Direct Oral Anticoagulants Versus Vitamin K Antagonists for the Management of Left Ventricular Thrombus After Myocardial Infarction: A Meta-Analysis

Christos Gogos, MD[a], Vasileios Anastasiou, MD[a], Andreas S. Papazoglou, MD[b], Stylianos Daios, MD[a], Matthaios Didagelos, MD, PhD[a], Nikolaos Kamperidis, MD, PhD[c], Vasileios Moschovidis, MD[d], Spyridon Filippos Papadopoulos, MD[a], Fotini Iatridi, MD[e], Pantelis Sarafidis, MD, PhD[e], George Giannakoulas, MD, PhD[a], Vasileios Sachpekidis, MD, PhD[d], Antonios Ziakas, MD, PhD[a], and Vasileios Kamperidis, MD, PhD[a,*]

Left ventricular (LV) thrombus formation remains a post-acute myocardial infarction (AMI) complication even in the modern era of early reperfusion. The optimal anticoagulation regimen in this clinical scenario is poorly defined. The present meta-analysis sought to investigate the efficacy and safety profile of direct oral anticoagulants (DOACs) compared with vitamin K antagonists (VKAs) for the management of LV thrombus after AMI. A systematic literature review was conducted in electronic databases to identify studies reporting efficacy and safety outcome data regarding the use of DOACs versus VKAs for patients with LV thrombus after AMI. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and random-effects meta-analyses were conducted to synthesize pooled ORs. Eight studies comprising a total of 605 patients were included. DOACs were associated with an almost twofold higher likelihood of thrombus resolution compared with VKAs (pooled OR 1.95 [1.25 to 3.04], p = 0.003, I^2 = 0%), and decreased the risk of systemic embolism by 70% (pooled OR 0.30 [0.12 to 0.75]; p = 0.01, I^2 = 0%). The use of DOACs was associated with a 54% lower risk of bleeding compared with VKAs (pooled OR 0.46 [0.26 to 0.84], p = 0.01, I^2 = 0%). Overall, patients receiving DOACs had a 63% lower risk of reaching the composite outcome of safety and efficacy compared with patients using VKAs (pooled OR 0.37 [0.23 to 0.60], p <0.0001, I^2 = 0%). In conclusion, DOACs appear to have a more favorable efficacy and safety profile compared with VKAs for the management of LV thrombus related to AMI. **(Am J Cardiol 2024;232:18−25)**

Keywords: direct oral anticoagulants, left ventricular thrombus, meta-analysis, myocardial infarction, vitamin K antagonists

Despite recent advances in early reperfusion strategies and antithrombotic therapies for the management of acute myocardial infarction (AMI), patients continue to suffer from a nonnegligible risk of complications.[1,2] Formation of left ventricular (LV) thrombus ranges from 0.4% to 26% after AMI,[3,4] and is a potentially life-threatening complication, augmenting 5.5-fold the risk of thromboembolic events.[5] The optimal anticoagulation regimen to prevent thromboembolism while retaining a low risk of bleeding remains poorly defined. Vitamin K antagonists (VKAs) have traditionally been recommended and used for the management of LV thrombus after AMI.[6] The 2023 European Society of Cardiology guidelines have challenged this approach by introducing the use of direct oral anticoagulants (DOACs) as a recommendation with the same class II and level of evidence C as VKAs after detection of LV thrombus after AMI.[7] Although studies on the role of DOACs in this setting have taken place,[8,9] these are nonrandomized and are limited by small numbers of patients included, therefore safe conclusions regarding the efficacy and safety of DOACs in this clinical setting, have not been drawn. The present meta-analysis sought to aggregate and quantitatively synthesize the existing literature regarding the efficacy and safety of DOACs for the management of LV thrombus after AMI in comparison to VKAs.

[a]1st Department of Cardiology, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece; [b]Athens Naval Hospital, Greece; [c]Department of IBD, St Mark's Hospital, Imperial College London, London UK; [d]Department of Cardiology, Papageorgiou Hospital, Thessaloniki, Greece; and [e]Department of Nephrology, Hippokration Hospital, School of Medicine, Aristotle University of Thessaloniki, Greece. Manuscript received August 1, 2024; revised manuscript received and accepted September 5, 2024.

Dr. Gogos and Dr. Anastasiou contributed equally to this manuscript and share first authorship.

Funding: none.

See page 23 for Declaration of Competing Interest.

*Corresponding author: Tel: +30 6932623300.

