Journal Pre-proof

One-year recurrence rate of new-onset atrial fibrillation after acute myocardial infarction

Alicia Prieto-Lobato MD Víctor Hidalgo Olivares MD PhD Manuel Gerónimo Pardo MD PhD Marta Cubells Pastor MD Francisco Manuel Salmerón Martínez MD Miguel José Corbí-Pascual MD

PII: S0870-2551(25)00156-8

DOI: https://doi.org/doi:10.1016/j.repc.2024.12.008

Reference: REPC 2440

To appear in: *Revista Portuguesa de Cardiologia*

Received Date: 31 July 2024

Accepted Date: 9 December 2024

Please cite this article as: Prieto-Lobato A, Olivares VH, Pardo MG, Pastor MC, Martínez FMS, Corbí-Pascual MJ, One-year recurrence rate of new-onset atrial fibrillation after acute myocardial infarction, *Revista Portuguesa de Cardiologia* (2025), doi: https://doi.org/10.1016/j.repc.2024.12.008

One-year recurrence rate of new-onset atrial fibrillation after acute myocardial infarction.

Taxa de recorrência num ano de fibrilhação auricular de novo após enfarte agudo do miocárdio.

Alicia Prieto-Lobato (MD)[a,1], Víctor Hidalgo Olivares (MD, PhD)[a], Manuel Gerónimo Pardo (MD, PhD)[b], Marta Cubells Pastor (MD)[a], Francisco Manuel. Salmerón Martínez (MD)[a], Miguel José Corbí-Pascual (MD)[a].

[a]Cardiology Department at Hospital General de Albacete, Albacete, Spain.

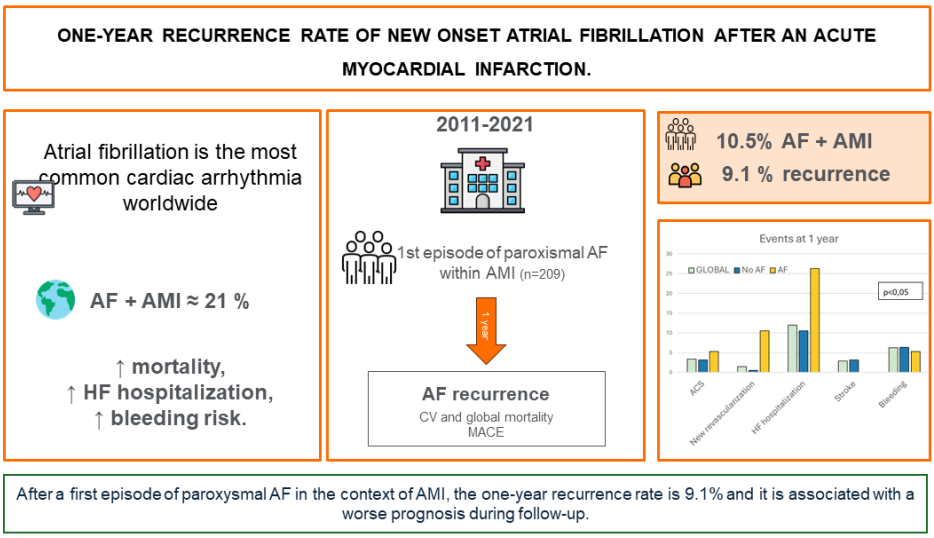
[b]Anesthesiology Department at Hospital General de Albacete, Albacete, Spain.

Address for correspondence:

Alicia Prieto Lobato,

email: alicia.prieto.lobato@psmar.cat

Graphical abstract



Graphical abstract. ACS: acute coronary syndrome; AF: atrial fibrillation; AMI: acute myocardial infarction; CV: cardiovascular; HF: heart failure; MACE: major cardiovascular adverse events; SCA: síndrome coronario agudo.

RESUMO

INTRODUÇÃO E OBJETIVOS:

A fibrilhação auricular (FA) é a arritmia cardíaca mais comum a nível mundial, com uma prevalência de até 21% na fase inicial do enfarte agudo do miocárdio (EAM). Os dados relativos à FA de início recente neste contexto são limitados, e o seu prognóstico a longo prazo permanece incerto.

MÉTODOS:

Realizámos um estudo de coorte observacional retrospetivo entre dezembro de 2011 e maio de 2021, incluindo doentes que apresentaram um primeiro episódio de FA paroxística durante a hospitalização por EAM. O resultado primário foi a taxa de recorrência de FA no primeiro ano após a alta hospitalar. Os resultados secundários incluíram mortalidade por todas as causas, mortalidade cardiovascular e um composto de eventos cardiovasculares adversos major.

RESULTADOS:

Um total de 209 doentes foi incluído. A recorrência de FA ocorreu em 19 doentes (9.1%, IC 95% 5.2-13.0%), com um tempo mediano até à recorrência de 84 dias [IQR 27.5-157.5]. Apesar da mortalidade no grupo com recorrência de FA ter sido numericamente superior à do grupo sem recorrência de FA, essa diferença não alcançou significância estatística (15.8% vs. 7.4%, p=0.19). Os doentes com recorrência de FA apresentaram um prognóstico significativamente pior (47,4% vs. 23,7%; p=0,04), principalmente devido ao aumento das hospitalizações por insuficiência cardíaca.

CONCLUSÕES:

Em doentes com um primeiro episódio de FA paroxística durante o EAM, a taxa de recorrência em um ano é relativamente baixa (9,1%), mas a recorrência de FA está

associada a um prognóstico significativamente pior, principalmente devido ao aumento das hospitalizações por insuficiência cardíaca.

PALAVRAS-CHAVE

Fibrilhação Auricular, Enfarte agudo do miocárdio, Insuficiência Cardíaca, Prognóstico

ABSTRACT

INTRODUCTION AND OBJECTIVES: Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide with a prevalence of up to 21% in the early phase of acute myocardial infarction (AMI). Data on new-onset AF in this context are limited, and long-term prognosis remains unclear.

METHODS: We conducted a retrospective observational cohort study from December 2011 to May 2021, including patients who experienced a first episode of paroxysmal AF during hospitalization for AMI. The primary outcome was the recurrence of AF within the first-year post discharge. Secondary outcomes included all-cause mortality, cardiovascular mortality, and a composite of major adverse cardiovascular events.

RESULTS: A total of 209 patients were included. There was AF recurrence in 19 patients, 9.1% (95% CI 5.2-13.0%) with a median time to recurrence of 84 days [interquartile range 27.5-157.5]. While mortality in the AF recurrence group was numerically higher than in the non-AF recurrence group, this difference did not achieve statistical significance (15.8% vs. 7.4%, p=0.19). Patients with AF recurrence had significantly worse prognosis (47.4% vs. 23.7%, p=0.04), primarily due to increased heart failure (HF) hospitalizations.

