localizing the culprit lesion and early risk stratification. (George, Arumugham, & Figueredo, 2010; Kireyev, Arkhipov, Zador, Paris, & Boden, 2010) The possible mechanism of lead aVR identifying left main coronary lesion may be as follows: Lead aVR captures the electrical activity of the right ventricular outflow tract and septum, which is also the upper right section of the heart. By influencing the blood flow

FIGURE 2 (Continued)

in the LAD and its branch, the occlusion of the LMCA can cause ischemia at the bottom of the interventricular septum resulting in STE in lead aVR (Gorgels et al., 2001; Wang, 2010). When a large left ventricle area is involved, as in acute coronary syndrome, due to incomplete left main obstruction (circumflex involvement), ST-T segment depression is seen in virtually all leads, except in aVR and sometimes, V1 and III. In these leads, STE is seen as a mirror pattern, since the ischemic vector is directed from the subepicardium toward the subendocardium in an upward, backward, and rightward direction; thus, ischemia generates a negative deflection in the majority of leads. (de Luna & Fiol-Sala, 2008).

Our meta-analysis including 27 studies (10,453 patients), focusing on ACS patient group, the prevalence of LMD was 12% (95% CI: 8%–16%); Prevalence of STE ≥ 0.05 mV subgroup was 26% (95% CI: 18%–34%); and in STE < 0.05 mV subgroup was 5% (95% CI: 3%–7%), indicated that patients with STE ≥ 0.05 mV were associated with a higher incidence rate of LMD. In addition, the degree of STE in lead aVR deviating from the baseline and LMD was positively correlated. Compared to $0.05 \leq \text{STE} < 0.1$ mV, the group of STE ≥ 0.1 mV was more frequently found in patients with LMD. Our findings are similar to those of D'Ascenzo et al. studies, the meta-analysis shows that patients with ACS have more common LMD or three-vessel disease than are generally perceived, with a prevalence rate of LMD of 12% (95% CI: 10.45%–13.5%). Studies have shown that the most powerful predictor of LMD or 3-vessel disease is diagnosis of heart failure and STE in lead aVR.

(D'Ascenzo et al., 2012) Although one of the recent studies showed that STE in lead aVR was only 10% associated with acute coronary occlusion, the study patient group included 854 STEMI-activated patients, 36% of whom showed cardiac arrest, and many patients showed shock, lactic acidosis, or respiratory failure that may result in this EKG pattern. (Harhash et al., 2019) So in this study, it is more important to find out the causes of respiratory and circulatory failure, not just to see if there is acute coronary occlusion.

Evidence showed that STE in lead aVR was more likely to reveal the LMD or 3-vessel coronary disease than ST-segment depression in other leads (Kosuge et al., 2005). Therefore, STE in lead aVR was an independent indicator of LMD. Except for diagnosis, STE could maybe also predict prognosis of non-ST-segment acute coronary syndromes (NSTEMI ACS). Filip found that patients with STE ≥ 0.05 mV had higher mortality in 30 days after the incidence of NSTEMI ACS (Szymanski, Grabowski, Filipiak, Karpinski, & Opolski, 2008).

In this meta-analysis, some possible limitations should be noted. First, according to different studies, the measurement of ST-T segment shift from baseline in the range of 20–80 ms after J point is inconsistent and may affect the result. Second, only published studies were used for data extraction. It is possible that negative results were hidden in some unpublished studies. Because of language barriers, some studies, which were written in Japanese, were excluded. Failure to include these results in the meta-analysis may overestimate the association between STE in lead aVR and LMD. Third, the

data quality differs among recruited studies. It was difficult to merge all data when some studies used different grouping scales in STE, so only 9 studies were included to analyze the association between LMD and the degree of STE in lead aVR. Finally, although some confounding factors, such as sample size, average age, sex ratio, number of smokers, number of patients with hypertension, hyperlipidemia and diabetes mellitus, were conducted by metaregression analysis, the sources of heterogeneity were not found. Due to the lack of original data of cardiovascular disease at baseline, a subgroup analysis was not performed. Further studies are needed to provide more clinical data and to comprehensively evaluate the influence of STE in lead aVR on LMD or myocardial infarction.

In conclusion, our findings suggest that in the ACS group, if there is STE in lead aVR, then the probability of LMD will be higher, and the higher the degree of elevation, the higher the probability. Similarly, if there is STE in lead aVR, the probability of myocardial infarction will be higher, so we conclude that STE in lead aVR is an independent predictor of LMD or myocardial infarction in the ACS group.

CONFLICT OF INTEREST

No competing interests.

ETHICAL APPROVAL

Not applicable.

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