E-mail address: vkamperidis@outlook.com (V. Kamperidis).

https://doi.org/10.1016/j.amjcard.2024.09.008

Methods

The current systematic review and meta-analysis were performed in accordance with a pre-specified research protocol registered a priori in the PROSPERO database (https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=502319, CRD42024502319). The reporting follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 reporting guidelines (Supplementary Table 1).[10]

A detailed description of the strategy followed for the literature search is presented in Supplementary Material. Observational (prospective or retrospective) cohort or randomized controlled studies were included in the meta-analysis if they reported the specific risk of the pre-defined clinical outcomes according to the received anticoagulant treatment. No restrictions were applied in terms of the type of DOAC or AMI type. Exclusion criteria of the meta-analysis were the following: (1) case reports, reviews, editorials, and practice guidelines; (2) studies not reporting raw prognostic data or reporting raw data not appropriate for synthesis; (3) studies not including a control group for comparison with the DOACs group, leading to inability to synthesize odds ratios (ORs) and 95% confidence intervals (CIs); (4) studies investigating anticoagulants other than the pre-specified; (5) nonhuman studies.

Details regarding the data extraction process are available in the Supplementary Material. Overall, 2 co-primary efficacy outcomes, 1 primary safety outcome, and a secondary composite outcome were examined. In terms of efficacy: (1) the difference in LV thrombus resolution between DOACs and VKAs, as defined by complete thrombus resolution on echocardiography or cardiac magnetic resonance during follow-up; (2) the incidence of any systemic embolic events, defined as any thromboembolic event/stroke/transient ischemic attack after the initiation of anticoagulation. The safety outcome comprised any major or clinically relevant nonmajor bleeding event, defined according to the criteria of the International Society on Thrombosis and Haemostasis,[11] Bleeding Academic Research Consortium score[12] or thrombolysis in MI bleeding criteria[13] or other criteria used by the authors. The composite outcome included any of the following**:** bleeding, systemic embolism, any cardiovascular hospitalization, and all-cause mortality. The quality assessment and data synthesis processes are described in detail in the Supplementary Material.

Results

The study selection process is summarized in Figure 1. Screening of databases identified a total of 4,227 studies; of these 40 were assessed for eligibility. After the exclusion of the studies including non-AMI populations and those providing inappropriate outcome data to produce ORs, a total of 8[8,9,14–19] studies were included in the meta-analysis with an overall sample of 605 patients with LV thrombus after AMI.

The baseline characteristics of the studies included are listed in Table 1. Four studies[8,9,16,17] included exclusively anterior ST-elevation MI patients whereas the rest had mixed AMI cohorts. Three[8,9,19] eligible studies were randomized control trials, and the rest were observational studies. The type of DOAC used was variable. Three studies[15,18,19] used exclusively rivaroxaban, 2 studies used exclusively apixaban,[8,9] and the remaining studies used any of the clinically available DOACs. Most patients followed an initial course of triple antithrombotic therapy after the diagnosis of thrombus. Transthoracic echocardiography was the primary imaging modality used to diagnose LV thrombus, with only 2[14,16] studies also employing cardiac magnetic resonance for certain patients.

Quality assessment of the included studies using the quality in prognostic studies tool is listed in Supplementary Table 2. Six of the included studies were considered as of moderate risk for bias[8,9,16–19] and 2 studies were considered as of low risk for bias,[14,15] mainly driven by domains of study attrition, prognostic factor measurement, study cofounding, and statistical analysis.

All 8 studies provided appropriate quantitative data regarding the resolution of LV thrombus after the initiation of anticoagulation. Patients receiving DOACs had an almost twofold higher chance of achieving thrombus resolution compared with patients treated with VKAs (pooled OR 1.95 [1.25 to 3.04], p = 0.003, I^2 = 0%) at follow-up (Figure 2). All included studies but one[19] provided appropriate outcome data to compare the risk of systemic embolism between DOACs and VKAs. DOACs demonstrated a 70% lower risk of systemic embolism compared with VKAs (pooled OR 0.30 [0.12 to 0.75], p = 0.01, I^2 = 0%) (Figure 2). Data from 7[8,9,14–18] studies could be synthesized to compare the risk of bleeding between DOACs and VKAs. The use of DOACs was associated with a 54% lower risk of bleeding compared with VKAs (pooled OR 0.46 [0.26 to 0.84], p = 0.01, I^2 = 0%) (Figure 2). Seven[8,9,14–18] studies were meta-analyzed to compare the composite risk of adverse events between DOACs and VKAs. Overall, patients receiving DOACs had a 63% lower risk of reaching the composite outcome of safety and efficacy compared with patients using VKAs (pooled OR 0.37 [0.23 to 0.60]; p <0.0001, I^2 = 0%) (Figure 2). All subgroup analyses performed are listed in Supplementary Table 3. The generated funnel plots suggested a small possibility of publication bias in all analyses (Supplementary Figures 1, 2, 3, and 4)

The quality of evidence, as assessed by the grading of recommendations, assessment, development, and evaluations tool, demonstrated a low risk of bias and low inconsistency for the 2 co-primary efficacy outcomes, the safety outcome, and the secondary composite outcome. No serious considerations were raised regarding the indirectness and imprecision of the results. Overall, the findings of these analyses were considered important with a moderate level of certainty (Supplementary Table 4).

