Temporal Relation Between Myocardial Infarction and New-Onset Atrial Fibrillation: Results from a Nationwide Registry Study

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Myocardial infarction (MI) and atrial fibrillation (AF) are commonly seen in the same patient. In this study, we evaluated the temporal relations and prognosis of MI and AF. This is a substudy of the nationwide registry−based Finnish Anticoagulation in Atrial Fibrillation (FinACAF) study, comprising all Finnish patients with new-onset AF from 2010 to 2017. Patients with MI and AF were divided into groups depending on the temporal relation between the disease onsets: (1) MI before AF (MI<AF), (2) MI ± 30 days before or after AF (MI=AF), (3) MI after AF (MI>AF), and (4) no MI. The 1-year mortality in the groups were studied with the Cox proportional hazards model. Of the 153,207 patients with new-onset AF (mean age 72.7 years, 50.0% women), 16,265 (10.6%) were diagnosed with MI. Altogether, 8,889 (54.7%) of the patients with MI were in the MI<AF group, 4,278 (26.3%) were in the MI=AF group, and 3,098 (19.1%) were in the MI>AF group. Of all MIs, 42.2% were diagnosed within 1 year from new-onset AF. The MI>AF group had the worst survival, with an adjusted hazard ratio for death of 3.08 (confidence interval [CI] 2.89 to 3.27) compared with patients without MI. For the MI<AF and MI=AF groups, the hazard ratios were 1.34 (CI 1.27 to 1.41) and 1.69 (CI 1.59 to 1.81). In conclusion, the diagnoses of MI and AF accumulated close to one another, and the survival of patients with concomitant AF and MI varied, with the worst outcome found in patients with MI diagnosed after the new-onset AF. **© 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)** **(Am J Cardiol 2024;211:49−56)**

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Myocardial infarction (MI) and atrial fibrillation (AF) commonly coexist in the same patient, with AF occurring in 6% to 21% of patients in the early setting of MI[1] and MI observed in 54% to 63% of patients previously diagnosed with AF.[2,3] AF and MI share common cardiovascular risk factors, such as increasing age, hypertension, obesity, and diabetes mellitus.[4,5] Although ischemia, MI, and left ventricular dysfunction are known triggers for AF, complex interplay of decreased blood flow, endothelial dysfunction, and increased thrombogenicity may favor plaque rupture in coronary arteries in patients with AF.[4,6] Limited data suggest clustering of disease onsets of AF and MI close to one another.[7,8] However, little is known about the temporal relation of the disease onsets of AF and MI and how this relation affects the prognosis of the patients. What seems to be clear is that patients with AF and MI have worse long- and short-term prognoses than patients with only 1 of either diagnosis.[1,9−12] Most of the studies on the association between AF and MI have been conducted on MI index cohorts. Large-scale population-based studies on the topic from an AF index perspective are lacking. The purpose of this study was to investigate the temporal relation of the disease onsets of AF and MI and the prognosis of these patients (patients with MI-AF) in a large, nationwide AF index cohort consisting of all diagnosed AF cases in the country.

Methods

The FinACAF (Finnish AntiCoagulation in Atrial Fibrillation) study is a retrospective nationwide registry-based cohort study comprising all patients with a diagnosis of AF from 2004 to 2018 in Finland. Patients were identified using data collected from 3 nationwide health care registries, including primary, secondary, and tertiary care: hospitalizations and outpatient specialist visits: CareRegister for Health Care (HILMO), primary health care: Register of

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See page 54 for Declaration of Competing Interest.

