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Incidence and Risk Factors of Left Ventricular Thrombus in Acute ST-Segment Elevation Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention: A Meta-Analysis

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Highlights of the Study

- We evaluated the incidence and risk factors of left ventricular thrombus after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction.
- Our results facilitate close monitoring and early prevention of patients with these risk factors in clinical practice.

Keywords
Left ventricular thrombus · Myocardial infarction · Percutaneous coronary intervention · Meta-analysis

Abstract

Objective: Left ventricular thrombosis (LVT) is a common complication of acute ST-segment elevation myocardial infarction (STEMI). This study attempted to synthesize the available evidence to understand the incidence and risk factors of LVT in acute STEMI patients undergoing primary percutaneous coronary intervention (PCI). ***Methods:*** We searched PubMed, Embase, Cochrane Library, and Web of Science for studies published from January 2001 to January 2022. The random-effects and fixed-effects model meta-analysis estimated pooled incidence, mean difference (MD), odds ratio (OR), and 95% confidence interval (CI). The Review Manager 5.4 software was used for meta-analysis performance. ***Results:*** The results of meta-analysis showed that the incidence of LVT in acute STEMI treated by primary PCI was 4% (95% CI [0.03, 0.05]), and the overall pooled incidence in patients with anterior STEMI was 10.0% (95% CI [0.07, 0.12]). Anterior STEMI (OR = 11.93, 95% CI [6.25, 22.78], $p = 0.0003$), left anterior descending-related infarct (OR = 6.85, 95% CI [3.70, 12.66], $p < 0.00001$), left ventricular wall motion abnormalities (OR = 7.53, 95% CI [3.18, 17.82], $p < 0.00001$), and lower post-PCI LVEF (MD = 13.78, 95% CI [12.15, 15.41], $p < 0.00001$) were risk factors for post-PCI LVT. ***Conclusion:*** The incidence of LVT after acute STEMI in the PCI era remains high. This study provides a preliminary overview of STEMI patients at risk for post-PCI LVT and will help the design of prospective randomized controlled trials for the management and prevention of LVT.

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Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is a disease with high morbidity and mortality, which seriously threatens human life and health. The incidence of STEMI continues to rise [1]. Although primary percutaneous coronary intervention (PCI) and dual antiplatelet therapy (DAPT) have improved survival in STEMI patients over the past 20 years, postinfarction complications remain an important cause of high mortality and disability [2]. The formation of left ventricular thrombosis (LVT) is one of the common complications of STEMI, which can embolize and lead to sudden death. Meanwhile, it increases the total length of hospital stay and the use of medical resources, resulting in excessive medical burden [3]. Cardiac magnetic resonance imaging (CMR) is the gold standard for the diagnosis of LVT, but its high cost and insufficient popularity make transthoracic echocardiography (TTE) the preferred screening method. Previous studies have showed that TTE has a sensitivity of 29% (95% confidence interval [CI]: 17–45%) and specificity of 98% (95% CI: 96–99%) compared to CMR, resulting in a 5% incidence of LVT after STEMI treated with PCI screened by TTE and a 12% incidence of CMR screening [4]. Although this implies that the incidence of LVT after STEMI is underestimated, it still indicates that with the improvement of reperfusion techniques and the standardization of drug therapy, the incidence of LVT after STEMI in the PCI era is lower than that in the thrombolytic era. However, a recent meta-analysis showed that LVT is associated with increased risk of embolic events and long-term mortality (hazard ratio [HR] = 3.97, 95% CI [2.68, 5.89], $p < 0.00001$; HR = 2.34, 95% CI [1.38, 3.69], $p = 0.002$), which warns us not to relax our vigilance [5]. Although studies on risk factors for LVT in STEMI patients are numerous, the results are diverse and require further evaluation [6]. At present, there is insufficient clinical evidence for its early prevention, which makes it imperative to develop effective prevention strategies for LVT [7]. Therefore, we conducted a meta-analysis to evaluate the incidence and risk factors of LVT in post-PCI STEMI patients, with the aim of providing a reference for higher quality research on early prevention and treatment of LVT.

Methods

Search Strategy

We conducted a comprehensive search of literature in four databases: PubMed, Embase, Cochrane Library, and Web of Science, which was searched from January 1, 2001, to January 31, 2022. A combination of title/keyword/abstract and Medical Subject Headings was used, and the following keywords were used: "myocardial infarction" and "left ventricular thrombus." We studied the references to identify supplementary research.

