

## Original article

# 12-month overall mortality in ST-elevation myocardial infarction with newly diagnosed atrial fibrillation and atrial flutter compared between early oral anti-coagulant initiation and delayed oral anti-coagulant initiation

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## Abstract:

**Background:** Atrial fibrillation (AF) is a common cardiac arrhythmia after ST elevation myocardial infarction (STEMI) leading to increased short-term and long-term mortality. Recent guidelines recommend starting oral anticoagulant (OAC) based on CHA<sub>2</sub>DS<sub>2</sub>-VASc in patients with STEMI and newly diagnosed AF without mentioning a proper time of the OAC initiation. **Objective:** To study the effect of early and delayed OAC initiation on 12-month overall mortality rate in patients with STEMI and newly diagnosed AF or atrial flutter. **Methods:** We conducted a retrospective cohort study involving hospitalized patients at Siriraj Hospital in Thailand spanning from January 2008 to 2022. Participants with STEMI and newly diagnosed AF or atrial flutter were included. Participants were divided into two groups: the «early OAC group» comprising individuals initiating OAC treatment within index hospitalization, and the «delayed OAC group» including those who did not. **Results:** We enrolled a total of 65 participants, with 16 in the early OAC group and 49 in the delayed OAC group. Warfarin is the primary OAC, with only 8.2% of participants in the delayed OAC group receiving warfarin. During the 1-year follow-up period, two deaths (12.5%) occurred in the early OAC group compared to sixteen deaths (32.7%) in the delayed OAC group. The hazard ratio for overall mortality was 0.35 [95% confidence interval (CI), 0.80-1.51; p-value = 0.16]. There were 4 nonfatal strokes, all of which occurred before OAC initiation. **Conclusion:** Due to limited sample size, we were unable to demonstrate a difference in 12-month overall mortality between early and delayed OAC initiation in patients with STEMI and newly diagnosed AF or atrial flutter. Therefore, the timing of OAC initiation in these patients remains at the discretion of the attending physician. Further prospective cohort study is necessary to provide more comprehensive insights into the optimal timing of OAC initiation in newly diagnosed AF or atrial flutter after STEMI and its pathophysiology.

**Keywords:** ● Stroke prevention in atrial fibrillation ● SPAF ● Newly diagnosed atrial fibrillation  
● STEMI ● ST elevation myocardial infarction

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## นิพนธ์ต้นฉบับ

# การศึกษาเปรียบเทียบอัตราการเสียชีวิตที่ 12 เดือนในผู้ป่วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้น และได้รับการวินิจฉัยภาวะหัวใจห้องบนสั่นพลิ้วครั้งแรก ในกลุ่มที่ได้รับยาละลายลิ่มเลือดเร็ว กับกลุ่มที่ได้รับยาละลายลิ่มเลือดช้า

