

Myocardial infarction secondary to coronary embolism: aetiology, clinical characteristics, and prognosis

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Aims

Limited data are available regarding aetiology, clinical characteristics, and prognosis of coronary embolism (CE). This study aimed to describe the clinical features of embolic myocardial infarction (MI) and compare them with non-embolic MI.

Methods and results

All admissions for acute MI in a single tertiary centre between January 2010 and December 2023 were reviewed. Coronary embolism was diagnosed by established criteria. Among 8160 patients, 89 (1.1%) were diagnosed with CE. The most common attributable cause was atrial fibrillation (AF) (52.8%), followed by prosthetic valve thrombosis (11.2%) and endocarditis (7.9%). Compared with the remaining patients, those with CE were more frequently female, had a lower prevalence of cardiovascular risk factors, and presented more often with ST-segment elevation (79.8 vs. 58.6%, $P < 0.001$). Coronary embolism patients had a high frequency of unsuccessful reperfusion and higher rates of mechanical complications (5.6 vs. 2.2%, $P = 0.031$) and strokes/transient ischaemic attacks (6.7 vs. 1.3%, $P < 0.001$) than those with non-CE MI, although in-hospital mortality was not statistically different (9.0 vs. 6.4%, respectively, $P = 0.321$). In a propensity-matched analysis among hospital survivors (77 in each group), no differences were observed over a median follow-up of 59.6 months in overall mortality or thrombo-embolic events after discharge, although more patients in the CE group were admitted for heart failure.

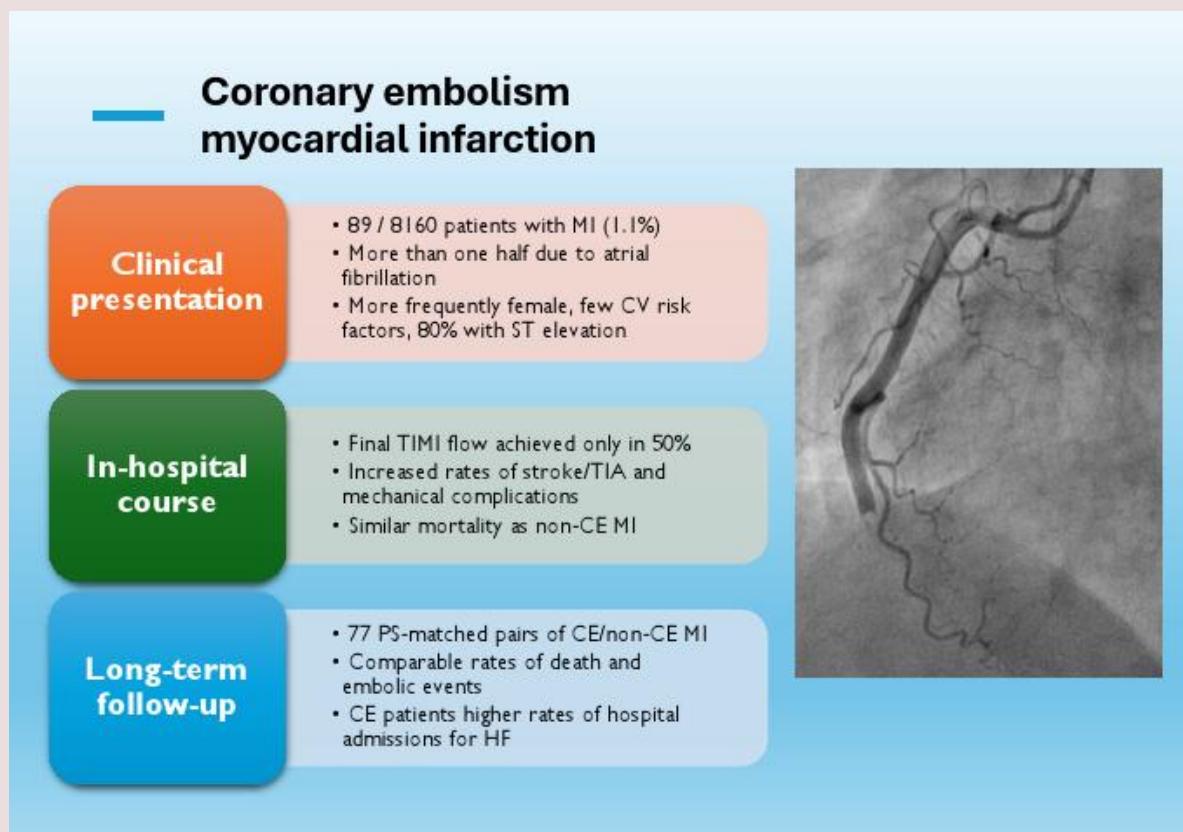
Conclusion

Coronary embolism is mostly caused by AF, usually presents with ST-segment elevation, and is associated with higher rates of mechanical complications and in-hospital embolic events, but not of recurrent thromboembolism after discharge. No significant differences in mortality were observed between CE and non-CE MI.