Eligibility Criteria

All included studies were cohort or case-control studies, which had to meet the following criteria to be eligible: (1) all patients were adults who met the STEMI diagnostic criteria and received only PCI revascularization combined with standard DAPT and no anticoagulation therapy; (2) the outcome of interest was whether new LVT occurred after PCI during the follow-up period, reporting the incidence and examining risk factors of LVT; (3) studies reported mean difference (MD), relative risk (RR), HR, odds ratio (OR), and 95% CI, which could also be calculated from data provided or obtained by data conversion. Studies containing the following items were excluded: (1) repeated reports, conference reports, and review literature; (2) literature with incomplete information and data that cannot be transformed; (3) the full literature could not be obtained; (4) the sample size was less than 50 cases; and (5) articles not written in English. We included only the most recent update if there were sequential updates and publications on the same study.

Quality Assessment and Data Extraction

Two researchers independently conducted a step-by-step screening based on inclusion and exclusion criteria. First, the title and abstract were read, and then the full text was read to determine whether the papers met the requirements. The Novus Ordo Seclorum scale was used to score the quality of the final included literature, and data were extracted from the literature of 6 stars or more. Differences were settled by consensus. If no consensus could be reached, disagreements were resolved by a third adjudicator. After the selected literature was identified, a predesigned data extraction table was used for data extraction, including first author, publication year, study type, sample size, the incidence of LVT, and risk factors. Risk factors included anterior STEMI, left anterior descending-related infarct, left ventricular wall motion abnormalities, and lower post-PCI LVEF. After data extraction, two researchers checked and summarized relevant results.

Statistical Analysis

The Review Manager 5.4 software was used for meta-analysis. MD was used to describe continuous variables, OR value was used to describe binary variables, and the combined effect size was calculated. The Q test and I^2 value were used to measure heterogeneity between studies. The fixed-effect model was used if there was no significant heterogeneity among studies ($p \geq 0.1$, $I^2 < 50\%$). The rest were analyzed by the random-effect model ($p < 0.1$, $I^2 \geq 50\%$). For results with heterogeneity, subgroup and sensitivity analyses were further performed. For each outcome, $p < 0.05$ was considered statistically significant. The potential for publication bias was evaluated via funnel plots, Begg's test, and Egger's test.