CONCLUSIONS: In patients with a first episode of paroxysmal AF during AMI, one-year recurrence is relatively low (9.1%); however; AF recurrence is associated with significantly worse prognosis, driven largely by HF hospitalizations.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide,[1] and occurrence in the setting of acute myocardial infarction (AMI) may impact prognosis. Although the prevalence of AF during AMI can reach up to 21%,[2] data on new-onset AF (NOAF) in this context remain limited, and long-term impact is not well understood. These patients are highly complex, as both conditions confer an elevated risk of thromboembolic events, which may lead to ischemic complications. Also, the use of antiplatelet and anticoagulant therapies, which are necessary to manage this risk, can exacerbate the likelihood of hemorrhagic complications.[1,3]

Several studies have reported a significant increase in mortality, heart failure (HF) hospitalization and clinically relevant bleeding in patients with AMI and AF compared to those without AF [4,5]. However, data specifically on NOAF in the context of AMI are limited and sometimes contradictory.[2,4,6–11] Some authors suggest that NOAF may be transient and self-limiting [12], which makes the long-term antithrombotic management of these patients controversial.

The introduction of direct oral anticoagulants (DOACs) has improved the management of embolic risk in AF patients. However, anticoagulant therapy, even with the safer profiles of DOACs, carries a significant risk of bleeding, which can have consequences comparable to recurrent ischemic events in terms of morbidity, mortality, and quality of life.[13] While several randomized trials have addressed anticoagulant and antiplatelet strategies in patients with a prior history of AF and AMI,[14–18] there is limited evidence on how to manage patients who develop AF for the first time during hospitalization for acute coronary syndrome (ACS).

This lack of robust evidence is reflected in current clinical guidelines, in which recommendations for antithrombotic management in this setting carry a weak level of evidence (IIaC).[1]

OBJECTIVES

The primary objective of this study was to evaluate the recurrence of AF within the first year after discharge in patients with AMI, who experienced a first episode of paroxysmal AF. For this study, the 'AF recurrence group' refers to patients who experienced a recurrence of AF during follow-up, while the 'non-AF recurrence group' refers to those who did not. To enhance readability, these groups will be referred to as the 'AF group' and 'non-AF group' from this point onward.

Secondary objectives include comparisons between the AF group and the non-AF group in terms of all-cause mortality, cardiovascular mortality, and a composite endpoint comprising hospitalization due to HF, new ACS, new revascularization, stroke, and major bleeding according to the BARC criteria (see S1. Secondary objectives)[19]. These outcomes were chosen based on prior evidence indicating their relevance in the prognosis of patients with AF and AMI.[4,5,8,20]

METHODS

Patients and study design

A retrospective observational cohort study was conducted, including consecutive patients admitted to the Cardiovascular Critical Care Unit (CCCU) of a tertiary care center from December 2011 to May 2021 with ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI) diagnosis who developed a first episode of paroxysmal AF during hospitalization.

Atrial fibrillation was defined according to current clinical practice guidelines,[1] as documented by a standard 12-lead electrocardiogram (ECG) or a single-lead ECG

tracing more than 30 seconds showing a cardiac rhythm with indiscernible P waves followed by irregular RR intervals. Paroxysmal AF was defined as AF that reverted spontaneously or required intervention within the first seven days after diagnosis[1]. Myocardial infarction was diagnosed by the attending physician according to current guidelines,[21,22] based on evidence of myocardial damage (elevated cardiac troponin levels >99th percentile of the upper reference limit), with evidence of necrosis in a clinical context consistent with myocardial ischemia. No restrictions were made regarding the type of AMI including types 1 to 5 as defined by the Universal Definition of Myocardial Infarction.[23] Coronary anatomy was assessed using diagnostic coronary angiography, and the number of diseased vessels and treated vessels was recorded. Complete revascularization was defined as the treatment of all vessels with a diameter >2 mm and lesions >70%, or >50% in the case of the left main coronary artery.

Exclusion criteria included patients with a history of prior AF (paroxysmal, permanent, or persistent even if they presented with sinus rhythm at admission), those who remained in AF at the time of discharge, and those for whom one-year follow-up was not possible. This included patients who had died during hospitalization and those who were treated in another healthcare system, as their medical records could not be reliably followed.

Demographic, laboratory, and echocardiographic data, along with interventional and pharmacological treatments during hospitalization and at discharge, were collected. All variables are defined in the supplementary material (see S2. Variable definitions). A minimum follow-up of one year from the date of hospital discharge was conducted by reviewing patients' medical records through the healthcare information system of the Castilla-La Mancha Health Service (SESCAM).

Statistical analysis

Categorical variables were expressed as number and percentage. Quantitative variables are expressed as median and interquartile range (IQR 25–75%). Normal distribution of quantitative variables was assessed using the Shapiro-Wilk test. Categorical variables were compared between groups using the χ2 test or Fisher's exact test, as appropriate. For normally distributed continuous variables, comparisons were made using Student's t-test, while the Mann-Whitney U test was used for non-normally distributed variables. Comparisons of continuous variables across independent groups were conducted using analysis of variance with Bonferroni correction for multiple comparisons. A two-sided p-value <0.05 was considered statistically significant. Survival outcomes were analyzed using Kaplan-Meier survival curves and Cox proportional hazards regression.

Multivariate regression analysis was performed, including variables related to the index event as reported in the literature,[6,24] as well as those variables that showed p<0.2 in the bivariate analysis. An additional regression analysis powered by bootstrap technique over 1000 samples was performed ad-hoc. All statistical analyses were performed using the Statistical Package for the Social Sciences software (SPSS v. 23.0 for Windows, SPSS Inc., Chicago, Illinois, USA). This article follows the STROBE recommendations [25] for reporting observational studies.

Ethics

The study was conducted in accordance with the principles of the Declaration of Helsinki and good clinical practice guidelines. It was approved by the hospital's Ethics Committee, which granted an exemption from the requirement to obtain informed consent from patients.

RESULTS

Between December 2011 and May 2021, a total of 5291 patients were admitted to the CCCU, of whom 3651 had a diagnosis of AMI. Among these, 269 patients with previous AF were excluded, leaving 3382 patients. From these, 354 developed a first episode of

AF (NOAF). After excluding patients with AF at discharge (n=87), in-hospital death (n=33), and those who were expected to be lost to follow-up due to being part of a different healthcare system (n=25), a total of 209 patients were included in the final analysis (Figure 1). Of these, 69.9% (146) were male, with a median age of 74 years [IQR 64-80].

Regarding the primary objective, 19 patients, 9.1% (confidence interval [CI] 5.2-13.0) presented a new episode of AF, of which 13 (68.4%) were paroxysmal. The median time to AF recurrence was 84 days [28–158] (S3. Kaplan-Meier analysis for AF recurrence). The clinical characteristics, ischemic event features, and treatments are detailed in Tables 1–3. Coronary angiography was performed in 98.6% of patients and percutaneous coronary intervention was the preferred revascularization strategy in both groups.