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Graphical Abstract



CE, coronary embolism; CV, cardiovascular; HF, heart failure; MI, myocardial infarction; PS, propensity score; TIA, transient ischaemic attack; TIMI, thrombolysis in myocardial infarction.

Keywords

Coronary embolism • Acute myocardial infarction • Prognosis

Introduction

Coronary embolism (CE) is a cause of non-atherosclerotic acute myocardial infarction (MI).^{1–4} In a seminal autopsy-guided study,⁵ CE accounted for 13% of infarcts, but its prevalence in clinical studies has been significantly lower, ranging between 0.2 and 2.9% of all MIs,^{6–8} or reportedly 4.3% in patients with ST-segment elevation MI (STEMI).⁹ Several clinical conditions have been associated with CE including atrial fibrillation (AF), presence of prosthetic heart valves, infective endocarditis, cardiomyopathies, atrial septal defect or patent foramen ovale (PFO), cardiac tumours, or hypercoagulable states.^{1,6,8–12} Atrial fibrillation appears to be the most common cause of CE, although its prevalence has varied widely (28.3–73.0%) among studies.^{6,8,9}

Available data on clinical characteristics and prognosis of patients with CE are based on limited-size case series (the largest including 53 patients) and case reports.^{6,8–10} Moreover, only one study has compared a CE cohort with a propensity score-matched non-CE acute MI cohort.⁶ In this relatively small sample size comparison, with 45 patients per group, a higher incidence of death and cardiac death was observed in the CE group at 5 years. However, cohorts were matched only by demographic variables, cardiovascular risk factors, and left ventricular ejection fraction, leaving unanswered the question whether the

results could have been different if the propensity score had included a broader number of variables.

The objective of the present study was to determine the predisposing factors, clinical characteristics, and short- and long-term outcomes of patients with CE in a larger, contemporary series of patients with this condition and to compare them with a cohort of patients with non-CE acute MI matched by a propensity score that also included comorbidities, GRACE score, and discharge therapies.

Methods

Study population

This retrospective observational study included all adult patients with acute MI admitted to the acute cardiac care unit of a tertiary hospital between January 2010 and December 2023. Acute MI diagnosis required the combination of a dynamic elevation of serum cardiac biomarkers with clinical symptoms and/or electrocardiographic signs of myocardial ischaemia.²

Patients presenting with persistent ST-segment elevation usually underwent an emergent coronary angiography and primary percutaneous coronary intervention (PCI), and an early invasive strategy was the preferred strategy in the remaining patients. Antithrombotic therapies were administered in accordance with clinical practice guidelines in force at the time of admission. During coronary angiography, thrombus aspiration, PCI, and

administration of intravenous antiplatelet agents were at the discretion of the operating interventional cardiologist. Revascularization strategies in complex cases were discussed in the Heart Team.

Demographic variables, cardiovascular risk factors, comorbidities, ongoing therapies, and data on clinical presentation and in-hospital course were prospectively collected. Standard blood tests were performed on admission. A transthoracic echocardiographic exam was routinely performed. Follow-up data were obtained by consulting electronic medical records.

Definition of coronary embolism

Coronary embolism diagnosis was based on coronary angiography data, except for one patient with active endocarditis complicated with various extracardiac embolisms, in whom the MI was considered embolic despite lacking a coronary angiography. All coronary angiographies of patients considered to have a definite or probable CE by the interventional cardiologist performing the procedure were reviewed for the purpose of this study by another experienced interventional cardiologist (Y.B.) and CE diagnosis was established only if both experts agreed. Coronary embolism was diagnosed in the presence of a thrombus—defined as a non-calcified filling defect outlined by contrast media or an abrupt occlusion in the absence of significant coronary atherosclerosis. Patients in whom doubts persisted after coronary angiography evaluation or those without an identifiable coronary thrombus were classified as CE only if they fulfilled the criteria for definite CE proposed by Shibata et al.⁶ and modified by Raphael et al.¹ The major criteria for CE are (i) angiographic evidence of embolus/thrombus; (ii) concomitant emboli in multiple coronary vascular territories; (iii) concomitant systemic embolization without left ventricular thrombus attributable to acute MI; (iv) histological evidence of venous origin of coronary embolic material; and (v) evidence of an embolic source on imaging techniques. The minor criteria are (i)<25% angiographic stenosis in non-culprit vessels; (ii) AF; and (iii) presence of embolic risk factors, cardiomyopathy, rheumatic heart disease, prosthetic valve, PFO, atrial septal defect, history of cardiac surgery, infective endocarditis, or hypercoagulability. According to this classification, diagnosis of definite CE requires the presence of ≥2 major criteria, 1 major criterion plus ≥2 minor criteria, or 3 minor criteria. Specific studies such as transoesophageal echocardiography, magnetic resonance imaging, bubble studies, or hypercoagulable disorder tests were performed according to the clinical suspicion and the treating physician's decision. Coronary embolism diagnosis was not made in the presence of pathological evidence of atherosclerotic thrombus, coronary artery ectasia, or plaque disruption or erosion detected by intravascular imaging of the culprit lesion.