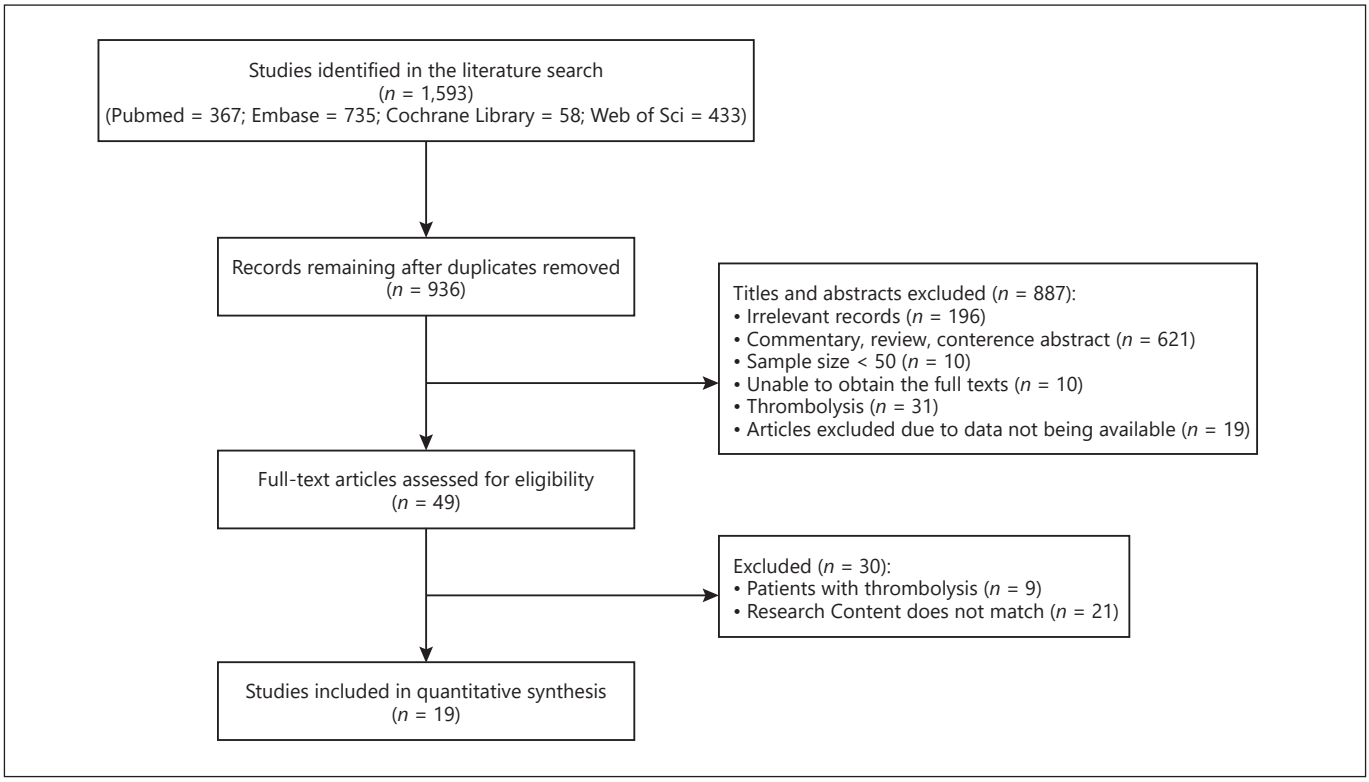

Fig. 1. Flowchart showing selection of studies.

Results

Study Selection and Characteristics

Initially, 1,593 potential references were identified through the database search. After eliminating duplicate articles and screening titles and abstracts, 1,544 articles were excluded. The full text of the remaining 49 papers was carefully reviewed, of which 30 were excluded. Finally, 19 studies met the criteria and were included in the meta-analysis. A summary of the overall screening process and results is shown in Figure 1.

Key characteristics and quality scores of the nineteen included studies are summarized in online supplementary Table 1 (see www.karger.com/doi/10.1159/000525943 for all online suppl. material). The studies were published between 2002 and 2021, including three cohort studies [8–10] and sixteen case-control studies [11–26]. There were ten studies from Asian countries such as China, Japan, Turkey, and Saudi Arabia, five from European countries such as the UK and Denmark, three from North America, and one from Australia. The total number of STEMI patients enrolled in the study was 1,050,484, of whom 2,909 developed LVT. The median age of the LVT (+) group and LVT (−) group was 54–64 and 54–63 years, and the male proportion was 69%~92% and 65%~89%, respectively. A total of eighteen studies [8–17, 19–26] reported the incidence of post-STEMI LVT, of which eight [8, 10, 12, 16, 17, 22, 23, 25] reported the incidence of LVT after anterior STEMI. Except for the two studies [14, 15] that included TTE and CMR in the diagnosis of LVT, all the other studies used TTE to screen LVT, and in three of them [14, 19, 21], some patients used echocardiographic contrast. Standard DAPT antithrombotic therapy was performed after PCI except for six studies [12, 14, 15, 19, 20, 26] that did not specify post-PCI antithrombotic drugs. The risk factors for LVT reported in more than three articles were anterior STEMI, left anterior descending-related infarct, left ventricular wall motion abnormalities, and lower post-PCI LVEF. The first two were risk factors related to coronary angiography (CAG), and the last two were related to TTE. All nineteen included studies had the NOS quality scores ≥7 according to the NOS quality assessment scale.

Incidence of LVT in STEMI Patients

The overall pooled incidence of LVT in patients with all STEMI was 4% (95% CI [0.03, 0.05]; I^2 = 97.6%), and