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## บทคัดย่อ

**ที่มาและความสำคัญ** ภาวะหัวใจห้องบนสั่นพลิ้วครั้งแรกพบได้บ่อยหลังเกิดโรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้น และส่งผลให้เกิดอัตราการตายที่สูงขึ้นทั้งในระยะสั้นและระยะยาว แนวทางเวชปฏิบัติในปัจจุบันแนะนำให้พิจารณาการให้ยาละลายลิ่มเลือดโดยใช้ CHA<sub>2</sub>DS<sub>2</sub>-VASc score แต่ไม่ได้ระบุถึงช่วงเวลาที่เหมาะสมในการเริ่มยาละลายลิ่มเลือด **วัตถุประสงค์** เพื่อเปรียบเทียบผลของการเริ่มยาละลายลิ่มเลือดเร็วกับช้าต่ออัตราการเสียชีวิตที่ 12 เดือนในผู้ป่วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้นและได้รับการวินิจฉัยภาวะหัวใจห้องบนสั่นพลิ้วครั้งแรก **วิธีดำเนินการวิจัย** ศึกษาแบบ retrospective cohort study ในผู้ป่วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้นและได้รับการวินิจฉัยภาวะหัวใจห้องบนสั่นพลิ้วครั้งแรกที่โรงพยาบาลศิริราช ตั้งแต่ปี พ.ศ. 2551-2565 โดยแบ่งผู้ป่วยออกเป็น 2 กลุ่ม ได้แก่ กลุ่มที่ได้รับยาละลายลิ่มเลือดเร็ว คือกลุ่มที่ได้ยาละลายลิ่มเลือดในช่วงที่รับการรักษาในโรงพยาบาลด้วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้น และกลุ่มที่ได้รับยาละลายลิ่มเลือดช้าคือกลุ่มที่ไม่ได้ยาละลายลิ่มเลือดในช่วงที่รับการรักษาในโรงพยาบาล **ผลการวิจัย** ผู้ป่วยทั้งหมด 65 ราย ประกอบด้วย 16 รายในกลุ่มที่ได้รับยาละลายลิ่มเลือดเร็ว และ 49 รายที่ได้รับยาละลายลิ่มเลือดช้า ยาละลายลิ่มเลือดที่ผู้ป่วยได้รับส่วนใหญ่เป็น warfarin ซึ่งในกลุ่มผู้ป่วยที่ได้รับยาละลายลิ่มเลือดช้า ได้รับ warfarin เพียงร้อยละ 8 ยาละลายลิ่มเลือดที่ผู้ป่วยได้รับส่วนใหญ่เป็น warfarin Hazard ratio ของอัตราการเสียชีวิตที่ 12 เดือนเป็น 0.35 (95% confidence interval 0.80-1.51; p-value 0.16) **สรุป** เนื่องจากขนาดกลุ่มตัวอย่างที่จำกัดทำให้ไม่สามารถแสดงความแตกต่างของอัตราการเสียชีวิตที่ 12 เดือนในผู้ป่วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้นและได้รับการวินิจฉัยภาวะหัวใจห้องบนสั่นพลิ้วครั้งแรกที่ได้รับยาละลายลิ่มเลือดเร็วกับช้าในเวลาที่เหมาะสมในการเริ่มยาละลายลิ่มเลือดจึงยังขึ้นอยู่กับการตัดสินใจของแพทย์เจ้าของไข้เป็นหลัก การศึกษาเพิ่มเติมแบบ prospective study จะเป็นส่วนสำคัญที่ช่วยบอกถึงช่วงเวลาที่เหมาะสมในการเริ่มยาละลายลิ่มเลือดและพยาธิสรีรวิทยา

**คำสำคัญ:** ● การป้องกันโรคหลอดเลือดสมองในภาวะหัวใจห้องบนสั่นพลิ้ว ● ภาวะหัวใจห้องบนสั่นพลิ้วครั้งแรก ● โรคหัวใจขาดเลือดเฉียบพลันชนิด ST segment ยกขึ้น

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ได้รับต้นฉบับ 8 กรกฎาคม 2567 แก้ไขบทความ 12 กันยายน 2567 รับลงตีพิมพ์ 19 กันยายน 2567

ต้องการสำเนาต้นฉบับติดต่อ นายแพทย์ณรงค์ชัย วัฒนวงศ์วรรณ สาขาวิชาเวชศาสตร์ป้องกันโรคหัวใจ หลอดเลือดและเมตะบอลิซึม ภาควิชาเวชศาสตร์ป้องกันและสังคม คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ถนนวังหลัง แขวงศิริราช เขตบางกอกน้อย กรุงเทพฯ 10700 โทร: 085-442-9255 E-mail: narongchai.wat@mahidol.ac.th, xfi5ng@gmail.com

## Background

Atrial fibrillation (AF) frequently occurs as a cardiac arrhythmia following ST elevation myocardial infarction (STEMI). The new-onset AF post-STEMI is associated with increased short-term and long-term mortality compared to STEMI patient without new-onset AF<sup>2-4</sup>. New-onset AF might be related to an increase in reinfarction of myocardial infarction (MI), stroke, and heart failure<sup>2,5</sup>. Current guidelines recommend commencing oral anticoagulant (OAC) therapy based on the CHA<sub>2</sub>DS<sub>2</sub>-VASc score for patients with STEMI and newly diagnosed AF. However, these guidelines do not specify the optimal timing for initiating OAC treatment<sup>9-10</sup>. According to literatures<sup>3-8</sup> only 11-32% of patients with STEMI and newly diagnosed AF were found to receive OAC as part of their home medication. We conducted a retrospective cohort study to investigate whether initiating OAC in patients with STEMI and newly diagnosed AF, or atrial flutter within index hospitalization would affect the 12-month overall mortality.

## Materials and methods

### Study design

The retrospective cohort study was performed in hospitalized patients with STEMI at Siriraj Hospital in Thailand from January 2008 to 2022. Participants were identified by ICD-10 (ICD10 I21.0, I21.1, I21.2, I21.3 for STEMI and ICD10 I48, ICD10 I48.0, ICD10 I48.4, ICD10 I48.9, ICD10 I48.91, ICD10 I48.92 for newly diagnosed AF and atrial flutter). This study received an approval from the Institutional Review Board, Faculty of Medicine, Siriraj Hospital (SIRB) (COA no. Si 118/2022).