Within one year of follow-up, 17 patients (8.1%) died, including 14 (7.4%) in the non-AF group and 3 (15.8%) in the AF group (p=0.19). Cardiovascular mortality was 3.8% (8 patients), with no significant differences between groups (p=0.35) (Figure 2). Cardiovascular deaths were primarily due to HF (4 patients) and sudden cardiac death (4 patients), while non-cardiovascular causes included infections (4 patients), cancer (4 patients), and pulmonary embolism (1 patient). Cox regression and other survival analyses showed no statistically significant differences in mortality (Figure 3). The Breslow and Tarone-Ware tests were also applied to detect significant differences at the beginning or end of the curves, but did not provide significant results.

Regarding major adverse cardiovascular events, 25.8% (54 patients) experienced at least one event. Stratification by AF recurrence showed that 47.4% of patients in the AF group had a cardiovascular event within the first year, compared to 23.7% in the non-AF group (p=0.003) (Figure 4).

Multivariate regression analysis identified a potential protective effect of angiotensin-converting enzyme inhibitors (ACEis) (b=-2.82; p=0.02) on AF recurrence (S4. Regression analysis). Additional ad hoc analysis using the bootstrap technique to artificially increase the sample size suggested a relationship between diabetes and AF recurrence (b=1.47; p=0.044), as well as protective effects of ACEis and mineralocorticoid receptor blockers (MRBs) (b=-2.77; p=0.002 and b=-1.94; p=0.047, respectively) (S5. Regression analysis with bootstrapping over 1000 samples)."

DISCUSSION

The main findings of our study can be summarized as follows: 1) prevalence of NOAF in the context of AMI in this cohort is approximately 10%; 2) patients with paroxysmal AF (sinus rhythm at discharge) experience recurrence of around 10% during the first year; 3) AF recurrence was associated with worse prognosis within one year of discharge.

1) Prevalence of NOAF in the context of AMI is approximately 10%

The relationship between AF and AMI has been widely studied due to the high prevalence of both conditions and their significant clinical and socioeconomic impact.[8,26,27] However, data on NOAF are more limited. The prevalence of NOAF in the context of AMI in our cohort was 10.5% (354 patients who developed a first episode of AF during hospitalization out of 3382 patients without a prior history of AF). This finding is similar to previous studies such as the RIMA registry (8.8%) and Batra et al. (7.6%).[9,10] A key distinction in our study is the inclusion of both STEMI and NSTEMI patients, whereas previous studies often focused solely on STEMI. Furthermore, we excluded other supraventricular arrhythmias, ensuring that our analysis was specific to NOAF. Additionally, we provided information on patients' heart rhythm at discharge, finding that most were cardioverted during hospitalization (spontaneously or actively), with 24.6% remaining in AF at discharge. These findings are consistent with other studies, while also offering additional insights into rhythm management during hospitalization.

2) Patients with paroxysmal AF (sinus rhythm at discharge) present recurrence near to 10% within one year.

To our knowledge, this is the first study specifically analyzing the recurrence of paroxysmal AF in the context of AMI. We observed recurrence of 9.1% during the first year. Although continuous electrocardiographic monitoring was not used, which could lead to missed self-limiting arrhythmic episodes, our results provide valuable insights into the clinical course of NOAF following AMI. It is well established that acute ischemic events can act as triggers for AF through mechanisms such as atrial ischemia, increased left ventricular filling pressures, and subsequent atrial dilation.[6] These factors may resolve after the acute phase, potentially preventing long-term structural damage, which could explain why many patients remain in sinus rhythm during follow-up. This recurrence raises important questions about the need for long-term anticoagulation in patients who maintain sinus rhythm, especially since most of these patients receive dual antiplatelet therapy for six to 12 months post-AMI. Identifying predictors of recurrence is crucial to guiding early anticoagulation strategies. In our study, multivariate logistic regression suggested a protective effect of ACEis on AF recurrence. Given the limitations of our sample size, a secondary analysis using bootstrapping was performed, which further suggested an association between diabetes and AF recurrence and confirmed the protective effect of ACEis and angiotensin II receptor blockers.

It is worth noting that there were no significant differences in baseline characteristics or treatment between patients with and without AF recurrence, which suggests that the perceived cardiovascular risk by the treating physicians was similar across groups. However, changes in clinical practice guidelines over the decade-long study period may have introduced some bias, particularly regarding newer treatments such as neprilysin inhibitors and SGLT2 inhibitors, which were not widely available at the start of the study.

3) Arrhythmic recurrence is associated with worse prognosis in the first year after discharge.

A prior history of AF has been historically associated with worse outcomes in patients with AMI, including higher mortality, hospitalizations, and reduced quality of life.[8,9,20,28] However, NOAF, which occurs in response to acute ischemic events, may have a different prognosis. Studies have reported conflicting results regarding the impact of NOAF recurrence on outcomes.[4,9,] The CREDO-Kyoto study[4] reported that both NOAF and chronic AF were associated with increased long-term mortality in AMI patients at five years, regardless of whether sinus rhythm was restored. However, in the RIMA registry,[9] NOAF was associated with worse cardiovascular outcomes only in the short-term, particularly in the first year following AMI (HR 2.49; 95% CI 1.32–4.67; p=0.004).

In our study, AF recurrence during the first year was associated with worse clinical outcomes, especially HF hospitalizations, compared to patients who maintained sinus rhythm. Although we did not find significant differences in overall mortality, likely due to the small sample size, there was a trend toward higher mortality in the AF group. This highlights the need for closer monitoring and management of HF in patients with AF recurrence following AMI.

Larger studies are necessary to confirm the long-term impact of AF recurrence and to determine whether early rhythm control or anticoagulation strategies could improve outcomes in this high-risk group.

Limitations

Our study has certain limitations inherent to its design. Firstly, as a retrospective observational study, the data were limited to the information available in the electronic medical records, which may introduce bias or incomplete data. Additionally, as it was a single-center study, the sample size was restricted, which could limit the ability to achieve statistical significance in some analyses. As such, these results should be interpreted as

hypothesis-generating. A prospective multicenter study would be valuable to further investigate the questions raised in this analysis. Moreover, the study spans a ten-year period, during which updates to clinical practice guidelines were made as new evidence emerged. This may have introduced variability in the management of patients over time, potentially affecting the consistency of treatments and outcomes.

CONCLUSIONS

Our study provides valuable data on the prevalence of NOAF in the context of AMI over a 10-year period, confirming its frequent occurrence in routine clinical practice. Importantly, we focused on patients discharged in sinus rhythm, a cohort underrepresented in the literature. We found that arrhythmic recurrence occurred in approximately 10% of these patients within the first year. Although cardiovascular, non-cardiovascular, and overall mortality were higher in patients with AF recurrence, statistical significance was not reached likely due to sample size limitations. Nonetheless, these patients had a significantly worse prognosis at one year, mainly driven by a higher incidence of HF hospitalizations.