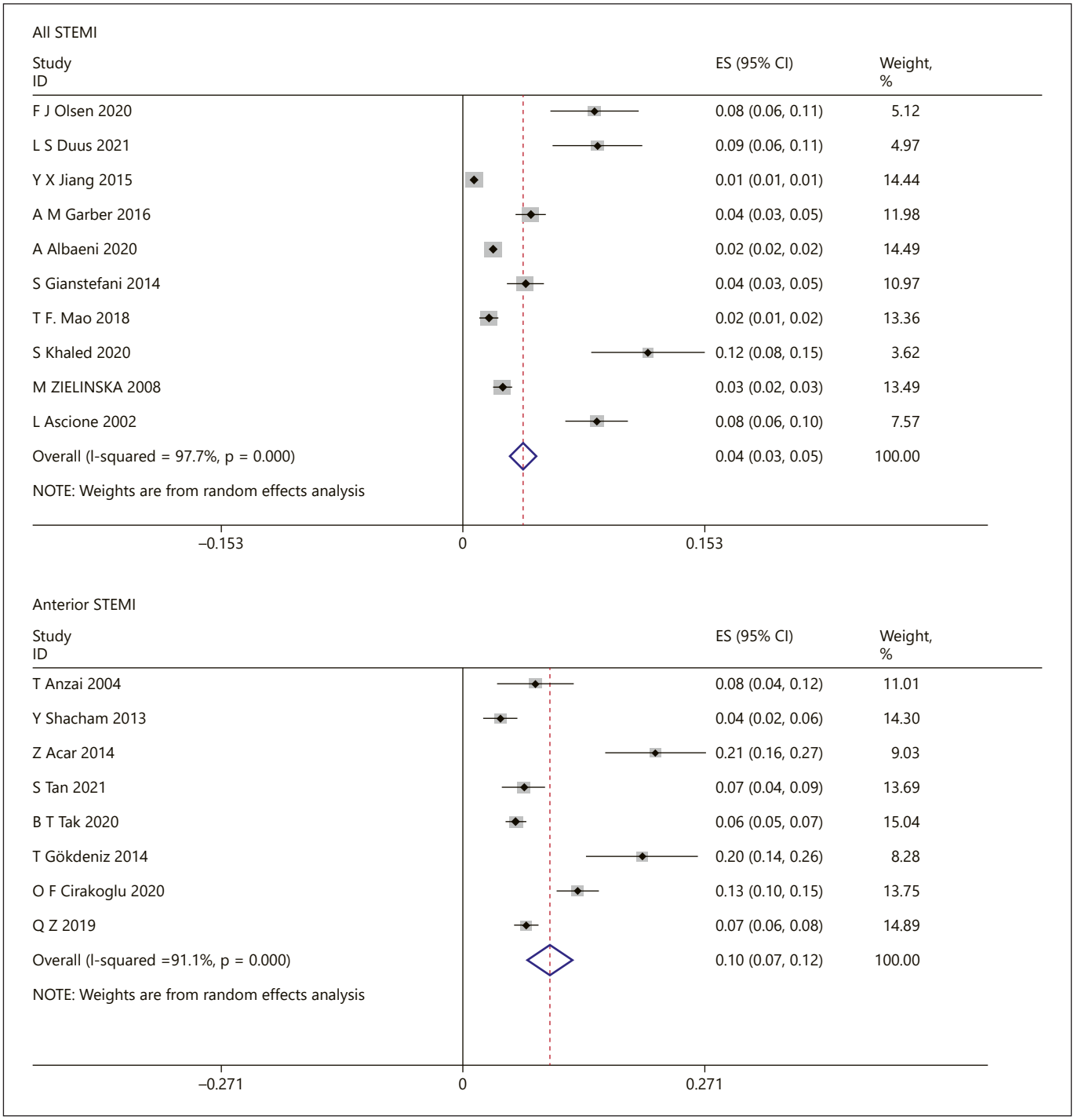

Fig. 2. Incidence of LVT in STEMI and anterior STEMI patients. STEMI, ST-segment elevation myocardial infraction.

the overall pooled incidence of LVT in patients with anterior STEMI was 10% (95% CI [0.07–0.12]; I^2 = 91%). Considering the high statistical heterogeneity, we chose the random-effects model. Our subgroup analysis according to the regions suggested that the incidence of LVT was 6% (95% CI [−0.05–0.17]; I^2 = 97.2%) in Asia,