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Primary Health Care Visits (AvoHILMO), and the National Reimbursement Register upheld by the Social Insurance Institute. The inclusion criteria and the definition of AF were International Classification of Diseases, Tenth Revision (ICD-10) code I48 in any of the nationwide health care registries. The details of the study design of FinACAF were previously described.[13]

In this prespecified FinACAF substudy, the exclusion criteria were (1) age <20 years at index date, (2) permanent migration abroad before January 1, 2019, (3) any use of oral anticoagulation (OAC) medication 365 days before cohort entry, (4) warfarin prescription during 2004 to 2006, (5) recorded AF diagnosis before 2007, (6) cohort entry before 2010, and (7) cohort entry after 2017. In this way, we could focus on patients with new-onset AF, in whom AF was diagnosed for the first time during the study period. By choosing the cohort entry time between 2010 and 2017, we ensured enough history information of the patients before cohort entry and at least 1 year of follow-up time to investigate the 1-year mortality. The flow chart of the selection of the study population appears in Figure 1.

We focused on patients with new-onset AF and their first MI. The definition of MI was the first ICD-10 code I21 found in the registry for hospitalizations: CareRegister for Health Care (HILMO). Patients were divided into different MI-AF groups, depending on the time of their first recorded MI diagnosis in the registry: (1) MI before cohort entry (MI<AF) if the patient had a recorded MI diagnosis before the new-onset AF, (2) MI at the time of cohort entry (MI=AF) if the first MI diagnosis was recorded within 30 days before or after the new-onset AF, (3) MI after cohort entry (MI>AF) if the first MI diagnosis was recorded more than 30 days later than the new-onset AF, and (4) no MI if no MI diagnosis was found in the HILMO registry from 2004 to 2017. To make sure that the MI diagnosis was the first 1 recorded, patients with other coronary artery disease diagnoses (ICD-10 codes I20, I22, I23, I24, I25, and Z95.1) in any registry before the time of the first registered MI diagnosis were excluded. Patients with ICD-10 code I21 found only in the primary health care registry (AvoHILMO) but not in HILMO were also excluded to ensure that the MI diagnoses were reliably registered. The baseline characteristics of the patients (Supplementary Table 1) were compiled using data from the registries from 2004 until cohort entry, that is, at the time of the new-onset AF. Information about OAC use was included if the patient had bought the prescribed OAC before the end of the 1-year follow-up.

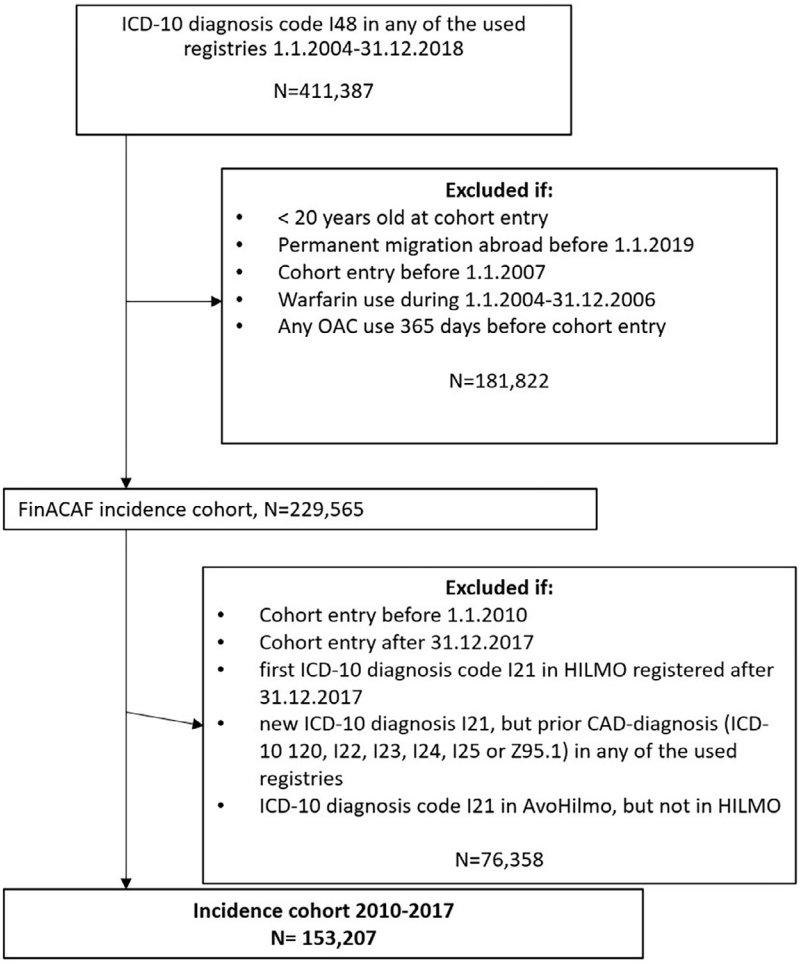

Figure 1. Flow chart of selection of the study population.