Larger multicenter studies are needed to better understand the factors that predispose patients to arrhythmic recurrence and worse outcomes, facilitating closer monitoring and tailored management for high-risk individuals.

Ética de la publicación

1. ¿Su trabajo ha comportado experimentación en animales?:

No

2. ¿En su trabajo intervienen pacientes o sujetos humanos?:

Sí

Si la respuesta es afirmativa, por favor, mencione el comité ético que aprobó la investigación y

el número de registro.:

Cómite Ético de la Gerencia de Atención Integrada de Albacete, estudio nº 2022-091

Si la respuesta es afirmativa, por favor, confirme que los autores han cumplido las normas

éticas relevantes para la publicación. :

Sí

Si la respuesta es afirmativa, por favor, confirme que los autores cuentan con el

consentimiento informado de los pacientes. :

Sí

3. ¿Su trabajo incluye un ensayo clínico?:

No

4. ¿Todos los datos mostrados en las figuras y tablas incluidas en el manuscrito se recogen en el

apartado de resultados y las conclusiones?:

Sí

REFERENCES

1. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2021;42(5):373–498.
2. Ruddox V, Sandven I, Munkhaugen J et al. Atrial fibrillation and the risk for myocardial infarction, all-cause mortality and heart failure: A systematic review and meta-analysis. Eur J Prev Cardiol. 2017;24(14):1555-1566.
3. Angiolillo DJ, Bhatt DL, Cannon CP, et al. Antithrombotic Therapy in Patients with Atrial Fibrillation Treated with Oral Anticoagulation Undergoing Percutaneous Coronary Intervention: A North American Perspective: 2021 Update. Circulation. 2021 Feb 9;143(6):583–96.
4. Obayashi Y, Shiomi H, Morimoto T, et al. Newly diagnosed atrial fibrillation in acute myocardial infarction. J Am Heart Assoc. 2021;10(18).
5. Luo J, Xu S, Li H, et al. Long-term impact of new-onset atrial fibrillation complicating acute myocardial infarction on heart failure. ESC Heart Fail. 2020 Oct 1;7(5):2762–72.
6. Belkouche A, Yao H, Putot A, et al. The multifaceted interplay between atrial fibrillation and myocardial infarction: A review. J Clin Med. 2021;10(2):1–15.
7. Feistritzer HJ, Desch S, Zeymer U, Fuernau G, et al. Prognostic Impact of Atrial Fibrillation in Acute Myocardial Infarction and Cardiogenic Shock: Results from the CULPRIT-SHOCK Trial. Circ Cardiovasc Interv. 2019;12(6):1–9.
8. Carnicelli AP, Owen R, Pocock SJ, et al. Atrial fibrillation and clinical outcomes 1 to 3 years after myocardial infarction. Open Heart. 2021 Dec 1;8(2).
9. Gourronc Y, Grall S, Ingremeau D, et al. De novo atrial fibrillation as an independent prognostic marker after ST-segment elevation myocardial infarction: Results from the RIMA registry. J Cardiol. 2019;74(2):123–9.
10. Batra G, Svennblad B, Held C, et al. All types of atrial fibrillation in the setting of myocardial infarction are associated with impaired outcome. Heart. 2016;102(12):926–33.
11. Pyka L, Gasior M. Atrial fibrillation and myocardial infarction – in constant need for new data. Eur J Prev Cardiol. 2019;26(13):1370–2.
12. Wang EY, Hulme OL, Khurshid S, et al. Initial Precipitants and Recurrence of Atrial Fibrillation. Circ Arrhythm Electrophysiol. 2020;13(3):e007716

13. De Caterina R, Agewall S, Andreotti F, et al. Great Debate: Triple antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting should be limited to 1 week. Eur Heart J. 2022;43(37):3512–27.

14. Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. The Lancet. 2019;394(10206):1335–43.

15. Cannon CP, Bhatt DL, Oldgren, et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. NEJM 2017;377(16):1513–24.

16. Gibson CM, Mehran R, Bode C, et al. Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI. NEJM. 2016;375(25):2423–34.

17. Lopes RD, Heizer G, Aronson R, et al. Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation. NEJM. 2019;380(16):1509–24.

18. Escobar C, Martí-Almor J, Pérez Cabeza A, et al. Direct Oral Anticoagulants Versus Vitamin K Antagonists in Real-life Patients With Atrial Fibrillation. A Systematic Review and Meta-analysis. Rev Esp Cardiol. 2019;72(4):305–16.

19. Mehran R, Rao S V., Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the bleeding academic research consortium. Circulation. 2011 Jun 14;123(23):2736–47.

20. Jabre P, Jouven X, Adnet F, et al. Atrial fibrillation and death after myocardial infarction: A community study. Circulation. 2011 May 17;123(19):2094–100.

21. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Vol. 39 Eur Heart J. 2018;39(2):119-177.

22. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42(14):1289–367.

23. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation. 2018 Nov 13;138(20):e618–51.

24. Schnabel RB, Yin X, Gona P, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: A cohort study. The Lancet. 2015 Jul 11;386(9989):154–62.

25. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for Reporting Observational Studies. J Clin Epidemiol. 2008; 61(4):344-349.

26. Kornej J, Börschel CS, Benjamin EJ et al. Epidemiology of Atrial Fibrillation in the 21st Century: Novel Methods and New Insights. Circ Res. 2020;127(1):4–20.

27. El-Shetry M, Mahfouz R, Frere AF, et al. The interplay between atrial fibrillation and acute myocardial infarction. Br J Hosp Med. 2021;82(2).

28. Jortveit J, Pripp AH, Langørgen J, et al. Poor adherence to guideline recommendations among patients with atrial fibrillation and acute myocardial infarction. Eur J Prev Cardiol. 2019;26(13):1373–82

FIGURE LEGENDS

Figure 1. Flow chart.

Flow of the patients included in the study.

Legend

AF: atrial fibrillation. AMI: acute myocardial infarction.

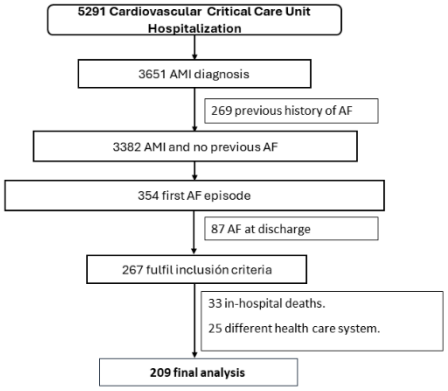


Figure 1. Flow chart of the patients included in the study.
AF: atrial fibrillation; AMI: acute myocardial infarction.

Figure 2. Mortality outcomes.

All-cause mortality, cardiovascular and non-cardiovascular mortality according to main objective (left) and Kaplan-Meier survival analysis (right).