### Study population

The study included hospitalized patients diagnosed with STEMI who were newly diagnosed with AF and atrial flutter. Participants were excluded from the study if they had rheumatic mitral stenosis, hypertrophic cardiomyopathy, a prosthetic heart valve, a history of OAC use, a previous diagnosis of AF or atrial flutter, or if they had a contraindication for OAC. The participants were categorized into 2 groups: the early OAC group, comprising those initiated with OAC during the index hospitalization, and the delayed OAC group, consisting of those not initiated with OAC during the index hospitalization. The participants were then observed for a period of 1 year.

### Outcomes

The primary outcome was 12-month overall mortality, while secondary outcomes included nonfatal stroke, recurrent MI, cardiovascular (CV) death, 3P-MACE which is a composite of CV death, nonfatal stroke and nonfatal MI, in-hospital mortality and bleeding events.

### Statistical analysis

In the sample-size calculation for the primary outcome, a hazard ratio of 0.663 was utilized, aiming for a statistical power of 90% at an alpha level of 5%. This calculation resulted in a target

sample size of 221 participants in each group. The sample-size calculation was conducted in the nQuery sample size software. The hazard ratios for both primary and secondary outcomes were analyzed using the Cox proportional-hazards model with assumption of proportional hazards assumption. The statistical analysis was conducted using Stata software version 15.1. In the statistical analysis, a two-sided *p*-value less than 0.05 was considered statistical significance.

## Results

### Study population

After applying the specified ICD-10 code, a total of 110 participants were identified as eligible for assessment. The study enrolled the remaining 65 participants who met the inclusion and exclusion criteria: 16 (24.6%) in the early OAC group and 49 (75.4%) in the delayed OAC group. The baseline characteristics of the participants are detailed in Table 1. In our study, warfarin was the primary OAC, used in 95% of cases, while the remaining participant received apixaban. Moreover, only 4 participants (8.2% of the delayed OAC group) received OAC after the index hospitalization.

**Table 1** Characteristics of the participants at baseline

Characteristic	Early OAC group (n = 16)	Delayed OAC group (n = 49)	<i>p</i> -value
Age (year) - mean $\pm$ SD	72.3 $\pm$ 10.1	68.7 $\pm$ 10.1	0.22
Male sex - no. (%)	12 (75.0)	35 (71.4)	0.78
Bodyweight (kg) - mean $\pm$ SD	62.8 $\pm$ 10.0	62.0 $\pm$ 11.0	0.81
Hypertension - no. (%)	11 (63.3)	31 (68.8)	0.69
Dyslipidemia - no. (%)	5 (31.3)	20 (40.8)	0.50
Diabetes mellitus - no. (%)	5 (28.6)	14 (31.3)	0.84
Mean GFR by Cockcroft-Gault	45.9 $\pm$ 16.7	56.3 $\pm$ 36.9	0.28
- CKD stage III - no. (%)	4 (25.0)	10 (20.4)	0.73
- ESRD - no. (%)	0	4 (8.2)	0.57
CAD - no. (%)	2 (12.5)	6 (12.2)	1.00
- PCI	0	4 (8.2)	0.57
- CABG	0	1 (2.0)	1.00
History of heart failure admission - no. (%)	0	2 (4.1)	1.00
History of ischemic stroke - no. (%)	2 (10.2)	5 (12.5)	1.00
History of hemorrhagic stroke - no. (%)	0	0	-
PAD - no. (%)	0	2 (4.1)	1.00
Cirrhosis - no. (%)	0	1 (2.0)	1.00
Cancer - no. (%)	0	3 (6.1)	0.57
History of GI bleeding - no. (%)	0	0	-
History of smoking - no. (%)	7 (43.8)	21 (42.9)	0.95