Study outcomes

The main goals were (i) to describe the underlying causes of CE; (ii) to compare the in-hospital complications of patients with CE and non-CE MI; and (iii) to analyse the medium-long-term prognosis of patients with CE compared with propensity score-matched non-CE MI patients, for recurrent embolic events, hospital admissions for heart failure, and mortality.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Institutional Review Board (PR[AG]374/2024).

Statistical analysis

The statistical analyses were performed using STATA BE 18 (StataCorp). Categorical variables are presented as count and percentage, and continuous variables as median [interquartile range (IQR)]. Comparisons between the CE cohort and the overall cohort were performed using the Student *t*-test or Wilcoxon rank-sum test for continuous variables or the χ^2 test or Fisher's exact test for categorical variables, as appropriate.

The non-CE and CE subjects with acute MI were matched based on a propensity score. The score was computed using a logistic regression model that included the following covariates: age, sex, ≥2 recent episodes of angina, previous MI, previous stroke, severe renal failure, chronic pulmonary disease, previous PCI, previous cardiac surgery, smoking status, diabetes mellitus, Killip class, heart rate and systolic blood pressure on admission, presenting symptom, ST-segment changes, initial creatinine and blood glucose levels, GRACE score, and pharmacologic treatment at hospital discharge. Each CE subject was matched with one non-CE subject using a 'nearest-neighbors' approach. Comparisons between propensity-matched pairs were performed by calculating standardized differences for variables included

Table 1 Underlying causes in the 89 cases of coronary embolism

Cause	Frequency
Atrial fibrillation, n (%)	47 (52.8) ^a
Prosthetic valve thrombosis, n (%)	10 (11.2) ^b
Infective endocarditis, n (%)	7 (7.9) ^c
Patent foramen ovale or atrial septal defect, n (%)	7 (7.9) ^d
Coagulopathy, n (%)	5 (5.6) ^e
Malignancy, n (%)	3 (3.4) ^f
Intracardiac thrombus, n (%)	1 (1.1)
Other, n (%)	4 (4.5) ^g
Unknown, n (%)	5 (5.6)

^aOne patient also had a PFO.

^bSix patients also had AF.

^cTwo patients also had AF.

^dOne patient had AF.

^eOne patient also had AF and one a PFO.

^fOne patient also had a PFO.

^gTwo patients also had AF.

in the score and by using a paired *t*-test for other continuous variables or the McNemar test for other categorical variables. Kaplan–Meier curves were used to represent the cumulative incidence of events over time. Differences between CE and non-CE patients were assessed using Cox regression analysis with paired data, employing the 'shared' option in STATA. A two-tailed *P*-value of <0.05 was considered statistically significant.

Results

Frequency and underlying cause of coronary embolism

Of 8160 patients with acute MI, 89 [1.1%, 95% confidence interval (CI) 0.9–1.3] were identified as having a CE. The prevalence of CE was 1.5% (95% CI 1.2–1.9) in the STEMI subgroup (67 of 4567 patients). The underlying causes of CE are displayed in Table 1. Atrial fibrillation was identified in 59 patients (66.3%, 95% CI 56.0–75.6). Among these, AF was previously known in 38 patients, diagnosed during admission in 16, and detected after discharge in 5. In 47 (52.8%) individuals, CE was solely attributed to AF—in 6 of them, an atrial appendage thrombus or spontaneous echo contrast were identified—and in the remaining 12, AF co-existed with other causes of CE. Ten (11.2%) embolisms were attributed to definite ($n = 3$) or probable ($n = 7$) prosthetic valve thrombosis. Seven (7.9%) were secondary to infective endocarditis (three involving the mitral valve, three involving the aortic valve, and one affecting both valves). Seven (7.9%) were due to paradoxical embolism in the presence of a PFO or atrial septal defect; however, three additional patients had PFO or atrial septal defect, but their emboli were attributed to AF, coagulopathy, or malignancy. Coagulopathy was identified as the underlying cause in five (5.6%) patients—one of whom also had AF and another had a PFO. This group comprised one patient with antiphospholipid syndrome, one with idiopathic thrombocytopenic purpura, two with protein C deficiency, and one with factor V Leiden. In three patients (3.4%), CE was attributed to malignancy and one patient (1.1%) had a left ventricular thrombus not attributable to the acute MI. Other causes of CE included one mitral fibroelastoma, one atheromatous plaque at the aortic sinotubular junction, one mitral calcification, and one CE post-transcatheter aortic valve implantation. Finally, in five (5.6%) patients, no embolic source was identified. Four patients had a history of

ischaemic ($n = 3$) or non-ischaemic ($n = 1$) cardiomyopathy but all of them had another underlying embolic source.