AF: atrial fibrillation.

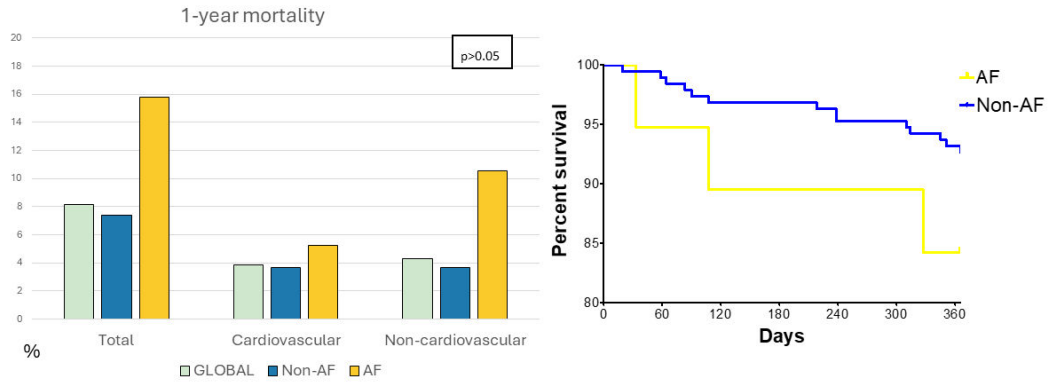


Figure 2. All-cause mortality, cardiovascular and non cardiovascular mortality according to main objective (left) and Kaplan-Meier survival analysis (right).

Figure 3. Cox proportional hazards regression.

Cox proportional hazards regression for mortality according to main objective.

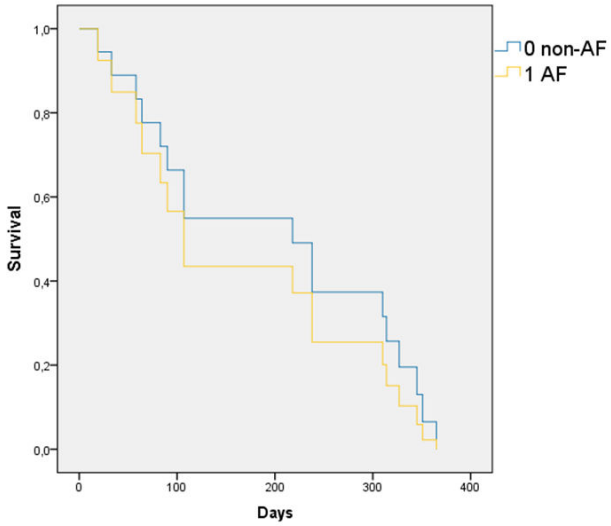


Figure 3. Cox proportional hazards regression for mortality according to main objective.

Figure 4. Outcomes at 1 year follow-up.

Events at one-year follow-up after hospitalization discharge.

Legend:

ACS: acute coronary syndrome; AF: atrial fibrillation; HF: heart failure.

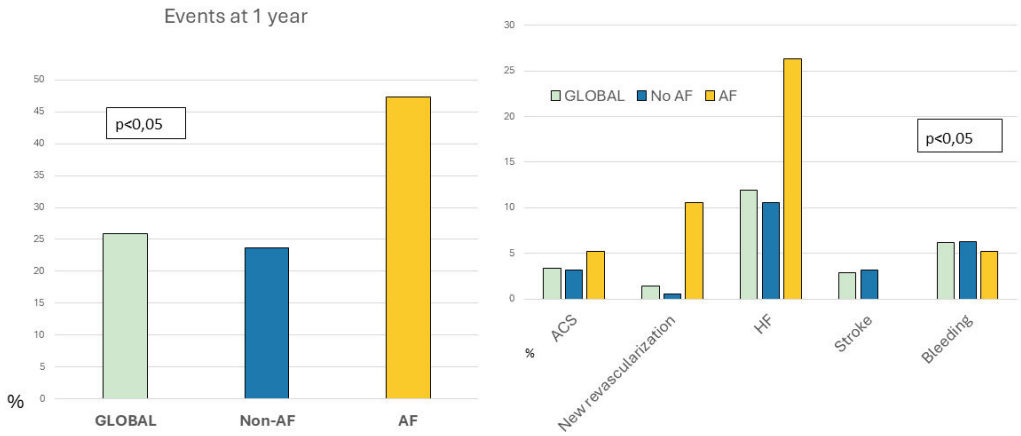


Figure 4. Events at 1 year follow-up after hospitalization discharge.
ACS: acute coronary syndrome; AF: atrial fibrillation; HF: heart failure.

TABLES

Characteristic	GLOBAL Median [Q1-Q3], n (%)	Non-AF Median [Q1-Q3], n (%)	AF Median [Q1-Q3], n (%)	p
Age, y	74 [64–80]	74 [64–81]	66 [62–76.5]	0.14
Male	146 (69.9)	134 (70.5)	12 (63.2)	0.60
Hypertension	154 (73.7)	141 (74.2)	13 (68.4)	0.59
Diabetes	72 (34.4)	68 (35.8)	4 (21.1)	0.31
HbA1ac [a]	6 [5.6–6.9]	6 [5.6–6.9]	6.2 [5.7–6.8]	0.80
Dyslipidemia	116 (55.5)	107 (56.3)	9 (47.4)	0.31
Smoker Former smoker	53 (25.4) 46 (22.0)	48 (25.3) 43 (22.6)	5 (26.4) 3 (15.8)	0.28
Coronary artery disease	27 (12.9)	25 (13.2)	2 (10.5)	0.48
Cerebral vascular disease	14 (6.7)	13 (6.8)	1 (5.3)	0.92
Peripheral vascular disease	13 (6.2)	12 (6.3)	1 (5.3)	0.49
Alcohol	11 (5.3)	9 (4.7)	2 (10.5)	0.74
Creatinine (mg/dL)	1 [0.81–1.27]	1 [0.82–1.27]	1 [0.79–1.23]	0.97
eGFR CKD-EPI (mL/min/1.73 m^2)	60 [50–75]	60 [50–75]	60 [55.7–73]	0.86
Glucose[b] (mg/dL)	165 [124–221]	166 [126–222]	147 [116–187]	0.21
Hemoglobin (g/dL)	13.6 [12.7–15.1]	13.6 [12.6–15.1]	13.9 [12.8–15.9]	0.42
LDL[c] (mg/dL)	92 [70.5–116]	92 [67–116]	92.5 [82–112]	0.39
HDL[d] (mg/dL)	43 [37–53]	43.5 [37–54]	41.5 [37–48]	0.41
CHA_2DS_2-VASC	3 [2–4]	3 [2–4]	2 [1–4]	0.12
Hospital stay (days)	9 [6–13]	9 [6–13]	9 [6.5–12.5]	0.83

Table 1. Baseline characteristic of the patients according to main objective.