**Table 1** Characteristics of the participants at baseline (continue)

Characteristic	Early OAC group (n = 16)	Delayed OAC group (n = 49)	p-value
History of alcohol drinking - no. (%)	4 (25.0)	12 (24.5)	1.00
CHA <sub>2</sub> DS <sub>2</sub> VASc score - mean $\pm$ SD	3.6 $\pm$ 1.5	3.2 $\pm$ 1.5	0.46
HAS-BLED score - mean $\pm$ SD	2.6 $\pm$ 1.0	2.6 $\pm$ 0.8	0.83
Fibrinolysis - no. (%)	1 (6.3)	11 (22.5)	0.27
- Time to fibrinolysis (hour) - mean $\pm$ SD	3	4 $\pm$ 2.0	-
PCI - no. (%)	12 (75.0)	39 (79.6)	0.73
- Time to PCI (hour) - mean $\pm$ SD	8.7 $\pm$ 7.6	7.5 $\pm$ 6.7	0.55
CABG - no. (%)	5 (25.0)	8 (16.3)	0.47
- Time to CABG (day) - mean $\pm$ SD	2.7 $\pm$ 3.1	2.5 $\pm$ 5.1	0.66
Atrial fibrillation			
- Time to AF after STEMI (day) - mean $\pm$ SD	2.7 $\pm$ 3.1	2.5 $\pm$ 5.1	0.086
- AF duration (hour) - mean $\pm$ SD	15.0 $\pm$ 26.1	7.9 $\pm$ 7.1	0.09
- AF recurrent - no. (%)	14 (87.5)	20 (44.9)	0.003
LVEF (%) - mean $\pm$ SD	42.9 $\pm$ 11.8	44.0 $\pm$ 13.7	0.79
- LVEF $\leq$ 40% - no. (%)	8 (50.0)	21 (42.9)	0.62
LA enlargement - no. (%)	14 (87.5)	47 (95.9)	0.25
LV thrombus - no. (%)	1 (2.0)	0	1.00
Medication at discharge - no. (%)	(n = 16)	(n = 40)	
- Aspirin	16 (100)	37 (92.5)	0.55
- P2Y12i	15 (93.8)	34 (85.0)	0.66
- Beta-blocker	14 (87.5)	31 (77.5)	0.48
- ACEI/ARB	9 (56.3)	20 (50.0)	0.67
- MRA	3 (18.8)	3 (7.5)	0.34
- SGLT2i	0	0	-
- Hydralazine/nitrate	1 (6.3)	4 (10.0)	1.00
- Amiodarone	4 (25)	4 (10.0)	0.21
- Digoxin	0	0	-
- PPI	14 (87.5)	27 (67.5)	0.19
- High intensity statin	12 (75.0)	27 (67.5)	0.75
- Moderate intensity statin	2 (12.5)	8 (20.0)	0.71
- Low intensity statin	3 (7.5)	0	0.55

### Primary outcomes

Throughout the 1-year follow-up period, a total of 18 deaths (27.7% of participants) from all causes occurred in both groups: 2 deaths (12.5%) in the early OAC group and 16 deaths (32.7%) in the delayed OAC group. The hazard ratio (HR) for overall mortality was 0.35 [95% confidence interval (CI), 0.80-1.51; *p*-value = 0.16]. (Figure 1) Among the 18 all-cause deaths, 8 were non-CV

deaths (44.4% of all-cause deaths). The primary causes of non-CV deaths were infection-related (75%), followed by pulmonary-related and hemorrhage-related causes. There were 9 in-hospital deaths (13.8% of participants) solely in the delayed OAC group, comprising of 6 CV deaths (66.7% of in-hospital deaths) and 3 infection-related deaths (33.3% of in-hospital deaths). The HR for overall mortality, after excluding of in-hospital mortality, was 0.75 (95%CI: 0.16-3.61;  $p$ -value = 0.72). (Figure 2)