Angiographic characteristics, specific exams, and discharge antithrombotic regimes in patients with coronary embolism

Table 2 summarizes the angiographic characteristics, the specific exams performed in search of the embolic source, and the discharge antithrombotic regimes in the 89 patients with CE. A coronary angiography was performed in 88 (98.9%) patients. In 71 (80.7%), coronary angiography was performed the day of admission and in the remaining patients between 1 and 10 days after admission. Seven patients did not have a visible CE at angiography but met the definite CE criteria for other reasons. Of the 81 patients with evidenced CE on angiography, CE was multivessel in 9 (11.1%), 53 (65.4%) had distal vessel involvement, and 75 (92.6%) had an initial TIMI 0 flow grade. The right coronary artery was the most affected vessel. Thrombectomy was performed in 56 patients (69.1%), PCI in 17, and stent implantation in 8. In two patients, the stent was implanted to treat a procedural complication (coronary dissection or perforation) and in the six other patients to stabilize coronary flow because it was not adequately restored or rapidly worsened after thrombectomy and/or balloon inflation. The final TIMI flow grade was 0 or 1 in 36 out of these 81 patients (44.4%) and only 41 (50.6%) achieved a TIMI flow Grade 3 at the end of the procedure.

A transoesophageal echocardiography was performed in 52 patients, a bubble echocardiography test in 20 (positive for PFO/atrial septal defect in 10), 6 underwent ambulatory Holter monitoring (which diagnosed 2 cases of AF), and 14 patients underwent thrombophilia testing (positive in 5 cases).

Among hospital survivors ($n = 81$, 91.0%), all but one (98.8%) were discharged on oral anticoagulation (OAC) therapy, associated or not with single or double antiplatelet therapy. Oral anticoagulation therapy was discontinued in eight patients a few months after discharge and was maintained as permanent therapy in the remaining patients. The reasons for not prescribing or discontinuing OAC therapy were infective endocarditis as underlying cause of CE ($n = 2$), PFO closure ($n = 2$), contraindication ($n = 1$), and unknown ($n = 4$).

There were no major changes in the diagnostic work-up throughout the study period. The use of vitamin K antagonists for anticoagulation declined from 90 to 60% during the second half of the study in favour of the direct anticoagulants.

Baseline characteristics, clinical presentation, and in-hospital course in patients with and without coronary embolism

Baseline characteristics, data on clinical presentation, and in-hospital course in patients with and without CE are summarized in **Table 3**. Compared with the remaining patients, those with CE were more frequently female and had a lower prevalence of diabetes mellitus, active smoking, previous angina, and peripheral artery disease. In contrast, they had higher rates of previous cardiac surgery (primarily non-bypass surgeries), previous stroke/TIA (including those occurring in the index admission prior to MI), and ongoing OAC therapy. Among patients ($n = 24$) on vitamin K antagonists at admission, the median initial INR value was 2.44 (IQR 1.89–3.27), with seven patients (29.2%) having an INR below 2. Of 38 patients with known AF, 21 were on OAC therapy (18 on vitamin K antagonists and 3 on direct anticoagulants) and 17 were not receiving OAC therapies on admission. Of these 17 patients, one was not taking the prescribed therapy, whereas OAC therapy was

Table 2 Angiographic characteristics, specific exams performed, and discharge antithrombotic regimens in patients with coronary embolism

	CE ($n = 89$)
Coronary angiography, n (%)	88 (98.9)
Angiographic evidence of CE, n (%)	
Yes	81 (92.0)
No	7 (8.0)
Abrupt occlusion, n (%)	57 (70.4)
Visible thrombus	40 (49.4)
‘Crab-claw’ sign	12 (14.8)
Multivessel CE, n (%)	9 (11.1)
Coronary vessel involved, n (%)	
Right coronary artery	34 (42.0)
Left anterior descending artery	26 (32.1)
Left circumflex artery	15 (18.5)
Left main stem	0 (0.0)
CE in distal segments, n (%)	53 (65.4)
Initial TIMI flow, n (%)	
0	75 (92.6)
1	2 (2.5)
2	1 (1.2)
3	3 (3.7)
Thrombectomy, n (%)	56 (69.1)
Percutaneous coronary intervention, n (%)	17 (21.0)
Distal embolization during thrombectomy, n (%)	15 (26.8)
Balloon angioplasty, n (%)	15 (16.9)
Stent implantation, n (%)	8 (9.0)
Final TIMI flow, n (%)	
0	25 (30.9)
1	11 (13.6)
2	4 (4.9)
3	41 (50.6)
Emboilic source study, n (%)	
Transthoracic echocardiography	89 (100.0)
Transoesophageal echocardiography	52 (58.4)
Bubble test echocardiography	20 (22.5)
Holter monitoring	6 (6.7)
Thrombophilia test	14 (15.7)
Long-term treatment (81 patients discharged alive), n (%) ^a	
OAC + DAPT <6 m → OAC + MAPT → OAC	4 (4.9)
OAC + DAPT <6 m → OAC + MAPT	1 (1.2)
OAC + MAPT	21 (25.9)
OAC + MAPT → OAC	19 (23.5)
OAC	27 (33.3)
OAC (± DAPT or MAPT) → MAPT	8 (9.9)
DAPT → MAPT	1 (1.2)

Data are shown as counts (%).