[a] n=194 patients; [b] n=203 patients; [c] n=200 patients; [d] n=200. Rest of the parameters were analyzed over total n=209.

Ischemic event characteristics				
	GLOBAL Median [Q1-Q3], n (%)	Non-AF Median [Q1-Q3], n (%)	AF Median [Q1-Q3], n (%)	p
LVEF (%)	45 [35–55]	45 [35–55]	50 [32.5–60]	0.48
STEMI NSTEMI	144 (68.9) 65 (31.1)	135 (71.1) 55 (29.0)	9 (47.4) 10 (52.6)	0.05
Killip class - I - II - III - IV	 76 (36.4) 72 (34.4) 20 (9.6) 41 (19.6)	 67 (35.3) 68 (35.8) 17 (8.9) 38 (20.0)	 9 (47.4) 4 (21.1) 3 (15.8) 3 (15.8)	0.43
Diagnostic coronariography	206 (98.6%)	187 (98.4)	19 (100.0)	0.58
Number of diseased vessels	1.5 [1–2]	2 [1–2]	1 [1–2]	0.09
PCI	170 (90.4)	156 (83.0)	14 (87.5)	0.91
CABG	9 (4.8)	8 (4.3)	1 (6.3)	0.60
Complete revascularization	113 (63.1)	103 (62.8)	10 (66.7)	0.77
Creatinine Kinase peak (U/L)	1140 [473–2730]	1151 [473–2730	1122 [510.4–2485.5]	0.99
hsTnT peak (ng/L)	2966 [1172–6551]	2988.5 [1201–6430]	2338 [899–10000]	0.77
Echocardiographic parameter				
	GLOBAL Median [Q1-Q3], n (%)	Non-AF Median [Q1-Q3], n (%)	AF Median [Q1-Q3], n (%)	p
LA (AP diameter, mm)	40 [36–43]	40 [36–43]	40 [38–45]	0.40
Mitral regurgitation (baseline) - No - Mild - Moderate - Severe	 35 (16.7) 107 (51.2) 47 (22.5) 20 (9.6)	 33 (17.4) 98 (51.6) 40 (21.1) 19 (10.0)	 2 (10.5) 9 (47.4) 7 (36.8) 1 (5.2)	0.41
Mitral regurgitation (follow-up) - No - Mild - Moderate - Severe	 36 (18.9) 112 (58.9) 35 (18.4) 7 (3.7)	 33 (19.3) 103 (60.2) 29 (19.9) 6 (3.5)	 3 (15.8) 9 (47.4) 6 (31.6) 1 (5.2)	0.44

LVEF (follow-up)	50 [45–60]	50 [45–60]	50 [37.5–60]	0.51

Table 2. Characteristics related to ischemic event and echocardiographic parameters according to main objective.
AP: anteroposterior; CABG: coronary artery bypass grafting; LA: left atrial; LVEF: left ventricle ejection fraction; hsTnT: high-sensitivity T troponin; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

TREATMENT	GLOBAL n (%)	Non-AF n (%)	AF n (%)	p
ACEI	148 (70.8)	131 (69.0)	17 (89.5)	0.07
ARB	23 (11.0)	21 (11.1)	2 (10.5)	0.94
Spironolactone	39 (18.7)	36 (19.0)	3 (15.8)	0.74
Furosemide	133 (63.6)	122 (64.2)	11 (57.9)	0.62
Betablockers	161 (77.0)	146 (76.8)	15 (79.0)	0.84
Amiodarone	151 (72.2)	137 (72.1)	14 (73.7)	1
Estatine	209 (100)	190 (100)	19 (100)	
Vasopressor drugs	71 (34)	66 (34.7)	5 (26.0)	0.61
ANTIPLATHELET DRUG	GLOBAL n (%)	Non-AF n (%)	AF n (%)	P
ASA	208 (99.5)	189 (99.5)	19 (100)	0.75
Clopidogrel	174 (83.3)	160 (84.2)	14 (73.7)	0.24
Prasugrel	38 (18.2)	33 (17.4)	5 (26.3)	0.34
Ticagrelor	28 (13.4)	24 (12.6)	4 (21.1)	0.30
ANTICOAGULANT	GLOBAL n (%)	Non-AF n (%)	AF n (%)	P
No	132 (63.2)	123 (64.7)	9 (47.4)	0.60
Dabigatran	12 (5.7)	10 (5.3)	2 (10.5)	
Apixaban	30 (14.4)	26 (13.7)	4 (21.1)	
Rivaroxaban	4 (1.9)	3 (1.6)	1 (5.3)	
Edoxaban	1 (0.5)	1 (0.5)	0	
VKA	30 (14.4)	27 (14.2)	3 (15.89)	

Table 3. Drug treatment according to main objective.

ACEI: angiotensin-converting enzyme inhibitors; blockers; ARB: angiotensin receptor blocker; ASA: acetylsalicylic acid; VKA: vitamin K antagonist.

GERENCIA DE ATENCIÓN INTEGRADA DE ALBACETE

sescam

INFORME DE LA UNIDAD DE INVESTIGACIÓN O COMISIÓN DE INVESTIGACIÓN DEL CENTRO:

La Comisión de Investigación, en la reunión de 11 de octubre de 2022, ha evaluado el proyecto nº 2022-091, titulado **"FIBRILACIÓN AURICULAR EN FASE PRECOZ DE INFARTO AGUDO DE MIOCARDIO. RECURRENCIA Y PRONÓSTICO A UN AÑO. ANÁLISIS DEL MANEJO ANTITROMBÓTICO".** Investigadora Principal: **Dña. Alicia Prieto Lobato,** MIR Cardiología.

Considerando que el mencionado proyecto es viable, siendo la capacidad del Investigador Principal y la disponibilidad de medios en la Gerencia de Atención Integrada de Albacete suficientes para llevarlo a cabo.

Por tanto esta Comisión informa favorablemente acerca del mencionado proyecto.

Albacete, 11 de octubre de 2022.

ROMERO ROMAN CARLOS - 42874561P

Firmado digitalmente por ROMERO ROMAN CARLOS - 42874561P
Fecha: 2022.11.02 10:11:06 +01'00'

Fdo.:
Presidente de la Comisión de Investigación

SUPPLEMENTARY MATERIAL

S1. Secondary objectives

Secondary outcomes were defined as follows:

- All-cause mortality: Defined as death from any cause, regardless of cardiovascular or non-cardiovascular origin, occurring within the follow-up period.

- Cardiovascular mortality: Defined as death attributable to cardiovascular causes, including fatal myocardial infarction, sudden cardiac death, stroke, or heart failure (HF). All deaths will be considered cardiac unless there is documentation to the contrary.