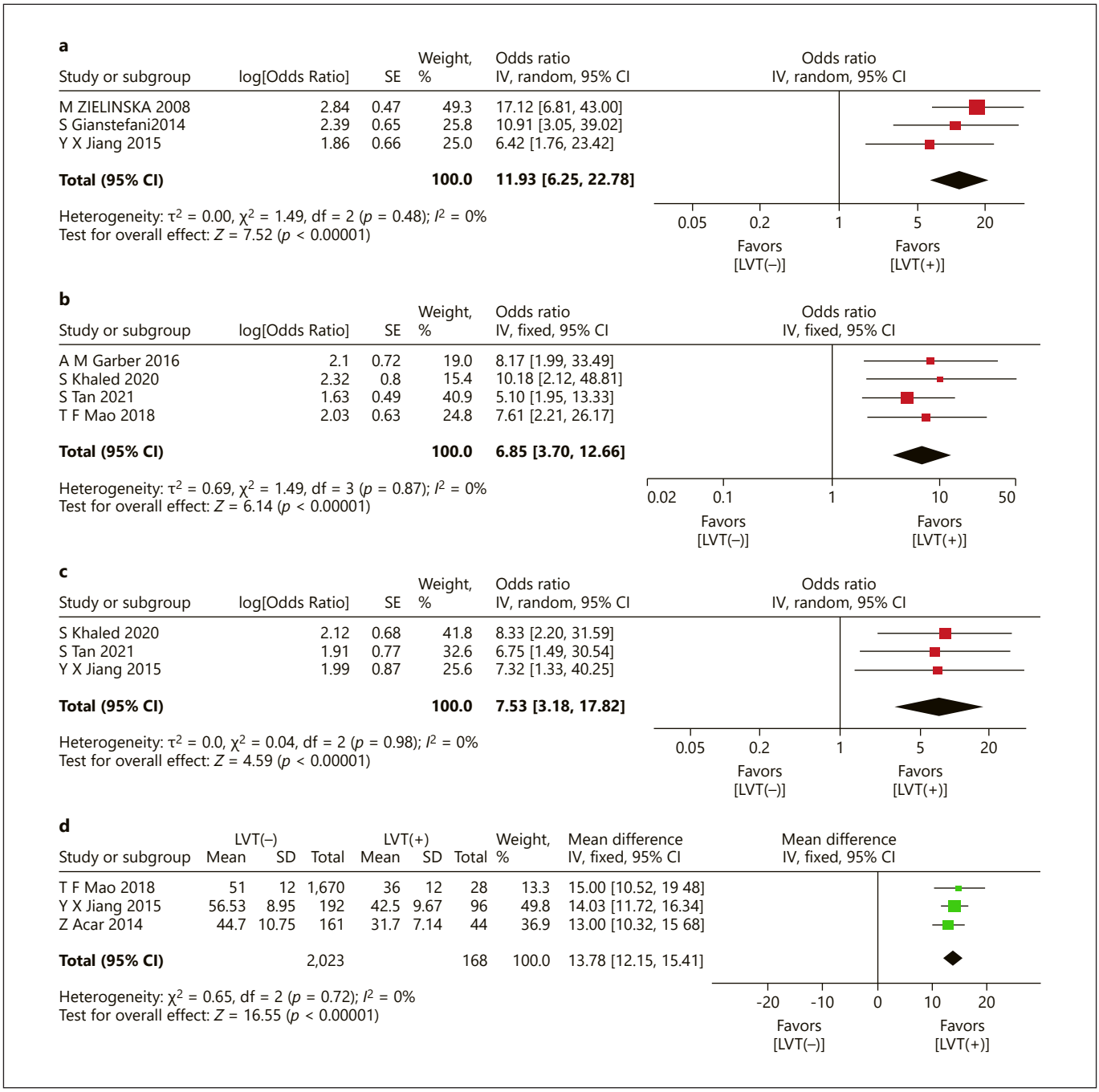

Fig. 3. Forest plot for the risk of LVT. **a** Forest plot for the association between anterior STEMI and the risk of LVT. **b** Forest plot for the association between LAD-related infarct and the risk of LVT. **c** Forest plot for the association between left ventricular wall motion abnormalities and the risk of LVT. **d** Forest plot for the association between lower post-PCI LVEF and the risk of LVT.

6% (95% CI [0.04–0.09]; I^2 = 93.3%) in Europe, and 3% (95% CI [−0.05–0.17]; I^2 = 91.7%) in North America. Sensitivity analysis found that the omission of any single study did not significantly change the pooled results, suggesting that the results of our analysis were stable. The incidence of LVT calculated from the above studies was shown by a forest plot (Fig. 2).