CE, coronary embolism; DAPT, dual antiplatelet therapy; n , number of patients; MAPT, mono antiplatelet therapy; OAC, oral anticoagulation.

^aDAPT was prescribed only in patients with a stent implanted.

Table 3 Baseline characteristics, clinical presentation, and in-hospital course in patients with and without coronary embolism

	CE MI (n = 89)	Non-CE MI (n = 8071)	P-value
Age, years	71.6 (57.5, 81.5)	65.2 (55.3, 75.7)	0.061
Female sex, n (%)	49 (55.1)	1961 (24.3)	<0.001
Body mass index (kg/m ²)	27.1 (23.8, 29.7)	27.1 (24.5, 30.1)	0.805
Arterial hypertension, n (%)	54 (60.7)	4961 (61.5)	0.872
Diabetes mellitus, n (%)	16 (18.0)	2418 (30.0)	0.014
Dyslipidaemia, n (%)	47 (52.8)	4759 (59.0)	0.238
Active smoking, n (%)	20 (22.5)	3026 (37.6)	0.003
Previous angina, n (%)	5 (5.6)	1248 (15.5)	0.010
Previous cardiac surgery, n (%)	20 (22.5)	349 (4.3)	<0.001
No, n (%)	69 (77.5)	7721 (95.7)	
Bypass grafting, n (%)	1 (1.1)	299 (3.7)	
Other surgery, n (%)	19 (21.4)	50 (0.6)	
Previous stroke/TIA, n (%)	18 (20.2)	609 (7.6)	<0.001
Peripheral artery disease, n (%)	3 (3.4)	778 (9.6)	0.046
Severe chronic kidney disease, n (%)	4 (4.5)	395 (4.9)	0.862
Anticoagulation treatment, n (%)	28 (31.5)	495 (6.1)	<0.001
ST-segment elevation MI, n (%)	67 (79.8)	4500 (58.6)	<0.001
Initial rhythm, n (%)			<0.001
Sinus rhythm	52 (58.4)	7256 (89.9)	
Atrial fibrillation/flutter	34 (38.2)	547 (6.8)	
Other	3 (3.4)	264 (3.3)	
Initial Killip class, n (%)			0.049
I	67 (75.3)	5932 (73.5)	
II	15 (16.8)	984 (12.2)	
III	0 (0.0)	563 (7.0)	
IV	7 (7.9)	590 (7.3)	
GRACE risk score	139 (111,155)	129 (103, 160)	0.170
Inotropic drugs, n (%)	10 (11.2)	1241 (15.4)	0.280
Glycoprotein IIb–IIIa inhibitors, n (%)	14 (16.1)	1615 (20.4)	0.319
Percutaneous intervention, n (%)	64 (71.9)	6348 (78.7)	0.121
In-hospital reinfarction, n (%)	0 (0.0)	237 (2.9)	0.116
In-hospital stroke/TIA, n (%) ^a	6 (6.7)	106 (1.3)	<0.001
Cardiogenic shock, n (%)	10 (11.2)	862 (10.7)	0.868
Mechanical complication, n (%)	5 (5.6)	178 (2.2)	0.031
In-hospital mortality, n (%)	8 (9.0)	516 (6.4)	0.321
Aspirin at discharge, n (%) ^b	46 (56.8)	7112 (94.2)	<0.001
P2Y ₁₂ inhibitor at discharge, n (%) ^b	15 (18.5)	6312 (83.6)	<0.001
Anticoagulation at discharge, n (%) ^b	73 (90.1)	912 (12.1)	<0.001
Left ventricular ejection fraction, n (%) ^c			0.279
>50%	47 (52.8)	4239 (53.1)	
41–50%	27 (30.3)	1943 (24.4)	
31–40%	12 (13.5)	1143 (14.3)	
<30%	3 (3.4)	653 (8.2)	

Data are shown as counts (%) or medians (IQR).

CE, coronary embolism; MI, myocardial infarction; n, number of patients; TIA, transient ischaemic attack.

^aOnly those stroke/TIA occurring after the MI and during the admission.^bPercentages with respect to patients discharged alive.^cData from 8067 patients (all patients with CE and 7978 with non-CE MI).

Table 4 Comparison of patients with coronary embolism with propensity score-matched patients with non-embolic acute myocardial infarction, including the most relevant covariates in the propensity score matching, other covariates and outcomes