Table 1
Baseline characteristics in atrial fibrillation (AF) patients with or without myocardial infarction (MI) at time of the new-onset AF. The different MI-groups were compared to the "No MI" group

	Total cohort (n=153,207)	No MI (n=136,942)	MI<AF (n=8,889)	MI=AF (n=4,278)	MI>AF (n=3,098)
Female	76,641 (50.0%)	69,131 (50.5%)	3,777 (42.5%) p<0.001	2,052 (48.0%) p=0.001	1,681 (54.3%) p<0.001
Mean age (SD)	72.7 (13.1)	72.1 (13.3)	77.8 (10.5) p<0.001	77.1 (10.9) p<0.001	77.2 (10.5) p<0.001
Mean CHA2DS2-VASc (SD)	3.4 (1.9)	3.3 (1.9)	5.0 (1.6) p<0.001	4.5 (1.7) p<0.001	3.8 (1.7) p<0.001
Mean modified HAS-BLED (SD)	2.1 (1.1)	2.1 (1.1)	2.7 (1.0) p<0.001	2.2 (1.1) p=0.01	2.3 (1.0) p=0.33
Comorbidities:					
Hypertension	115,196 (75.2%)	101,878 (74.4%)	7,707 (86.7%) p<0.001	3,036 (71.0%) p<0.001	2,575 (83.1%) p<0.001
Congestive heart failure	26,151 (17.1%)	20,657 (15.1%)	3,596 (40.5%) p<0.001	1,327 (31.0%) p<0.001	571 (18.4%) p<0.001
Hyperlipidemia	75,216 (49.1%)	63,624 (46.5%)	8,049 (90.6%) p<0.001	2,148 (50.2%) p<0.001	1,395 (45.0%) p=0.11
Diabetes mellitus	33,858 (22.1%)	28,870 (21.1%)	3,069 (34.5%) p<0.001	1,112 (26.0%) p<0.001	807 (26.1%) p<0.001
Ischemic stroke/TIA	24,188 (15.8%)	20,960 (15.3%)	1,954 (22.0%) p<0.001	700 (16.4%) p=0.06	574 (18.5%) p<0.001
Other vascular disease	7,801 (5.1%)	6,062 (4.4%)	1,192 (13.4%) p<0.001	338 (7.9%) p<0.001	209 (6.8%) p<0.001
Thyrotoxicosis	1,531 (1.0%)	1,379 (1.0%)	94 (1.1%) p=0.65	36 (0.8%) p=0.29	22 (0.7%) p=0.10
Abnormal renal function	6,324 (4.1%)	5,022 (3.7%)	873 (9.8%) p<0.001	273 (6.4%) p<0.001	156 (5.0%) p<0.001

Data presented as mean (standard deviation) or number of patients (percent). A p-value < 0.05 was considered statistically significant.

AF = atrial fibrillation; CHA2DS2-VASc = congestive heart failure, hypertension, age ≥ 75 years, diabetes, history of stroke or TIA, vascular disease, age 65−74 years, sex category (female); MI = myocardial infarction; MI<AF = MI registered before AF; MI=AF = MI registered within 30 days from AF; MI>AF = MI registered after AF; modified HAS-BLED score, hypertension, abnormal renal or liver function, prior stroke, bleeding history, age > 65 years, alcohol abuse, concomitant antiplatelet/NSAIDs (no labile INR, max score 8); No MI = AF-patients without MI-diagnosis; TIA = transient ischemic attack.