**Note: Deaths due to pulmonary thromboembolism were categorized as non-cardiovascular, as their primary cause is thromboembolic, often associated with systemic or non-cardiovascular risk factors (e.g., immobility, surgery, hypercoagulable states such as neoplasia). While ischemic strokes also have a thromboembolic origin, they are included as cardiovascular deaths due to their frequent direct relationship with cardiac or arterial events. In contrast, pulmonary thromboembolism originates in the venous system, involving a distinct physiopathology that is not directly related to the arterial or cardiac systems.

- New acute coronary syndrome: Defined as the occurrence of unstable angina, ST-segment elevation myocardial infarction (STEMI), or non-ST-segment elevation myocardial infarction (NSTEMI), confirmed by clinical symptoms, ECG changes, and elevated cardiac biomarkers, requiring medical intervention.

- Heart failure hospitalization: Defined as any hospitalization where the primary diagnosis was acute decompensated HF, requiring intravenous diuretics, inotropes, or mechanical ventilation.

- New revascularization: Defined as any additional percutaneous coronary intervention or coronary artery bypass grafting performed during the follow-up period due to symptomatic coronary artery disease or documented ischemia.

- Stroke: Defined as any new, sudden-onset neurological deficit lasting more than 24 hours, confirmed by imaging studies (computed tomography or magnetic resonance imaging) and attributable to either ischemic or hemorrhagic causes.

- Major bleeding: Defined according to the Bleeding Academic Research Consortium criteria as type 3 or higher, which includes overt bleeding with a drop in hemoglobin of ≥3 g/dL, any bleeding requiring transfusion or surgical intervention, or any fatal bleeding event.[1]

S2. Variable definitions

Main variable

Recurrence of atrial fibrillation (AF) during follow-up documented by a healthcare professional in the first year after discharge. The presence of AF was defined according to current guidelines by the presence of a standard 12-lead ECG or a single-lead ECG tracing of more than 30 seconds showing a cardiac rhythm with unidentifiable P waves followed by irregular RR intervals.

Secondary variables:

• Age (years).

• Female gender.

• Hypertension: previous diagnosis of hypertension, treatment with antihypertensive drugs or presence of systolic blood pressure (SBP) >140mmHg and/or diastolic blood pressure (DBP) >90mmHg on two or more occasions during hospitalization, without any intervening factors justifying the elevated blood pressure readings.

• Diabetes: Previously diagnosed diabetes or presence during hospitalization of fasting glucose levels ≥ 126 mg/dl on at least two separate occasions, or glucose levels ≥200 mg/dl at any time during hospitalization accompanied by classic symptoms of hyperglycemia or hyperglycemic crisis, or the finding of an HbA1c ≥6.5%. Additionally, the type of hypoglycemic treatment (oral antidiabetic drugs or insulin) was recorded.

• HbA1c (%).

• Dyslipidemia: previous diagnosis according to current dyslipidemia management guidelines.

• Smoking: defined as active cigarette consumption at the time of admission or within the 12 months prior to admission. Former smoker was defined as a patient who had not smoked in the last 12 months.

• History of previous coronary artery disease obtained from the medical history or patient interview.

• History of peripheral arterial disease obtained from patient's medical history or interview.

• Alcohol consumption: alcoholism was defined as daily alcohol intake exceeding 50 g in women and 70 g in men, guided by patient and family interviews.

• Creatinine values at admission (laboratory reference value of 0.7 to 1.3 mg/dL) and estimated glomerular filtration rate by the CKD-EPI method.

• Glucose at admission (laboratory reference value of 74-109 mg/dL).

• Levels of HDL cholesterol (laboratory reference value of 45-65 mg/dL) and LDL cholesterol (laboratory reference value of 50-130 mg/dL).

• Hemoglobin at admission (laboratory reference value of 12-16 g/dL).

• Hospital stay (days): calculated by recording the admission and discharge dates.

• CHA2DS2-VASC score at discharge.

CHA2DS2VASC		
Risk factor		Score
C	Congestive heart failure	1
H	Hypertension	1
A	Age>75 years	2
D	Diabetes	1
S	Stroke / transient ischemic attack / systemic thromboembolism (prior)	2
V	Vascular disease (myocardial infarction / peripheral artery disease / aortic plaque).	1
A	Age 65–75 (inclusive)	1
Sc	Sex category, female	1

CHA2DS2VASc score adapted from Lip et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach 2010;137(2):263-272.

• Killip classification:

KILLIP	SYMPTOMS	MORTALITY
I	No signs of heart failure.	6%
II	Rales or crackles in the lungs, an S3 gallop, and elevated jugular venous pressure.	17%
III	Manifest acute pulmonary edema.	38%
IV	Cardiogenic shock	81%

Killip and Kimball classification for acute myocardial infarction, adapted from Killip Iii T, Kimball JT, York N. Treatment of Myocardial Infarction in a Coronary Care Unit A Two Year Experience with 250 Patients.

• Left ventricle ejection fraction measured via echocardiogram at admission and at follow-up.

• Peak creatine kinase (laboratory reference range 26–140 U/L).

• Peak high-sensitivity T troponin (upper limit of normal 14 ng/L).

• Left atrial size considering the anteroposterior diameter from the parasternal long-axis view, or alternatively from the four-chamber view.

• Mitral regurgitation diagnosed by transthoracic or transesophageal echocardiogram according to clinical practice guidelines upon admission and during follow-up.

• Treatment during admission or at discharge with angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, mineralocorticoid receptor antagonists, loop diuretics or thiazides, beta-blockers, ivabradine, amiodarone, and statins.

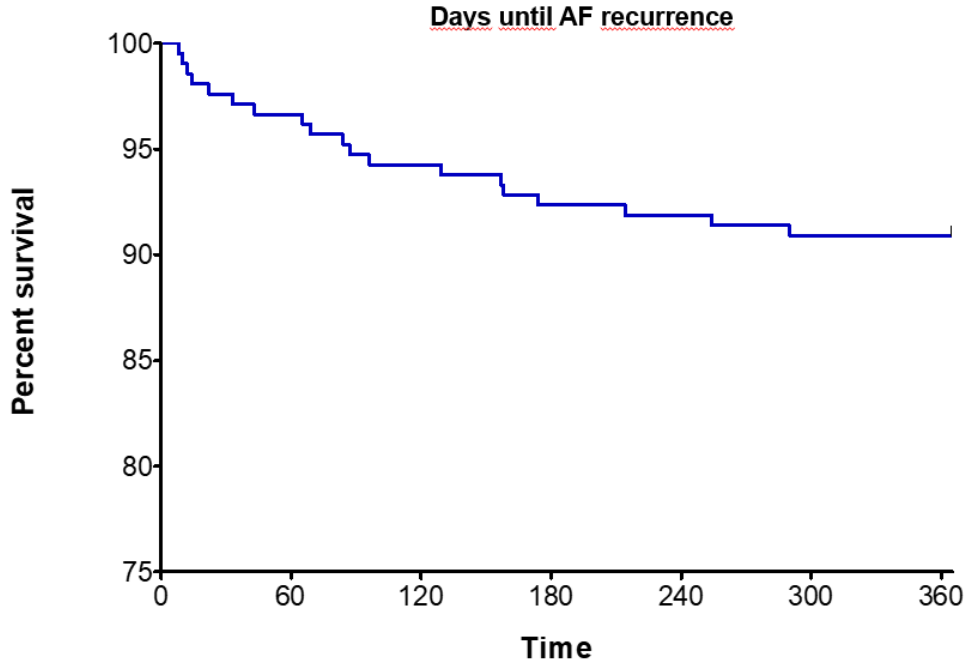
• Need for vasopressor support during admission: defined by the use of noradrenaline, dopamine, and/or dobutamine.