PS included covariates	CE group (n = 77)	Non-CE group (n = 77)	Standardized difference	
Age (years)	71.6 (58.7, 81.1)	70.5 (59.5, 79.9)	0.17	
Female sex, n (%)	40 (52.0)	35 (45.5)	0.13	
Active smoking, n (%)	17 (22.1)	23 (29.9)	0.18	
Diabetes mellitus, n (%)	13 (16.9)	15 (19.5)	0.07	
STEMI, n (%)	58 (75.3)	49 (63.6)	0.26	
AAS at discharge, n (%)	45 (58.4)	57 (74.0)	0.33	
P2Y ₁₂ inhibitor at discharge, n (%)	69 (89.6)	63 (81.8)	0.22	
Anticoagulation at discharge, n (%)	70 (90.9)	61 (79.2)	0.33	
Characteristics not included in the PS and in-hospital outcomes				
Body mass index (kg/m ²)	27.2 (23.6, 29.8)	26.0 (23.7, 29.2)	0.362	
Arterial hypertension, n (%)	48 (62.3)	52 (67.5)	0.480	
Dyslipidaemia, n (%)	42 (54.6)	37 (48.0)	0.384	
Initial TIMI flow 0, n (%)	65 (92.9)	37 (50.7)	<0.001	
Final TIMI flow 3, n (%)	35 (50.0)	67 (91.8)	<0.001	
CHADS2-VASc score	5 (3, 6)	4 (2, 5)	0.018	
In-hospital thromboembolism, n (%)	13 (16.9)	4 (5.2)	0.029	
Stroke/TIA	10 (13.0)	3 (3.9)	0.052	
Pulmonary embolism	4 (5.2)	0 (0.0)	0.125	
Other systemic embolism	2 (2.6)	0 (0.0)	0.500	
LV ejection fraction (%)	52 (45, 58)	50 (40, 57)	0.317	
Outcomes during follow-up				
		Hazard ratio (95% CI)	P-value	
Myocardial infarction, n (%)	3 (3.9)	7 (9.7)	0.45 (0.12–1.75)	0.251
Thrombo-embolic event, n (%)	15 (19.5)	10 (13.0)	1.92 (0.83–4.43)	0.126
Stroke/TIA	8 (10.4)	8 (10.4)		
Coronary embolism	3 (3.9)	0 (0.0)		
Pulmonary embolism	0 (0.0)	1 (1.3)		
Venous thrombosis/systemic embolism, n (%)	4 (5.2)	1 (1.3)		
Heart failure admission, n (%)	21 (27.3)	12 (15.6)	2.96 (1.39–6.31)	0.005
Death, n (%)	24 (31.2)	32 (41.6)	0.81 (0.48–1.39)	0.454
Cardiovascular death, n (%)	4 (5.2)	1 (1.3)	4.30 (0.48–38.5)	0.192
Bleeding BARC score >1, n (%)	5 (6.5)	8 (10.4)	0.66 (0.19–2.21)	0.498

Data are shown as counts (%) or medians (IQR).

CE, coronary embolism; MI, myocardial infarction; n, number of patients; PS, propensity score; TIA, transient ischaemic attack.

never prescribed in 7 patients and had been stopped in 9 (in 4 due to contraindications and in 5 for unknown reasons).

Patients with CE presented more often than the remaining patients with persistent ST-segment elevation and with AF or flutter in the initial electrocardiogram. Advanced Killip class on admission was less common in these patients, although both groups had a similar GRACE score.

With respect to in-hospital complications, patients with CE had higher rates of stroke/transient ischaemic attack (TIA) and mechanical complications than those without CE but comparable rates of cardiogenic shock. Fourteen (15.7%, 95% CI 9.6–24.7%) patients with CE

experienced 19 thrombo-embolic episodes during admission, including 11 strokes/TIAs, 4 pulmonary embolisms, 3 other systemic embolisms, and 1 venous thrombosis. Four patients had ≥2 embolic events during admission, excluding CE. No patient in the CE group experienced a recurrent CE or reinfarction during admission, while 2.9% (95% CI 2.6–3.3) of patients in the non-CE group had a reinfarction ($P=0.116$). In-hospital mortality rates in patients with CE and non-CE MI were 9.0% (95% CI 5.9–7.0) and 6.4% (95% CI 4.6–16.7), respectively ($P=0.321$). Among the eight patients with CE who died during admission, the underlying cause of CE was endocarditis in three patients, with a

mortality rate of 42.9% (95% CI 15.8–75.0) in the endocarditis group (3 out of 7), and AF in five patients.

There were no significant differences between groups in left ventricular ejection fraction. Among hospital survivors, most patients in the CE group (90.1%) were discharged on OAC treatment compared with 12.1% in the non-CE MI group ($P < 0.001$), while the opposite trends were observed for antiplatelet drugs.

Long-term prognosis

For the follow-up analysis, a propensity score-matched cohort consisting of 77 patients with CE and 77 patients without CE was selected. Table 4 summarizes the main clinical characteristics and the post-discharge evolution in both cohorts.

During a median follow-up of 59.6 (IQR 31.4–91.4) months, 15 patients (19.5%) in the CE group experienced new thrombo-embolic events: 8 (10.4%) strokes/TIAs, 3 (3.9%) probable CEs, and 4 (5.2%) other systemic or venous thromboembolisms. In the non-CE group, 10 patients (13.0%) experienced new thrombo-embolic events, including 8 (10.4%) strokes/TIAs, 1 (1.3%) pulmonary embolism, and 1 (1.3%) systemic thromboembolism. There were no statistically significant differences in the rate of new thrombo-embolic events between the two groups [hazard ratio (HR) 1.92, 95% CI 0.83–4.43, $P = 0.126$] (Figure 1A). During follow-up, 21 patients (27.3%) in the CE group were admitted due to heart failure, compared with 12 patients (15.6%) in the non-CE group (HR 2.96, 95% CI 1.39–6.31, $P = 0.005$) (Figure 1B). Finally, 24 patients from the CE group (31.2%) died during follow-up (16.7% from cardiac causes), compared with 32 (41.6%) in the non-CE group (HR 0.81, 95% CI 0.48–1.39, $P = 0.454$) (Figure 1C).