Discussion

This is the first meta-analysis to comprehensively examine the role of DOACs in patients with LV thrombus as a complication of AMI, by aggregating evidence from 8 studies with an overall sample size of 605 patients. Its main finding is that DOACs achieved a twofold higher rate of LV thrombus resolution during follow-up while demonstrating

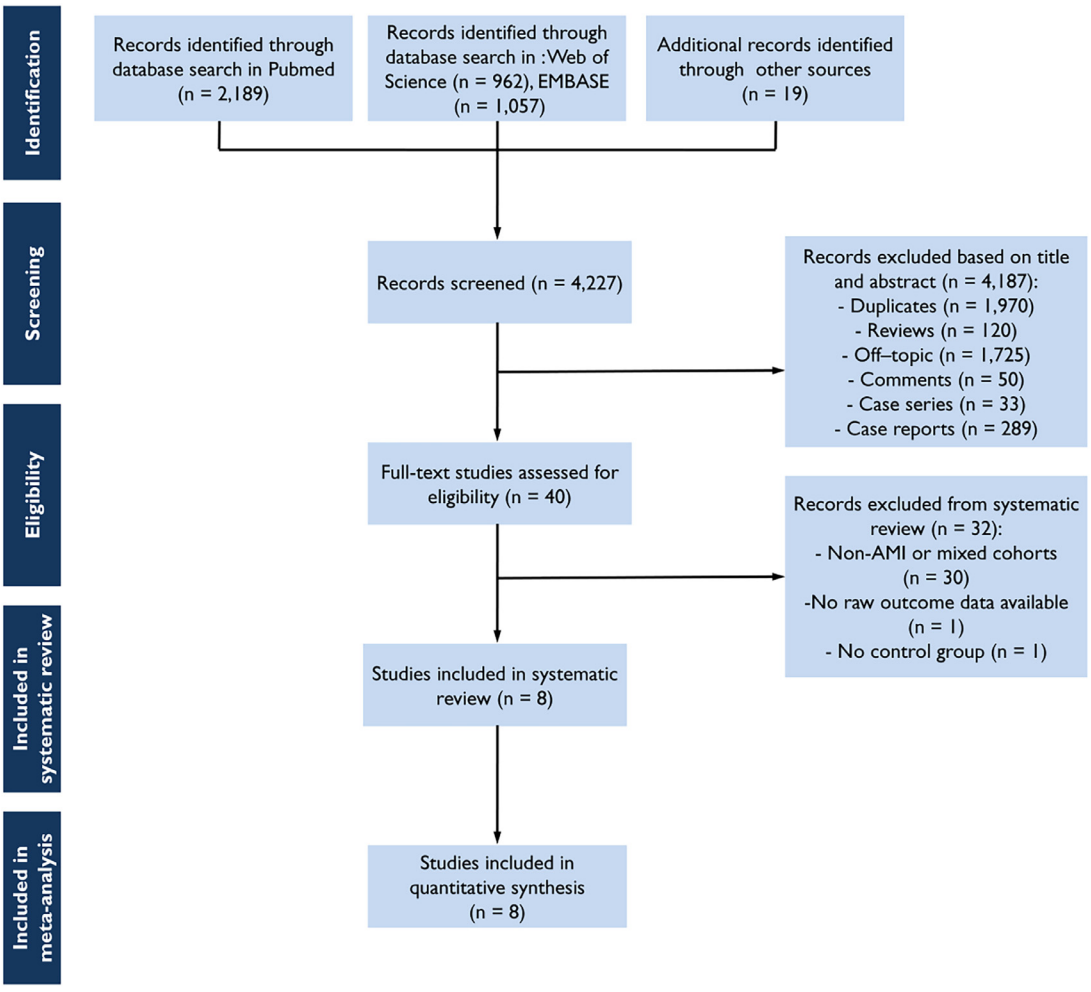

Figure 1. Study flow chart for study selection

a 70% lower risk of systemic embolism compared with VKAs. With respect to their safety profile, DOACs had a 54% lower risk of bleeding compared with VKAs. When the composite efficacy and safety outcome were examined, DOACs outperformed VKAs reaching an overall 63% lower risk of events.