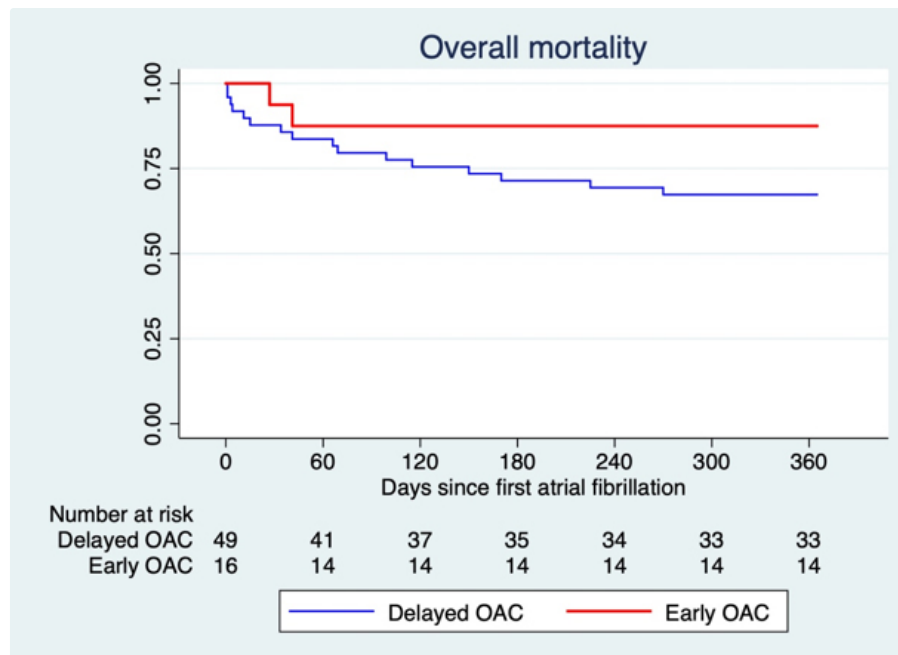


Figure 1 Overall mortality

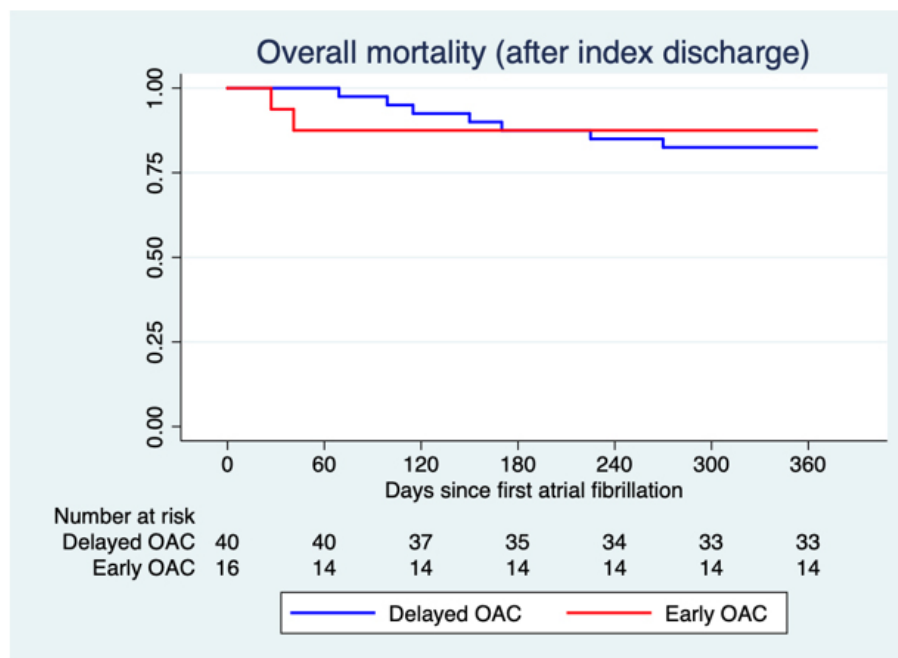


Figure 2 Overall mortality (after index discharge)

## Secondary outcomes

During the 1-year follow-up, there were 1 nonfatal stroke (6.3%) in the early OAC group and 3 nonfatal strokes (6.1%) in the delayed OAC group. The HR for nonfatal stroke was 1.03 (95%CI: 0.11-9.93;  $p$ -value = 0.98). (Figure 3) The details of 4 participants developing nonfatal stroke are described in Table 2. There were 1 CV death (6.3%) in the early OAC group and 9 CV deaths (18.4%) in the delayed OAC group. The HR for CV death was 0.32 (95%CI: 0.41-2.55;  $p$ -value