Discussion

The main findings of this study are: (i) CE accounts for ~1% of admissions for acute MI (a proportion somewhat larger for STEMI); (ii) the most frequent cause of CE is, by large, AF; (iii) CE is associated with a distinct clinical profile, presents more frequently as STEMI, and final TIMI 3 flow is only achieved in half of the patients; (iv) compared with non-CE MI patients, those with CE have higher rates of thrombo-embolic events (mainly strokes or TIAs) and mechanical complications but similar rates of cardiogenic shock and mortality during admission; and (v) during a 5-year follow-up, rates of thrombo-embolic events and mortality are comparable in patients with CE and non-CE MI, although the former more frequently require hospitalizations for heart failure.

To our knowledge, this is the largest reported series of CE. For this reason, it adds significantly to previous knowledge on the frequency, aetiology, and outcomes of CE.^{6,8–11} The prevalence of CE in the present study was comparable to that found in some previous series⁸ but lower than that reported by others.^{6,9} The fact that we only included cases of definite CE may help explain these differences.

In over one-half of the patients, CE was solely attributed to AF. This strengthens the results of previous studies^{6,8,9} that also identified AF as the main cause of CE and suggests that the primacy of endocarditis observed in some case reviews^{10,11} may have been influenced by publication bias. In about one-third of patients with AF, the arrhythmia was diagnosed during or after hospital admission, which stresses the importance of active rhythm monitoring in patients with definite or suspected CE. Prosthetic valve thrombosis, endocarditis, and paradoxical embolism through a PFO or an atrial septal defect were other relatively frequent causes of CE, but at a great distance from AF. Diagnosis of paradoxical embolism is challenging, as a PFO is a present in about one quarter of normal individuals.¹³ The presence of a PFO should raise suspicion of paradoxical embolism, especially in younger patients and in those with high-risk characteristics of the PFO,^{14,15} but other underlying causes should be investigated. In the present study, a PFO or atrial septal defect was diagnosed in 10 patients with CE (11.2%), of whom 1

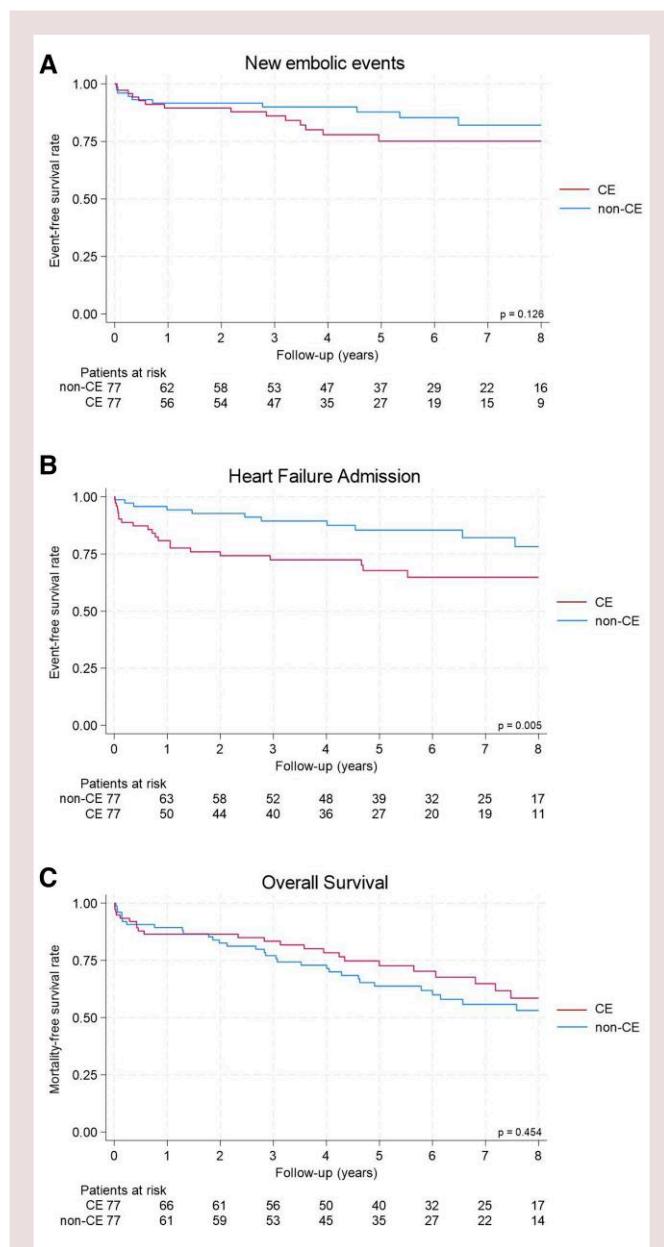


Figure 1 Kaplan–Meier curves for new embolic events (A), heart failure admission (B), and overall mortality (C).

had AF (in another patient AF was detected after PFO closure), 1 had a coagulopathy, and 1 had a malignant tumour. However, only 20 patients underwent a bubble test, presumably those patients in whom no alternative cause of CE was found. In our series, 4.5% of patients had cardiomyopathy but all of them had an additional underlying embolic source.