The pathophysiology of LV thrombus formation after AMI is complex and is based on Virchow's triad of thrombogenesis as the interplay of 3 factors: (1) endothelial injury, (2) blood stasis, and (3) hypercoagulability triggered by inflammation. Each of these factors further serves as a therapeutic target in the management of LV thrombus after AMI. Patients with AMI are known to have increased concentrations of prothrombin, fibrinopeptide A, and von Willebrand factor.[20] Endothelial injury in the setting of AMI triggers an inflammatory and prothrombotic state by exposing the subendothelial tissue to monocytes and macrophages.[21] This state predisposes to increased levels of circulating C-reactive protein, fibrinogen, D–dimer, and anti−cardiolipin antibodies (immunoglobulin M and immunoglobulin G), which are independent predictors of early LV thrombus formation after AMI.[22,23]

Nonetheless, it should be emphasized that there are intrinsic pathophysiological differences between AMI-related LV thrombus, mainly caused by acute endocardial injury/inflammation, and chronic heart failure-related LV thrombus, primarily caused by stasis. These differences in thrombogenesis may reasonably be translated into differences in treatment strategy.[24]

The treatment of LV thrombus after AMI remains challenging because of a lack of large randomized clinical trials to guide anticoagulation therapy. VKAs act by inhibiting the activation of multiple clotting factors (II, VII, IX, X) and proteins (C, S) and have historically been used and recommended for the treatment of LV thrombus.[6,25] However, their use is associated with considerable disadvantages including the need for close monitoring, dose adjustments, and multiple drug interactions.[25] Conversely, DOACs are highly selective direct inhibitors of coagulation, targeting the factor Xa or thrombin, and can overcome these limitations.[26]

Although the safety and efficacy profile of DOACs in atrial fibrillation has been well established,[26] data on the role of DOACs for LV thrombus are contradictory.[27−29] In an observational study Fleddermann et al[30] reported that DOACs achieved thrombus resolution in 83% of a cohort with LV thrombus with minimal bleeding complications. Robinson et al[28] demonstrated in a large multicenter

Table 1
Baseline characteristics of the included studies

Author	Year	Population	Design	No. of patients	Age, years	Male, %	Imaging modality for the diagnosis of LV thrombus	DOAC	Antiplatelets	LVEF, %	Follow-up period, months
Chao et al[18]	2018	AMI	Retrospective, observational	126	61±9.5	79.3	TTE	Rivaroxaban (100%)	NR	40.4±8	18
Jaidka et al[17]	2018	AMI (100% anterior STEMI)	Retrospective, observational	49	60.3±11.4	75.5	TTE or/and Contrast TTE	NR	Triple therapy (100%)	34.5±9.6	6
Jones et al[14]	2021	AMI (87% anterior STEMI)	Prospective, observational,	101	60	85	TTE or CMR	Rivaroxaban (58.5%) Apixaban (36.5%) Edoxaban (5%)	Triple therapy (70%) Anticoagulation+single antiplatelet (22%) Anticoagulation only (8%)	34.5±9.6	18
Zhang et al[15]	2021	AMI (91% anterior STEMI)	Retrospective, observational	64	60.7±11.9	74	TTE	Rivaroxaban (100%)	Triple therapy (100%) with median duration 8.5 months	42.1±11.9	24
Liang et al[16]	2022	AMI (100% anterior STEMI)	Retrospective, observational	128	55.1±11.2	86	TTE (only 2 patients underwent CMR)	Rivaroxaban (84.5%) Dabigatran (14.5%)	Triple therapy (95%) Anticoagulation and single antiplatelet (5%)	43.0±9.4	12
Alcalai et al[8]	2022	AMI (100% anterior STEMI)	RCT	35	57	80	TTE	Apixaban (100%)	Triple therapy (100%), aspirin was stopped after 1 month	36.0± 6	3
Youssef et al[9]	2023	AMI (100% anterior STEMI)	RCT	50	52±8.1	NR	TTE	Apixaban (100%)	Triple therapy (100%) for a maximum of 3 months, unless the clinical condition or bleeding risk mandated the modification of this policy	26.9±7.7	6
Mansouri et al[19]	2024	AMI	RCT	52	56.5±10.03	84.6	TTE	Rivaroxaban (100%)	Triple therapy (100%), aspirin was stopped after 1 month.	30.42±7.84	3

Continuous variables are reported as median (IQR) or mean ± SD and categorical variables as percentages.

AMI = acute myocardial infarction; CMR = cardiac magnetic resonance; DOAC = direct oral anticoagulant; LVEF = left ventricular ejection fraction; LV = left ventricular; NR = not reported; RCT = randomized controlled clinical trial; STEMI = ST-segment elevation myocardial infarction; TTE = transthoracic echocardiography.