Cohort entry date was the date of the new-onset AF. Patients were followed up 365 days starting from the date when the patient fulfilled the criterium of the combination of AF and MI diagnoses. In MI<AF patients, no patients with MI, and MI=AF with MI diagnosed <30 days before or the same day as the new-onset AF, the start of the 1-year follow-up was the cohort entry date. To avoid survival bias in our analyses, in MI>AF patients and MI=AF with MI diagnosed within 30 days after the new-onset AF, the follow-up started from the date of the first recorded MI after the AF diagnosis. The primary outcome was all-cause death. The information about the outcome was obtained from the National Causes of Death Register and Statistics Finland.

The FinACAF study was approved by the ethics committee of the Medical Faculty of Helsinki University, Helsinki, Finland (number 15/2017) and granted institutional approval from the Helsinki University Hospital (HUS/46/2018). Respective approvals were obtained from the Finnish registry holders Social Insurance Institute (138/522/2018), THL: Terveyden ja Hyvinvoinnin Laitos (2101/5.05.00/2018), Population Register Centre (VRK/1291/2019-3), and Statistics Finland (TK-53-1713-18/u1281). All patient data were pseudonymized, ensuring full data protection of the patients according to the European General Data Protection Regulation.

Statistical analyses were performed with the IBM SPSS Statistics software (version 27.0, SPSS Inc, IBM Corp, Armonk, NY) and R (R Core Team, version 4.3.0, Vienna, Austria). A p value <0.05 was considered statistically significant. The normality and distribution of the data were assessed. Qualitative variables were described as frequencies and percentages and quantitative variables with normal distribution as means ± SD. The chi-square test was used to compare differences between proportions and independent samples *t* test was used to compare continuous variables with normal distribution. A multivariable analysis for 1-year mortality in the groups of interest was performed using a Cox proportional hazards model, where the results were adjusted for all relevant baseline characteristics to obtain adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). To depict the 1-year survival in the different groups, Kaplan−Meier curves were constructed.

Results

Between 2010 and 2017, 153,207 patients with new-onset AF were identified. The mean age was 72.7 (13.1) years, and 50.0% (n = 76,641) of the patients were women (Table 1). A total of 16,265 patients (10.6%) were diagnosed with MI at any time point. The mean ages of patients with AF with or without MI were 77.5 (10.6) years and 72.1 (13.3) years, and the proportions of women were 7,510 (46.2%) and 69,131 (50.5%), respectively. At the time of cohort entry, patients in the MI<AF group had a higher burden of co-morbidities than those in the MI=AF and MI>AF groups. The mean congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke or transient ischemic attack, vascular disease, age 65−74 years, gender category (female) score (4.6 ± 1.7 vs 3.3 ± 1.9) and the modified hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol score (2.5 ± 1.0 vs 2.1 ± 1.1) were higher in patients with MI versus no MI. Especially in the MI<AF group, the mean congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke or transient ischemic attack, vascular disease, age 65 to 74 years, gender category (female) (5.0 ± 1.6, 4.5 ± 1.7, 3.8 ± 1.7) and modified HAS-BLED scores (2.7 ± 1.0, 2.2 ± 1.0, 2.3 ± 1.0) were higher than those in MI=AF and MI>AF groups. Before the end of the 1-year follow-up, 98,220 patients (64.1%) initiated OAC therapy, of whom 71.9% (n = 70,583) started warfarin and 28.1% (n = 27,637) started nonvitamin K antagonist oral anticoagulant (apixaban, rivaroxaban, dabigatran, or edoxaban).