As previously reported,^{6,8} in our study, patients with CE were more frequently females and had fewer cardiovascular risk factors than those with atherosclerotic MI. Also in agreement with previous series,^{6,9} the occurrence of other thrombo-embolic events during admission was frequent. Notably, our study is the first to report a higher incidence of mechanical complications in CE patients. This finding can be explained by the fact that most patients presented with STEMI and that, despite thrombectomy being routinely attempted, a TIMI flow 0–1 at the end of the procedure was frequent. This rate of unsuccessful reperfusion is much higher than that observed in unselected STEMI patients¹⁶ and was related to distal vessel involvement or to distal embolization during

thrombectomy. The short-term prognostic implications of CE have differed among previous studies.^{6,8,9,17} In ours, in-hospital mortality was numerically higher in CE patients than in those with non-CE MI, but this difference was not statistically significant. However, as previously mentioned, among the eight who died, three had endocarditis, which suggests that the risk of death may be related to the underlying cause of CE.

Regarding long-term follow-up, we observed similar rates of recurrent thrombo-embolic events and mortality in patients with CE than in propensity-matched patients with non-CE MI, although the former were hospitalized more frequently for heart failure. Notably, the incidence of follow-up strokes/TIAs was identical in both groups. Only three patients in the CE group experienced recurrent myocardial infarction, all of embolic origin, compared with eight patients with non-CE MI. In previous studies, recurrent thromboembolism occurred with variable frequency,^{6,8,9} and two of these studies^{6,9} reported higher mortality rates in patients with CE than in those with non-CE MI on the long-term follow-up. In a recent study on patients with STEMI, the combination of CE and AF was associated with a more severe clinical presentation and poorer outcomes.¹⁷

The rate of hospitalizations for heart failure in CE patients was comparable to that observed by Jerónimo et al.,⁸ the only study reporting this event. The differences in long-term events between our study and previous studies^{6,9} may be explained in part by differences in patient's selection, medical treatment, and propensity score matching. Firstly, we only included patients with definite CE. Secondly, in our series, 90.9% of patients in the propensity-matched CE cohort were discharged on OAC therapy. In contrast, in the series by Popovic et al.,⁹ 21 out of 53 patients were prescribed long-term OAC therapy at discharge. In the series by Shibata et al.,⁶ recurrent thromboembolism occurred exclusively in AF patients and the mean international normalized ratio at the time of the recurrent event was below recommended values. In all, these findings underscore the importance of appropriate anticoagulation in patients with CE. Finally, at variance with previous studies,^{6,9} we compared CE patients with a non-CE MI cohort matched with a propensity score that, in addition to demographic variables and cardiovascular risk factors, included comorbidities, previous cardiac history, GRACE score, and discharge therapies. This increased the comparability of both cohorts, made that control patients were a higher-risk population (79.2% discharged on OAC for any reason), and may help explain the lack of differences in mortality after discharge observed herein.

Limitations

Several methodological considerations and limitations must be discussed. Firstly, although this is the largest reported series on CE, the number of patients included is still limited. Secondly, because of its retrospective design, the explorations in search of the embolic source were those performed according to the judgement of the treating physicians. A multicentre study including a large number of patients studied prospectively with a uniform protocol would be necessary to provide a definitive characterization of this clinical entity. And, thirdly, it may be challenging to differentiate CE from other entities such as erosion of a minimal plaque with local thrombosis or spontaneous coronary dissection, or to diagnose CE in the presence of a normal coronary angiogram. To circumvent these limitations, we relied on the consensus of expert interventional cardiologists for angiographic evaluation and only diagnosed CE if established criteria for definite CE¹ were fulfilled, although the validation for this classification is limited. However, it seems unlikely that we misdiagnosed a significant number of patients with CE, because CE prevalence in our series was lower than in other series^{6,9} and also because, in most cases, an embolic source was identified.

Conclusion

Coronary embolism accounts for ~1% of all acute MIs. The most common cause is AF. Patients with CE exhibit distinct clinical characteristics

and, when compared with patients with non-CE MI, present more frequently with STEMI, have a higher frequency of unsuccessful reperfusion, and have higher rates of recurrent embolic events and mechanical complications during index admission. Short-term mortality may be related to the underlying cause of CE. Long-term rates of thrombo-embolic events and mortality are not different from those of MI patients with comparable clinical profiles. Larger multicentre registries and trials are needed to confirm these findings and to establish optimal diagnostic protocols and treatment strategies.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding authors.

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