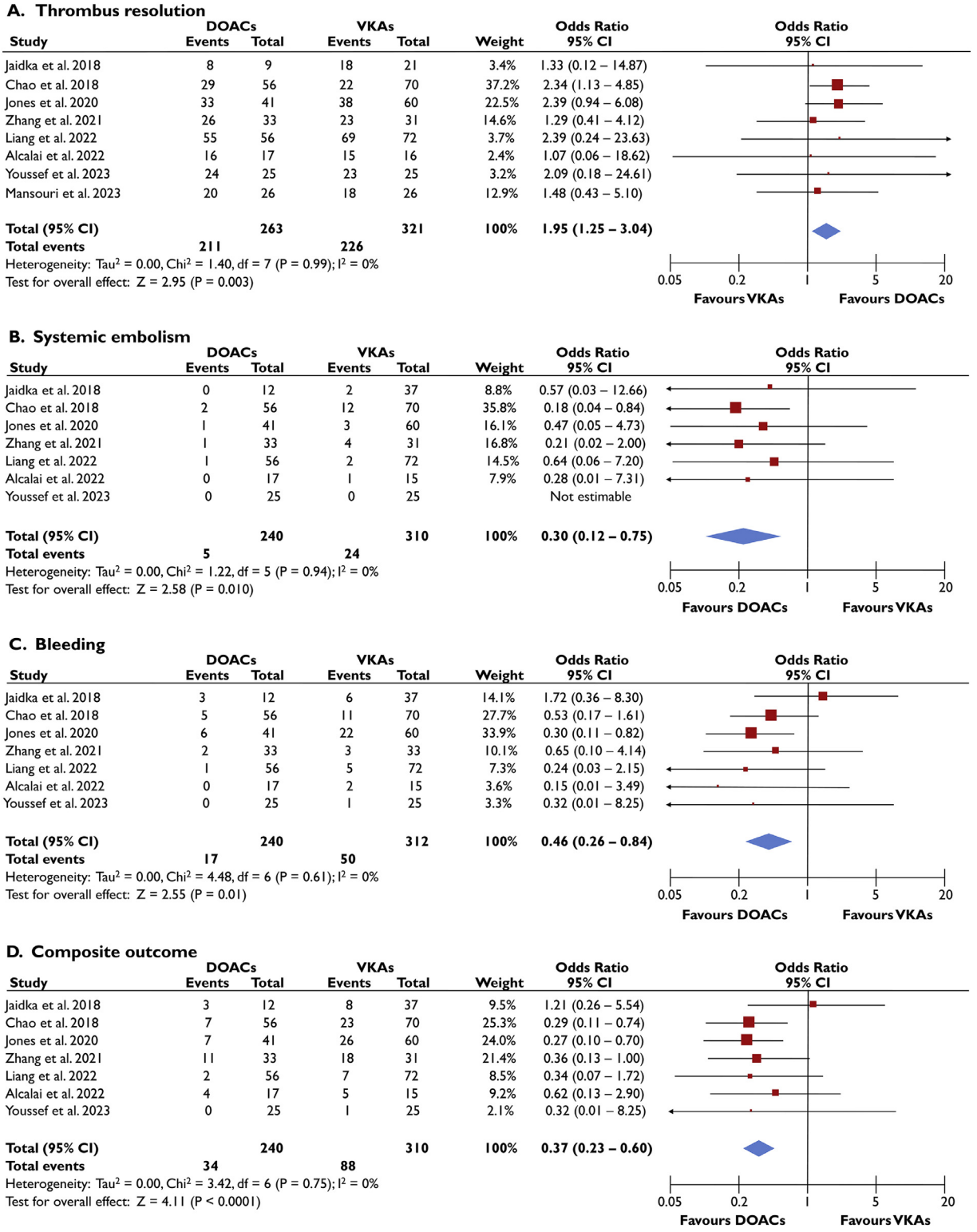

Figure 2. Comparison of DOACs versus VKAs for the incidence of thrombus resolution *(A)*, systemic embolism *(B)*, bleeding *(C)*, and the composite outcome *(D)* in patients with left ventricular thrombus after acute myocardial infarction. The forest plot displays the odds ratio and the corresponding 95% confidence interval (CI) of each study, indicating respectively the rate of thrombus resolution (*A*), the risk of systemic embolism (*B*), the risk of any major or clinically relevant nonmajor bleeding event (*C*), and the risk of composite efficacy and safety outcome (*D*) for patients receiving DOACs compared with patients receiving VKAs.