• Antiplatelet therapy with acetylsalicylic acid, clopidogrel, prasugrel, or ticagrelor.

• Anticoagulant therapy at discharge with vitamin K antagonist, direct-acting oral anticoagulant (rivaroxaban, apixaban, edoxaban, or dabigatran), or low-molecular-weight heparin.

• Mortality during follow-up, distinguishing between cardiovascular or any other etiology.

S3. Kaplan Meier analysis for atrial fibrillation recurrence.



AF: atrial fibrillation

S4. Regression analysis

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	209	100.0
	Missing Cases	0	.0
	Total	209	100.0
Unselected Cases		0	.0
Total		209	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The category variable statin is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Classification Table[a,b]

Observed			Predicted		
			0=no 1=AF recurrence		Percentage Correct
			0	1	
Step 0	0=no 1=AF recurrence	0	190	0	100.0
		1	19	0	.0
	Overall Percentage				90.9

a. Constant is included in the model.

b. The cut value is .500

AF: atrial fibrillation

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)
Step 0 Constant	-2.303	.241	91.578	1	.000	.100

Variables not in the Equation[a]

		Score	df	Sig.
Step 0 Variables	Age>65(1)	3.556	1	.059
	Female sex(1)	.445	1	.505
	Hypertension(1)	.299	1	.585
	Diabetes(1)	1.661	1	.197
	Smoker(1)	.010	1	.920
	Killip III-IV(1)	.058	1	.810
	hS TnT peak	.668	1	.414
	CK peak	.062	1	.804
	Vasoactive drugs (1)	.546	1	.460

	ACEis(1)	3.521	1	.061
	ARB (1)	.005	1	.944
	LVEF <50% (1)	2.570	1	.109
	LA >40mm (1)	.008	1	.930
	Mitral regurgitation > moderate(1)	.969	1	.325

a. Residual Chi-Squares are not computed because of redundancies

ACEis: angiotensin convertase enzyme inhibitors; hsTnT: high-sensitivity troponin T; LA: left atria; LVEF: left ventricle ejection fraction; MRB: mineralocorticoid receptor blockers.

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	24.924	14	.035
	Block	24.924	14	.035
	Model	24.924	14	,035

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	102.413[a]	.112	.246

a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.

Classification Table[a]

	Observed		Predicted		
			0=no 1=AF recurrence		Percentage Correct
			0	1	
Step 1	0=no 1=AF recurrence	0	189	1	99.5
		1	17	2	10.5
	Overall Percentage				91.4

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	Age>65(1)	1.261	.656	3.696	1	.055	3.529	.976	12.764
	Female sex(1)	-.732	.656	1.247	1	.264	.481	.133	1.738

	Hypertension(1)	.308	.649	.225	1	.635	1.361	.381	4.853
	Diabetes(1)	1.436	.762	3.554	1	.059	4.205	.945	18.722
	Smoker(1)	.665	.703	.896	1	.344	1.944	.491	7.705
	Killip III-IV(1)	-1.428	.883	2.614	1	.106	.240	.042	1.354
	hS TnT peak	.000	.000	4.388	1	.036	1.000	1.000	1.000
	CK peak	.000	.000	2.187	1	.139	1.000	.999	1.000
	Vasoactive drugs (1)	.881	.830	1.126	1	.289	2.414	.474	12.289
	ACEis(1)	-2.820	1.224	5.313	1	.021	.060	.005	.656
	MRB (1)	-2.015	1.306	2.382	1	.123	.133	.010	1.723
	LVEF <50% (1)	1.023	.621	2.718	1	.099	2.782	.824	9.387
	LA >40mm (1)	-.274	.614	.199	1	.656	.761	.228	2.536
	Mitral regurgitation > moderate(1)	-.583	.643	.823	1	.364	.558	.158	1.967
	Constant	-1.579	1.785	.782	1	.377	.206		

ACEis: angiotensine convertase enzime inhibitors; hsTnT: high-sensitivity troponine T; LA: left atria; LVEF: left ventricle ejection fraction; MRB: mineralocorticoid receptor blockers.

S5. Regression analysis with bootstrapping over 1000 samples

Bootstrap for Variables in the Equation

		B	Bootstrap[a]				
			Bias	Std. Error	Sig. (2-tailed)	95% Confidence Interval	
						Lower	Upper
Step 0	Constant	-2.297	-.021	.247	.001	-2.885	-1.866

a. Unless otherwise noted. bootstrap results are based on 1000 bootstrap samples

Bootstrap for Variables in the Equation

		B	Bootstrap[a]				
			Bias	Std. Error	Sig. (2-tailed)	95% Confidence Interval	
						Lower	Upper
Step 1	Age>65(1)	1.177	.319	1.376	.121	-.385	3.954
	Female sex(1)	-.819	-.185	1.049	.167	-2.709	.402
	Hypertension(1)	.307	-.024	1.312	.698	-1.677	2.395
	Diabetes(1)	1.467	.893	3.690	.044	.038	9.743
	Smoker(1)	.538	.291	1.918	.498	-1.056	3.414
	Killip III-IV(1)	-1.406	-.444	1.820	.161	-5.373	.536
	hS TnT peak	.000	.000	.000	.064	.000	.001
	CK peak	.000	.000	.000	.119	-.001	.000
	Vasoactive drugs (1)	.855	.431	1.615	.266	-.497	3.980
	ACEis(1)	-2.764	-4.395	7.169	.002	-21.148	-1.732
	MRB (1)	-1.939	-.972	7.886	.047	-20.577	15.758
	LVEF <50% (1)	.905	.239	.941	.169	-.433	3.167
	LA >40mm (1)	.052	.006	.077	.353	-.072	.228
	Mitral regurgitation > moderate(1)	-.439	-.154	1.089	.576	-2.710	1.581
	Constant	-3.715	-.890	10.843	.112	-29.875	17.262

a. Unless otherwise noted. bootstrap results are based on 1000 bootstrap samples

ACEis: angiotensine convertase enzime inhibitors; hsTnT: high-sensitivity troponine T; LA: left atria; LVEF: left ventricle ejection fraction; MRB: mineralocorticoid receptor blockers.