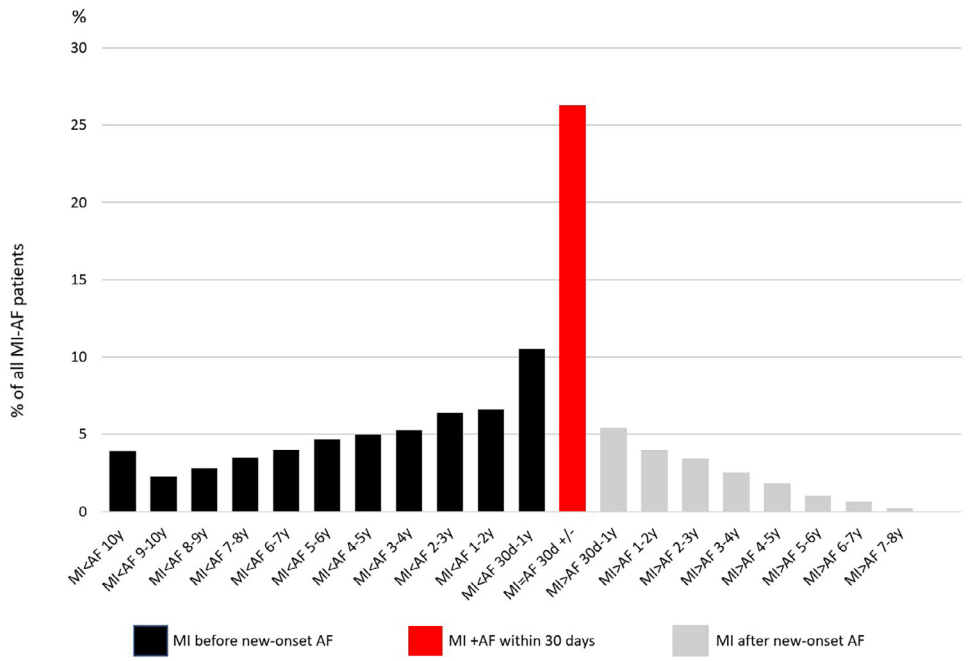

Figure 2. Temporal relation between disease onsets of first MI and new-onset AF. Frequency of first-time diagnosed MI (*y* axis) according to the temporal distance (*x* axis) from new-onset AF within 10 years preceding or 8 years after new-onset AF (n = 16,265).

The temporal relation between new-onset AF and the first MI is described Figure 2, Supplementary Table 2. Altogether, 8,889 patients with MI-AF (54.7%) had a history of established MI diagnosis (MI<AF), whereas 4,278 (26.3%) were diagnosed with MI during the same hospitalization period as new-onset AF or within 30 days (MI=AF) and 3,098 (19.1%) 30 days or later after the new-onset AF (MI>AF). A total of 6,866 of all MI diagnoses (42.2%) were diagnosed within 1 year from new-onset AF.

During the 1-year follow-up, we identified 17,972 deaths (11.7%) in the whole cohort. MI was associated with an increased 1-year mortality risk compared with patients with AF with no MI. The highest mortality was observed in the MI>AF group, with a 3-fold HR (3.08, CI 2.89 to 3.27) compared with patients with no MI. For the MI<AF group, the HR was 1.34 (CI 1.27 to 1.41) and for the MI=AF group, the HR was 1.69 (CI 1.59 to 1.81) (Figure 3, Table 2). The largest number of deaths was found in the MI>AF group (n = 1,109, 35.8%). The most common underlying cause of death in the whole cohort was atherosclerotic heart disease (n = 2,154, 12.0%), whereas the most common immediate cause of death in the whole cohort was pneumonia (n = 2,012, 11.2%). In the MI<AF and no MI groups, the most common underlying and immediate cause of death were the same: atherosclerotic heart disease and pneumonia (n = 527, 28.4% and n = 1,363, 9.7%). In the MI=AF and MI>AF groups, the most common underlying and immediate cause of death was acute MI I21.9 (n = 160, 16.6% and n = 184, 16.6%) (Table 3).

Discussion

The main findings of this nationwide AF cohort study were that the disease onsets of AF and MI tend to accumulate close to one another: 1 in 4 of all MIs were diagnosed within a ±30-day time window of the new-onset AF. Patients with AF and MI were older and had a higher burden of co-morbidities than patients with AF without MI. The co-occurrence of AF and MI was associated with a worse prognosis, especially in those with MI diagnosed more than 30 days after the new-onset AF.