retrospective cohort that DOACs were associated with an increased risk of stroke or systemic embolism compared with VKAs. However, given the lack of randomization in this study residual confounding could impact the authors' conclusions, as the DOACs group appears to have more patients with traditional risk factors for stroke, whereas intracranial bleeding, which is usually reduced in patients treated with DOACs compared with VKAs, was not evaluated.[28] In another multicenter retrospective cohort Seiler et al[29] questioned the efficacy of DOACs, by reporting a higher rate of thrombus resolution within 1 month with VKAs compared with DOACs. A major and common limitation of the previously mentioned studies was the substantial heterogeneity of the included population, which poses a challenge to reaching robust conclusions about AMI patients with LV thrombus. Specifically, these studies enrolled patients with LV thrombus induced by any cause such as heart failure or AMI. However, the present meta-analysis enrolled only studies with AMI-related LV thrombus, which have significantly different pathophysiology and treatment strategy compared with heart failure patients, because they usually require oral anticoagulation in combination with antiplatelet agents.[31]

There are only limited organizational guideline recommendations regarding LV thrombus in an AMI context, which reflects the lack of robust evidence and the necessity of such an analysis. Previously, both the European and American guidelines for the management of ST-elevation MI did not include the DOACs as an anticoagulant choice for the treatment of LV thrombus.[6,32,33] In 2022, a scientific statement from the American Heart Association indicated that DOACs were considered to be a reasonable alternative to VKAs in patients with LV thrombus and may be particularly attractive in cases where therapeutic international normalized ratio range is difficult to achieve consistently or its monitoring is impractical.[24] More recently, the 2023 European Society of Cardiology guidelines for the management of acute coronary syndromes recommended DOACs as an equal option to VKAs in patients with LV thrombus after AMI.[7] However, this recommendation stems from randomized data on LV thrombus treatment in a heterogeneous cohort that is not post-AMI-specific.[34] This meta-analysis provides, for the first time in an AMI population, comprehensive evidence in favor of DOACs compared with VKAs, both in terms of efficacy and safety.

The results of this meta-analysis are subject to several inherent limitations, which should be acknowledged. Random-effects meta-analyses were executed based on unadjusted OR and CI. These were calculated using raw events which could lead to residual confounding. Moreover, the pooling of both randomized and observational studies adds to the risk for residual confounding, although the calculated I^2 for all analyses indicated low heterogeneity. Any subgroup analyses provided are even more subject to cofounding because of the very small sample of studies, and their results should be interpreted with caution.

In conclusion, this is the first meta-analysis attempting to elucidate the efficacy and safety of using DOACs versus VKAs for the management of LV thrombus after AMI. DOACs appear to achieve higher rates of thrombus resolution and to be associated with a lower risk of thromboembolic events and bleeding, outperforming VKAs. This meta-analysis emphasizes the need for further randomized clinical trials to determine the most effective and safe treatment strategy for LV thrombus management related to AMI.

Declaration of competing interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

Christos Gogos: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Vasileios Anastasiou:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Andreas S. Papazoglou:** Writing – original draft, Supervision, Software, Methodology, Formal analysis, Data curation. **Stylianos Daios:** Validation, Software, Methodology, Investigation, Formal analysis, Data curation. **Matthaios Didagelos:** Methodology, Investigation. **Nikolaos Kamperidis:** Writing – review & editing. **Vasileios Moschovidis:** Validation, Supervision. **Spyridon Filippos Papadopoulos:** Data curation, Conceptualization. **Fotini Iatridi:** Investigation, Formal analysis. **Pantelis Sarafidis:** Validation, Software, Conceptualization. **George Giannakoulas:** Project administration, Conceptualization. **Vasileios Sachpekidis:** Validation, Methodology. **Antonios Ziakas:** Writing – review & editing, Conceptualization. **Vasileios Kamperidis:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Data curation, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2024.09.008.

1. Smedegaard L, Charlot MG, Gislason GH, Hansen PR. Temporal trends in acute myocardial infarction presentation and association with use of cardioprotective drugs: a nationwide registry-based study. *Eur Heart J Cardiovasc Pharmacother* 2018;4:93–101.
2. Moschovidis V, Papadopoulou SL, Gogos C, Kantartzi V, Styliadis I, Sachpekidis V. Usefulness of contrast echocardiography for detection of left ventricular thrombus in a real-world population with acute anterior myocardial infarction. *Eur Heart J Cardiovasc Imaging* 2023;24 (suppl 1). jead119.380.
3. Meurin P, Brandao Carreira V, Dumaine R, Shqueir A, Milleron O, Safar B, Perna S, Smadja C, Genest M, Garot J, Carette B, Payot L, Tabet JY, College National des Cardiologues Français, Collège National des Cardiologues des Hôpitaux Français, Paris, France. Incidence, diagnostic methods, and evolution of left ventricular thrombus in patients with anterior myocardial infarction and low left ventricular ejection fraction: a prospective multicenter study. *Am Heart J* 2015;170:256–262.
4. Greaves SC, Zhi G, Lee RT, Solomon SD, MacFadyen J, Rapaport E, Menapace FJ, Rouleau JL, Pfeffer MA. Incidence and natural history of left ventricular thrombus following anterior wall acute myocardial infarction. *Am J Cardiol* 1997;80:442–448.
5. McCarthy CP, Vaduganathan M, McCarthy KJ, Januzzi JL Jr, Bhatt DL, McEvoy JW. Left ventricular thrombus after acute myocardial