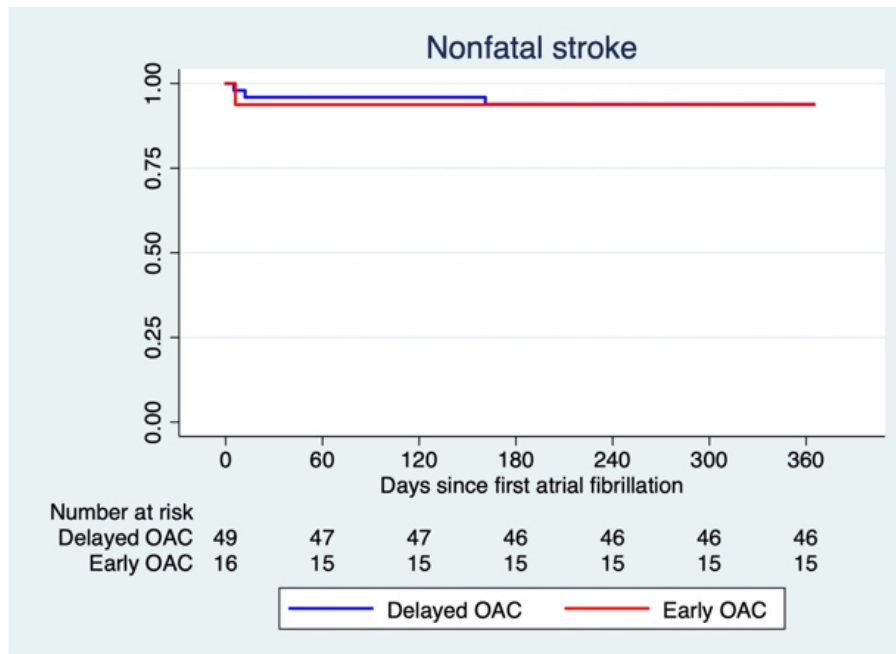


Figure 3 Nonfatal stroke

Table 2 Nonfatal stroke

Case	Sex	Age	Underlying disease	CHA <sub>2</sub> DS <sub>2</sub> -VASc score	HAS-BLED score	AF duration (hour)	Stroke after AF onset (day)	AF recurrence	OAC
1	Female	59	Hypertension T2DM Dyslipidemia	4	1	1.5	6	Yes	Delayed <sup>§</sup>
2	Female	76	Hypertension T2DM Dyslipidemia CKD stage III	6	2	5	161	No	Delayed <sup>§</sup>
3	Male	61	Current smoker	1	3	4	5	No	Delayed*
4	Female	70	Hypertension T2DM Old CVA	6	4	7.5	12	Yes	Early*

\*Warfarin was started after nonfatal stroke; <sup>§</sup>OAC was not started due to thrombocytopenia