Temporal relation between MI and AF has most often been described based on an MI index cohort.[8,9,11,14–17] To the best of our knowledge, this is the first nationwide study in which the investigation of the temporal relation of AF and MI has been performed based on an AF index cohort, which includes all diagnosed AF cases in the country.

The temporal relation between AF and MI has earlier been described in the retrospective BiomarCaRE (Biomarkers for Cardiovascular Risk Assessment in Europe) study, where 108,363 patients from 6 different European population-based cohorts were analyzed starting from patients without AF and MI[7] and in a community-based cohort of 3,220 patients hospitalized for their first-ever MI.[8] Our findings of the clustering of the new-onset AF and MI are similar to earlier findings, where the most recent findings were that 37%[7] and 46%[8] of AF and MI diagnoses occur within 30 days from one another. The reasons for the accumulation of AF and MI are speculative and 1 explanation is that the patients might be more frequently followed up in the clinic after the onset of 1 disease and, therefore, the other disease is more likely diagnosed.

The rate of MI diagnoses 30 days to 1 years before the new-onset AF was higher than MI diagnoses 30 days to 1 years after the new-onset AF. This could partly be explained by MI eventually being more often an underlying trigger to AF in those susceptible to the arrhythmia than AF being an underlying trigger to plaque rupture and MI.