infarction: screening, prevention, and treatment. *JAMA Cardiol* 2018;3:642–649.
6. O'Gara PT, Kushner FG, Ascheim DD, Jr Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW, American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;127:e362–e425.
7. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, Gilard M, Hinterbuchner L, Jankowska EA, Jüni P, Kimura T, Kunadian V, Leosdottir M, Lorusso R, Pedretti RFE, Rigopoulos AG, Rubini Gimenez M, Thiele H, Vranckx P, Wassmann S, Wenger NK, Ibanez B, ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J* 2023;44:3720–3826.
8. Alcalai R, Butnaru A, Moravsky G, Yagel O, Rashad R, Ibrahimli M, Planer D, Amir O, Elbaz-Greener G, Leibowitz D. Apixaban vs. warfarin in patients with left ventricular thrombus: a prospective multicentre randomized clinical trial‡. *Eur Heart J Cardiovasc Pharmacother* 2022;8:660–667.
9. Youssef AA, Alrefae MA, Khalil HH, Abdullah HI, Khalifa ZS, Al Shaban AA, Wali HA, AlRajab MR, Saleh OM, Nashy BN. Apixaban in patients with post-myocardial infarction left ventricular thrombus: a randomized clinical trial. *CJC Open* 2023;5:191–199.
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Br Med J (Clin Res Ed)* 2021;372:n71.
11. Schulman S, Kearon C. Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *J Thromb Haemost JTH* 2005;3:692–694.
12. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, Serebruany V, Valgimigli M, Vranckx P, Taggart D, Sabik JF, Cutlip DE, Krucoff MW, Ohman EM, Steg PG, White H. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation* 2011;123:2736–2747.
13. Chesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, Dalen J, Dodge HT, Francis CK, Hillis D, Ludbrook P. Thrombolysis in myocardial infarction (TIMI) trial, phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. *Circulation* 1987;76:142–154.
14. Jones DA, Wright P, Alizadeh MA, Fhadil S, Rathod KS, Guttmann O, Knight C, Timmis A, Baumbach A, Wragg A, Mathur A, Antoniou S. The use of novel oral anticoagulants compared to vitamin K antagonists (warfarin) in patients with left ventricular thrombus after acute myocardial infarction. *Eur Heart J Cardiovasc Pharmacother* 2021;7:398–404.
15. Zhang Z, Si D, Zhang Q, Qu M, Yu M, Jiang Z, Li D, Yang P, Zhang W. Rivaroxaban versus vitamin K antagonists (warfarin) based on the triple therapy for left ventricular thrombus after ST-Elevation myocardial infarction. *Heart Vessels* 2022;37:374–384.
16. Liang J, Wang Z, Zhou Y, Shen H, Chai M, Ma X, Han H, Shao Q, Li Q. Efficacy and safety of direct oral anticoagulants in the treatment of left ventricular thrombus after acute anterior myocardial infarction in patients who underwent percutaneous coronary intervention. *Curr Vasc Pharmacol* 2022;20:517–526.
17. Jaidka A, Zhu T, Lavi S, Johri A. Treatment of left ventricular thrombus using warfarin versus direct oral anticoagulants following anterior myocardial infarction. *Can J Cardiol* 2018;34(suppl 1):S143.
18. Chao P LJ, Chen X, Wang Y, Ren P. Incidence of systemic embolism in patients with left ventricular thrombus after myocardial infarction treated with new oral anticoagulants or vitamin K antagonists. *Chin Circ J* 2018;12:1184–1188.
19. Mansouri P, Jazi ZA, Mansouri MH, Dehghan H, Zavar R, Hashemi SM, Sattar F, Sadeghi M, Amirpour A, Abdar M. Evaluation of the efficacy and safety of Rivaroxaban compared to warfarin in patients with left ventricular apical thrombus: a randomized clinical trial. *Thromb J* 2024;22:66.
20. Solheim S, Seljeflot I, Lunde K, Bratseth V, Aakhus S, Forfang K, Arnesen H. Prothrombotic markers in patients with acute myocardial infarction and left ventricular thrombus formation treated with pci and dual antiplatelet therapy. *Thromb J* 2013;11:1.