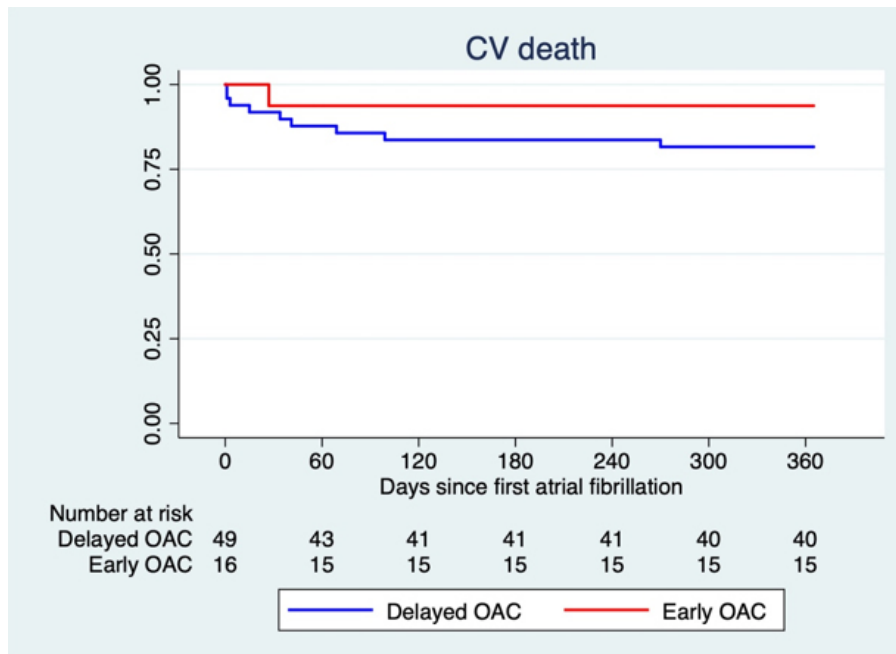


Figure 4 CV death

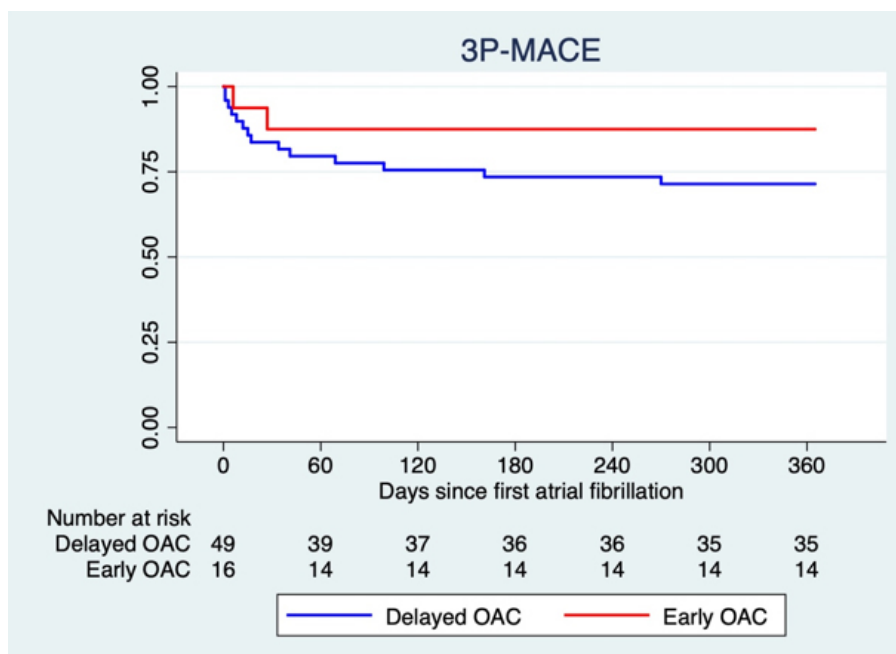


Figure 5 3P-MACE

= 0.28). (Figure 4) There were 2 recurrent MI (4.1%) only in the delayed OAC group. There were 2 3P-MACE (12.5%) in the early OAC group and 14 3P-MACE (28.6%) in the delayed OAC group. The HR for 3P-MACE was 0.41 (95%CI: 0.09-1.79;  $p$ -value = 0.23). (Figure 5) There were 3 bleeding events (6.1%) only in the delayed OAC group. All the above results are shown in the Table 3.



**Table 3** Outcome

Outcome	Early OAC group	Delayed OAC group	Hazard ratio	p-value
Overall mortality				
- No. of patient with event/ total no. (%)	2/16 (12.5)	16/49 (32.7)	0.35 (0.80-1.51)	0.16
Nonfatal stroke				
- No. of patient with event/ total no. (%)	1/16 (6.3)	3/49 (6.1)	1.03 (0.11-9.93)	0.98
CV death				
- No. of patient with event/ total no. (%)	1/16 (6.3)	9/49 (18.4)	0.32 (0.41-2.55)	0.28
Recurrent MI				
- No. of patient with event/ total no. (%)	0	2/44 (4.1)	-	-
3P-MACE				
- No. of patient with event/ total no. (%)	2/16 (12.5)	14/49 (28.6)	0.41 (0.09-1.79)	0.23
Overall mortality (after index discharge)				
- No. of patient with event/ total no. (%)	2/16 (12.5)	7/40 (17.5)	0.75 (0.16-3.61)	0.72
In-hospital mortality				
- No. of patient with event/ total no. (%)	0	9/49 (18.4)	-	-
Bleeding event				
- No. of patient with event/ total no. (%)	0	3/49 (6.1)	-	-

### Discussion

In our study, only 16 participants (24.6%) received OAC initiation within index hospitalization, which is lower than anticipated. Our study recruited participants from 2008 to 2022, under 2 different guidelines: ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation, and ESC 2017 guidelines for the management of acute myocardial infarction in patients presenting ST-segment elevation. The ACC/AHA/ESC 2006 guidelines recommended long-term treatment with OAC along with anti-platelet in patient with AF after revascularization with a potential of increased bleeding risk<sup>9</sup>. The ESC 2017 guidelines recommended considering long-term oral anticoagulation based on CHA<sub>2</sub>DS<sub>2</sub>VASc score and advice taking concomitant antithrombotic therapy into account. Importantly, the guidelines do not provide specific detailed regarding the timing of the OAC initiation<sup>10</sup>. According to the literature review, only 11-38%<sup>3-7</sup> of patients with STEMI and newly diagnosed AF received OAC at the time of discharge. These results are consistent with our study, demonstrating a comparable prevalence of OAC utilization upon discharge.

The 1-year overall mortality in the early OAC group (12.5%) appeared to be lower when compared to the delayed OAC group (32.7%). Unfortunately, we were unable to demonstrate a statistically significant difference in overall mortality between early and delayed OAC initiation in patients with STEMI and newly diagnosed AF or atrial flutter during first year after hospital discharge primarily due to limited sample size, which could be attributed by several factors. Firstly, there

may be misclassified ICD coding leading to a shortage of participants. Moreover, a brief transient episode of paroxysmal AF or atrial flutter might be overlooked. Furthermore, a substantial number of participants were referred back to their primary hospital after PCI for post-PCI care. It might be possible that newly diagnosed AF occurred after the referral, contributing to the limited participants in the study. Lastly, during the COVID-19 pandemic, Siriraj Hospital did not receive STEMI referral from nearby primary hospitals which could also be a reason for the limited number of the STEMI cases.