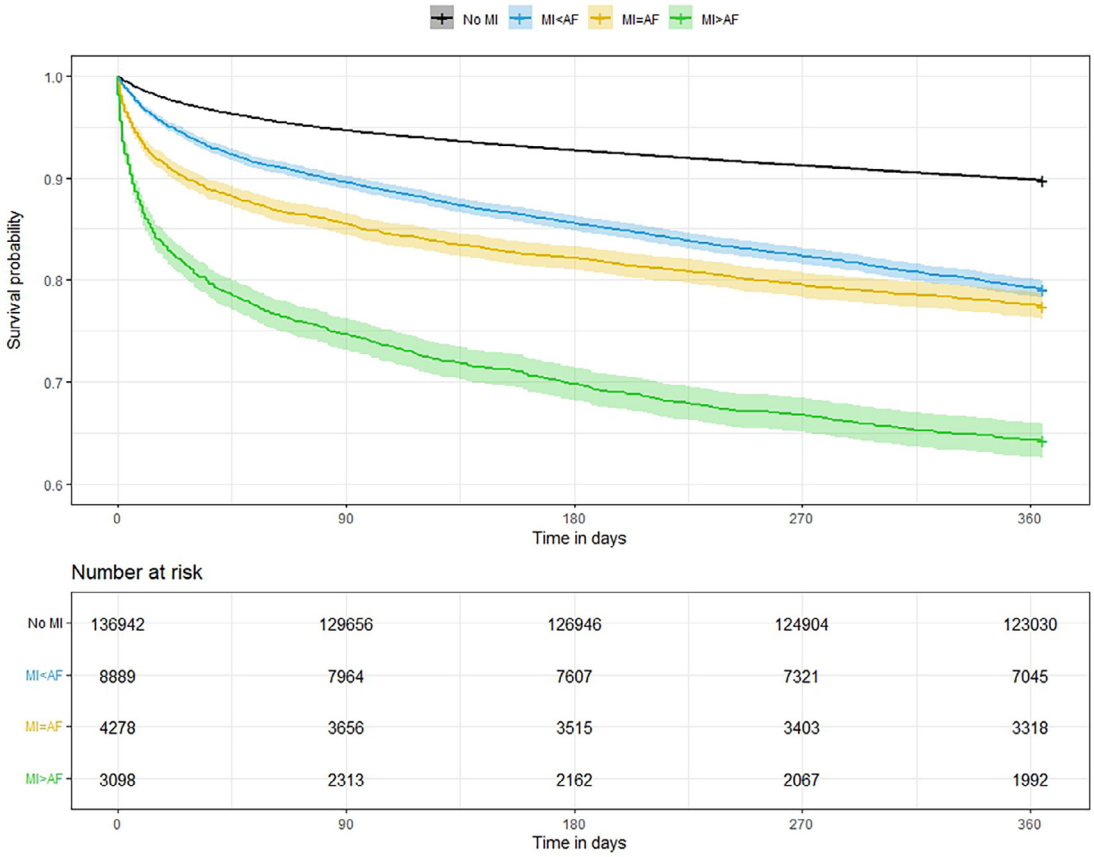

Figure 3. Kaplan−Meier curves of 1-year survival in patients with their first MI temporally associated with new-onset AF. MI<AF if MI was diagnosed before new-onset AF, MI=AF if both diseases were diagnosed within 30 days, and MI>AF if MI was diagnosed more than 30 days after new-onset AF.

Patients with MI are more frequently followed up the first years after the MI than patients with AF, which might lead to AF after MI being more frequently recognized.

It is well known that a combination of AF and MI is associated with a poor prognosis.[6,9−11,18,19] This was seen also in our study, and patients with this combination had a higher 1-year mortality than patients with AF without MI. The worst prognosis was found in the MI>AF group, which differs from previous studies, where some have reported a higher mortality in patients with new-onset AF during MI than previous AF and MI.[12,14,15,18,20] It is noteworthy that our results are not directly comparable with these earlier

Table 2
Multivariable adjusted Cox regression analysis on the association of the first myocardial infarction (MI) temporally associated with new-onset atrial fibrillation (AF) with one-year all-cause mortality

Covariate	Adjusted Hazard ratio	95% Confidence Interval	p-value
No MI	**Reference**		
MI<AF	1.34	1.27−1.41	<0.001
MI=AF	1.69	1.59−1.81	<0.001
MI>AF	3.08	2.89−3.27	<0.001
Female sex	0.77	0.75−0.80	<0.001
Hypertension	0.87	0.83−0.90	<0.001
Congestive heart failure	2.07	2.01−2.14	<0.001
Hyperlipidemia	0.72	0.70−0.74	<0.001
Diabetes mellitus	1.19	1.15−1.24	<0.001
Ischemic stroke/TIA	1.48	1.43−1.53	<0.001
Other vascular disease	1.47	1.40−1.54	<0.001
Thyrotoxicosis	0.19	0.84−1.12	0.66
Abnormal renal function	1.81	1.72−1.90	<0.001
Age when registered diagnosis of both AF and MI	1.07	1.07−1.07	<0.001

AF = atrial fibrillation; MI = myocardial infarction; MI<AF = MI registered before AF; MI=AF = MI registered within 30 days from AF; MI>AF = MI registered after AF; No MI = AF-patients without MI-diagnosis; TIA = transient ischemic attack.

Table 3
Top-5 causes of death after one-year follow-up in atrial fibrillation (AF) patients with or without myocardial infarction (MI). The total number of deaths in the whole cohort after one year follow-up was 17,972 (11.7%).