21. Okuyan E, Okcun B, Dinçkal MH, Mutlu H. Risk factors for development of left ventricular thrombus after first acute anterior myocardial infarction-association with anticardiolipin antibodies. *Thromb J* 2010;8:15.
22. Shacham Y, Leshem-Rubinow E, Ben Assa E, Rogowski O, Topilsky Y, Roth A, Steinvil A. Comparison of C-reactive protein and fibrinogen levels in patients having anterior wall ST-Segment elevation myocardial infarction with versus without left ventricular thrombus (from a primary percutaneous coronary intervention cohort). *Am J Cardiol* 2013;112:57–60.
23. Camaj A, Fuster V, Giustino G, Bienstock SW, Sternheim D, Mehran R, Dangas GD, Kini A, Sharma SK, Halperin J, Dweck MR, Goldman ME. Left ventricular thrombus following acute myocardial infarction: JACC state-of-the-art review. *J Am Coll Cardiol* 2022;79:1010–1022.
24. Levine GN, McEvoy JW, Fang JC, Ibeh C, McCarthy CP, Misra A, Shah ZI, Shenoy C, Spinler SA, Vallurupalli S, Lip GYH. American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; and Stroke Council. Management of patients at risk for and with left ventricular thrombus: a scientific statement from the American Heart Association. *Circulation* 2022;146:e205–e223.
25. Huang L, Tan Y, Pan Y. Systematic review of efficacy of direct oral anticoagulants and vitamin K antagonists in left ventricular thrombus. *ESC Heart Fail* 2022;9:3519–3532.
26. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, Camm AJ, Weitz JI, Lewis BS, Parkhomenko A, Yamashita T, Antman EM. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014;383:955–962.
27. Iqbal H, Straw S, Craven TP, Stirling K, Wheatcroft SB, Witte KK. Direct oral anticoagulants compared to vitamin K antagonist for the management of left ventricular thrombus. *ESC Heart Fail* 2020;7:2032–2041.
28. Robinson AA, Trankle CR, Eubanks G, Schumann C, Thompson P, Wallace RL, Gottiparthi S, Ruth B, Kramer CM, Salerno M, Bilchick KC, Deen C, Kontos MC, Dent J. Off-label use of direct oral anticoagulants compared with warfarin for left ventricular thrombi. *JAMA Cardiol* 2020;5:685–692.
29. Seiler T, Vasiliauskaite E, Grüter D, Young M, Attinger-Toller A, Madanchi M, Cioffi GM, Tersalvi G, Müller G, Stämpfli SF, de Boeck B, Suter Y, Nossen J, Toggweiler S, Wuillemin WA, Cuculi F, Kobza R, Bossard M. Direct oral anticoagulants versus vitamin K antagonists for the treatment of left ventricular thrombi-insights from a Swiss multicenter registry. *Am J Cardiol* 2023;194:113–121.
30. Fleddermann AM, Hayes CH, Magalski A, Main ML. Efficacy of direct acting oral anticoagulants in treatment of left ventricular thrombus. *Am J Cardiol* 2019;124:367–372.
31. Zhou XD, Chen QF, Katsouras CS, Nijjar PS, Zheng KI, Zhu H, Gong M, Lin Q, Jin Y, Huang W, Shan P. Clinical outcome after left ventricular thrombus resolution: who needs long-term or lifetime use of anticoagulants? *J Am Heart Assoc* 2023;12:e029070.
32. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P, ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:119–177.

33. Bejjani A, Khairani CD, Assi A, Piazza G, Sadeghipour P, Talasaz AH, Fanikos J, Connors JM, Siegal DM, Barnes GD, Martin KA, Angiolillo DJ, Kleindorfer D, Monreal M, Jimenez D, Middeldorp S, Elkind MSV, Ruff CT, Goldhaber SZ, Krumholz HM, Mehran R, Cushman M, Eikelboom JW, Lip GYH, Weitz JI, Lopes RD, Bikdeli B. When direct oral anticoagulants should not be standard treatment: JACC state-of-the-art review. *J Am Coll Cardiol* 2024;83:444–465.
34. Abdelnabi M, Saleh Y, Fareed A, Nossikof A, Wang L, Morsi M, Eshak N, Abdelkarim O, Badran H, Almaghraby A. Comparative study of oral anticoagulation in left ventricular thrombi (No-LVT trial). *J Am Coll Cardiol* 2021;77:1590–1592.