Risk Factors of LVT in STEMI Patients Treated by Primary PCI

CAG-Related Factors

Four studies [20, 21, 24, 26] explored the association between anterior STEMI and the risk of LVT, and the pooled analysis showed heterogeneity (I^2 = 79%>50%) (as shown in online suppl. Table 2). Further sensitivity analysis revealed that one of the studies [26] was the source of heterogeneity, and the pooled results after exclusion showed that the risk of LVT in patients with anterior STEMI was significantly higher than that in other infarction locations (OR = 11.93; 95% CI [6.25, 22.78]; Z = 7.52; p < 0.0003; I^2 = 0%) (Fig. 3a). Four studies [9, 12, 15, 19] reported the association between left anterior descending-related infarct and LVT in STEMI patients, and the pooled results revealed that the risk of LVT in STEMI patients with left anterior descending-related infarct was significantly higher than in other branches of the coronary arteries (OR = 6.85; 95% CI [3.70, 12.66]; Z = 6.14; p < 0.00001; I^2 = 0%)(Fig. 3b).

TTE-Related Factors

Four studies [12, 15, 20, 26] analyzed the association between left ventricular wall motion abnormalities and the risk of LVT, and the pooled analysis showed heterogeneity (I^2 = 85%>50%) (as shown in online suppl. Table 2). Further sensitivity analysis revealed that one of the studies [26] was the source of heterogeneity; the pooled results after exclusion showed that the risk of LVT in patients with left ventricular wall motion abnormalities was significantly higher than that in patients with normal left ventricular wall motion (OR = 7.53; 95% CI [3.18, 17.82]; Z = 4.59; p <0.00001; I^2 = 0%) (Fig. 3c). Seven studies [14, 18–20, 22–24] reported associations between post-PCI LVEF and LVT in STEMI patients, of which five [18–20, 22, 23] examined the association between lower post-PCI LVEF levels and the risk of LVT. The pooled results of the above five studies showed heterogeneity (I^2 = 90%>50%) (as shown in online suppl. Table 2). After further sensitivity analysis and exclusion of two heterogeneous source studies [18, 23], the final pooled results indicated that lower post-PCI LVEF was associated with LVT (MD = 13.78, 95% CI [12.15, 15.41], p < 0.00001) (Fig. 3d).

Publishing Bias

We evaluated the publication bias of the results of more than ten articles. A funnel plot was drawn for the publication bias test for the incidence of all STEMI, which showed that each study site's left and right distribution was asymmetrical, revealing that publication bias might exist. However, the p values of Egger's and Begg's tests are 0.12 and 0.24, indicating that the possibility of publication bias is low. The funnel plot is shown in online supplementary Figure 1.

Discussion

Considering the high risk of systemic embolism caused by LVT and the lack of evidence-based data on prevention strategies, we conducted a comprehensive meta-analysis combining results from multiple centers to assess the incidence of LVT and related risk factors in post-PCI STEMI patients. Our results showed that the incidence of LVT in post-PCI STEMI patients was about 4%, and the incidence in anterior STEMI patients was about 10%. This is similar to the results of previous studies [4, 27] which reported that the incidences of LVT in STEMI patients were 6.3% and 2.7%, while the incidence of LVT in anterior STEMI patients was 12.2% and 9.1%, respectively. The higher incidence of the former may be due to the use of CMR to screen for LVT in the included studies. In contrast, the lower incidence of the latter may be since some studies using heparin or other anticoagulant drugs after PCI were not excluded. In the studies included by us, some patients in two studies [14, 15] received both TTE and CMR for the diagnosis of LVT; in the other three studies [14, 19, 21], some patients received echocardiographic contrast during the diagnosis of LVT with TTE; conventional TTE was used for the diagnosis of LVT in the rest of the studies. Although we were unable to conduct a subgroup analysis for these special patients due to insufficient data, the vast majority of patients in our study adopted conventional TTE as the diagnostic method of LVT, which made the results of our study more general. Similarly, we selected the patients treated with DAPT as the only post-PCI antithrombotic therapy, which also made the results of our study more general [1]. Due to the significant difference in reports of LVT detection time in various studies and the lack of complete data to support our meta-analysis, we were only given a time range of 3–30 days, most of which was within 2 weeks. The detection time window is consistent with a previous report [14], but the specific occurrence time of LVT after STEMI and the optimal detection time need to be evaluated by further large-scale prospective studies.