Our study revealed a 1-year overall mortality rate of 27.7% for AF following STEMI, which is higher than the mortality rates reported in previous studies (17-20%)<sup>6,11-12</sup>. There are several potential explanations for the poorer outcome. Firstly, our participants had a high prevalence (44.6%) of individuals with reduced left ventricular ejection fraction (LVEF < 40%), contributing to the higher mortality rate<sup>11,13-14</sup>. Additionally, 93.8% of our participants had a left atrium enlargement which is a marker of long-standing pressure overload in the left atrium and associated with increased mortality in acute myocardial infarction<sup>15-16</sup>. The timing of newly diagnosed AF post-STEMI was also identified as a potential factor associated with increased mortality. In our study, newly diagnosed AF or atrial flutter occurred after STEMI, with an average onset of 2.5 days. Previous research showed that patients developing AF post-STEMI within the 24-72 hours after admission experienced the highest 30-day mortality compared to those who developed AF either within less than 24 hours after admission or more than 72 hours after admission<sup>17</sup>. These findings underscore the significance of considering the temporal aspect of AF occurrence in the post-STEMI period as a predictor of adverse outcomes. Lastly, 50% of the deaths in our study occurred in-hospital, potentially obscuring any benefits of early OAC initiation

There was a significantly higher recurrence rate of AF or atrial flutter in the early OAC group (87.5%) compared to the delayed OAC group (44.9%). Furthermore, AF or atrial flutter in the early OAC group tended to last longer (15 hours) compared to those in the delayed OAC group (7.9 hours). Additionally, there was a participant with left ventricular thrombus only in the early OAC group. These findings could potentially be attributed to the attending physician's treatment approach, particularly early initiation of OAC.

The mean CHA<sub>2</sub>DS<sub>2</sub>VASc score in both groups was approximately 3.3, predicting a stroke risk of 3.2-4.8% per year<sup>18</sup>. Over the 1-year follow-up period, a total of 4 nonfatal strokes occurred (6.1% per year), with 3 nonfatal strokes in the delayed OAC group (6.1% per year) and 1 nonfatal stroke in the early OAC group (6.3% per year). However, all nonfatal strokes occurred before OAC initiation, with only 2 participants receiving OAC afterward, as described in Table 3. The observed stroke rate was higher than expected based on CHA<sub>2</sub>DS<sub>2</sub>VASc score. Stroke risk factors beyond CHA<sub>2</sub>DS<sub>2</sub>VASc score, such as left atrium enlargement<sup>19-21</sup>, were observed in almost all of our

participants. However, we were unable to demonstrate significant clinical or statistical difference, mainly due to limited sample size as discussed earlier.

The mean HAS-BLED score was approximately 2.6, predicting a bleeding risk of 4.1-5.8% per year<sup>22</sup> or 1.88-3.72 bleed events per 100 patient-years<sup>23</sup>. In our study, there were only 3 bleeding events in the delayed OAC group (4.6% of all participants) which is comparable to the predicted bleeding risk based on the HAS-BLED score. All bleeding events occurred in the index hospitalization, resulting in no OAC initiation afterward. We assumed that additional risk factors beyond the HAS-BLED score might have been considered by the attending physician when predicting the bleeding risk. For example, the delayed OAC group included more participants with end-stage renal disease, cirrhosis, and cancer. Furthermore, participants in the delayed OAC group tended to receive more fibrinolysis (22.5%) compared to the early OAC group (6.3%). Attending physicians likely refrained from early initiation of OAC, or even any OAC initiation, due to the high bleeding risk associated with these underlying diseases. Similarly to our study, the majority of participants (91.8%) in the delayed OAC group did not receive any OAC after in the index hospitalization. The observed effect in this group may therefore reflect patients who did not receive OAC at all.

## Conclusions

We were unable to demonstrate a significant difference in 12-month overall mortality between early and delayed initiation of OAC in patients with STEMI and newly diagnosed AF or atrial flutter, primarily due to underpowered analysis. Nevertheless, no nonfatal stroke occurred after OAC initiation. The timing of OAC initiation in these patients remains at the discretion of the attending physician, balancing the thrombotic and bleeding risks. Further prospective cohort studies are necessary to provide more comprehensive insights into the optimal timing of OAC initiation in newly diagnosed AF or atrial flutter after STEMI and its pathophysiology.

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