In addition, we also confirmed several factors related to LVT in post-PCI STEMI patients. Among CAG-related factors, anterior STEMI and LAD-related infarct were

associated with increased risk of LVT, while TTE-related factors associated with increased risk of LVT in post-PCI STEMI patients included left ventricular wall motion abnormalities and lower post-PCI LVEF. Whether these identified risk factors are merely risk markers for LVT or are causal remains to be further determined. However, there are possible mechanistic pathways that could explain some of the documented associations. Anterior STEMI, LAD-related infarct, and left ventricular wall motion abnormalities in our study were related to the increased risk of LVT formation. This may be because the anterior wall is the part of the heart that does the most work in systolic activity. Therefore, anterior STEMI, LAD-related infarct, and left ventricular wall motion abnormalities could have the greatest impact on the heart function and are more likely to thrombose due to reduced myocardial contractility, uncoordinated ventricular wall movement, and blood flow stasis [28]. Previous studies [3] have found that STEMI patients with lower post-PCI LVEF have larger myocardial infarction areas, decreased myocardial contractility, significant pump dysfunction, left ventricular blood flow stagnation, and LVT proneness. In our study, a similar conclusion was reached that lower post-PCI LVEF increased the risk of LVT. Due to the limitations of the included data, we did not conduct a stratified analysis of LVEF, thus making it impossible to determine its critical value.

Clinical hazards of LVT mainly lie in the rupture and shedding of thrombus, which will cause embolization of peripheral arteries and essential organs and cause a high risk of disability or death to patients. Therefore, it is of great significance to identify the incidence and risk factors of LVT in STEMI patients and take early treatment for high-risk patients to prevent severe embolism events. At present, many clinical studies have analyzed the risk factors of LVT, but no unified conclusion has been reached. The specific reasons are unclear and may be partly due to differences in patient selection and drug treatment strategies. Many researchers also have tried to summarize the incidence and risk factors of LVT in STEMI patients and reported relevant findings, but these results are not universal. We consider that most STEMI patients do not routinely use anticoagulant drugs such as heparin post-revascularization but receive DAPT-based antithrombotic therapy and the more widely used TTE to monitor cardiac function. Therefore, our meta-analysis attempted to evaluate and synthesize the incidence of LVT and several factors related to it in the largest proportion of STEMI patients. Our findings are clinically relevant because we have identified several potential risk factors that can help physicians monitor high-risk patients and implement early thromboprophylaxis.

At the same time, we acknowledge that this study has some limitations. First, the studies we included are mainly case-control studies, with few cohort studies and a lack of cross-sectional studies, which may lead to insufficiently comprehensive arguments. Most of the studies we included adopted the low-sensitivity TTE diagnostic method for LVT, which resulted in LVT missed detection and a major bias of underestimation. Secondly, due to the limitations of single rate meta-analysis studies and differences in follow-up time, the results are highly heterogeneous. Subgroup analysis failed to identify the source of heterogeneity. Thirdly, some risk factor indices were included in only a few of the papers, which makes it impossible for us to accurately assess publication bias. The colinearities of related risk factors may affect our analysis results, just as lower post-PCI LVEF and left ventricular wall motion abnormalities, both of which could exacerbate each other by causing ventricular vortices. Finally, most of the studies we included were from Asia, so factors such as medical level and ethnicity may have influenced our results. The APERITIF trial (NCT05077683) is currently underway to compare the 1-month incidence of LVT under DAPT versus triple therapy with very low-dose rivaroxaban (2.5 mg twice daily) and DAPT in patients with acute anterior MI. We believe that based on these data, we can analyze more accurate risk factors and implement better management and prevention for high-risk groups.

Conclusions

Our findings indicate that LVT is still a relatively common complication in STEMI patients, especially in anterior STEMI patients. We also confirmed that the risk factors related to LVT in post-PCI STEMI patients are anterior STEMI, LAD-related infarct, left ventricular wall motion abnormalities, and lower post-PCI LVEF. Patients with these high-risk factors should receive close monitoring and early prevention in clinical practice.

Statement of Ethics

This meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO no. CRD 42021267240) and conducted according to the PRISMA and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) statement.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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Author Contributions

Study concept and design: P. Wang and Z. Zhang; data collection: P. Wang, X. Ye, and D. Yan; data analysis: P. Wang and X. Ye; first draft: P. Wang and X. Ye; manuscript revision: P. Wang, X. Ye, D. Yan, Y. Peng, and Z. Zhang. All the authors approved the final version to be submitted.

Data Availability Statement

All data relevant to this study are available with the corresponding author.

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