Top-5 causes of death	Total cohort (n=17,972; 11.7%)	No MI (n=14,038; 10.3%)	MI<AF (n=1,859; 20.9%)	MI=AF (n=965; 22.6%)	MI>AF (n=1,109; 35.8%)
1. Underlying cause of death	I25.1 (n=2,154; 12.0%)	I25.1 (n=1,363; 9.7%)	I25.1 (n=527; 28.4%)	I21.9 (n=160; 16.6%)	I21.9 (n=184; 16.6%)
1. Immediate cause of death	J18.9 (n=2,012; 11.2%)	J18.9 (n=1,626; 11.6%)	J18.9 (n=218; 11.7%)	I21.9 (n=106; 11.0%)	I21.9 (n=128; 11.5%)
2. Underlying cause of death	I21.9 (n=733; 4.1%)	I11.0 (n=666; 4.7%)	I21.9 (n=112; 6.0%)	I25.1 (n=130; 13.5%)	I21.4 (n=176; 15.9%)
2. Immediate cause of death	I50.9 (n=896; 5.0%)	I50.9 (n=647; 4.6%)	I50.9 (n=135; 7.3%)	I21.4 (n=69; 7.2%)	I21.4 (n=126; 11.4%)
3. Underlying cause of death	I11.0 (n=725; 4.0%)	I63.9 (n=604; 4.3%)	I25.9 (n=95; 5.1%)	I21.4 (n=128; 13.3%)	I25.1 (n=134; 12.1%)
3. Immediate cause of death	I21.9 (n=539; 3.0%)	I50.0 (n=328; 2.3%)	I21.9 (n=90; 4.8%)	J18.9 (n=68; 7.1%)	J18.9 (n=100; 9.0%)
4. Underlying cause of death	I63.9 (n=706; 3.9%)	I63.4 (n=470; 3.4%)	I21.4 (n=90; 4.8%)	I21.0 (n=54; 5.6%)	I21.0 (n=60; 5.4%)
4. Immediate cause of death	I50.0 (n=459; 2.6%)	J15.9 (n=257; 1.8%)	I21.4 (n=69; 3.7%)	I50.9 (n=59; 6.1%)	I50.9 (n=55; 5.0%)
5. Underlying cause of death	I25.9 (n=537; 3.0%)	G30.1 (n=439; 3.1%)	I63.9 (n=54; 2.9%)	I21.1 (n=35; 3.6%)	I25.9 (n=40; 3.6%)
5. Immediate cause of death	J15.9 (n=316; 1.8%)	I21.9 (n=215; 1.5%)	I50.0 (n=60; 3.2%)	I21.0 (n=35; 3.6%)	I21.0 (n=43; 3.9%)

Data presented as n = absolute number of deaths in the specific group, %= relative amount of the deaths in the specific group. The diagnoses of death are based on the International Classification of Diseases, 10th Revision.

G30.1 = Alzheimer disease with late onset; I11.0 = Hypertensive heart disease with (congestive) heart failure; I21.0 = Acute transmural myocardial infarction of anterior wall; I21.1 = Acute transmural myocardial infarction of inferior wall; I21.4 = Acute subendocardial myocardial infarction; I21.9 = Acute myocardial infarction, unspecified; I25.1 = Atherosclerotic heart disease; I25.9 = Chronic ischemic heart disease, unspecified; I50.0 = Congestive heart failure; I50.9 = Heart failure, unspecified; I63.4 = Cerebral infarction due to embolism of cerebral arteries; I63.9 = Cerebral infarction, unspecified; J15.9 = Bacterial pneumonia, unspecified; J18.9 = Pneumonia, unspecified. AF = atrial fibrillation; MI = myocardial infarction; MI<AF = MI registered before AF; MI=AF = MI registered within 30 days from AF; MI>AF = MI registered after AF; No MI = AF-patients without MI.

studies because our index cohort focuses on patients with new-onset AF and, therefore, all patients included in the MI<AF group must have survived from the time of MI until the new-onset AF and cohort entry. In contrast, in the MI>AF group, the 1-year follow-up starts from the time of the MI diagnosis because all patients in the MI>AF group are patients who have survived from the new-onset AF until the diagnosis of the MI. In the Supplements, we have demonstrated the survival curves if the 1-year follow-up would have started from the diagnosis of new-onset AF in all MI groups and in the MI>AF group. Here, we can see that the mortality would be significantly lower in this particular group (Supplementary Tables 1 and 3). The MI>AF group, which had the worst 1-year survival, showed a 20% mortality rate within the first 30 days after the MI (Figure 3). A possible explanation for the significantly higher mortality in the MI>AF group could be their older age at start of the follow-up than the other MI-AF groups (Supplementary Table 4), but it tells us also about the problems we are facing when it comes to the clinical care of patients with AF with acute MI.[21]

Comparing the causes of death in the different MI-AF groups, the deaths related to MI were more prominent in the MI=AF and MI>AF groups than in the MI<AF and no MI groups. This finding denotes earlier findings about the vulnerability of patients with AF who experienced an MI: patients with AF often have a more severe infarction than patients without AF.[11,19,22]

Because our study is based on registry data, our findings are reliant on the general limitations of such approaches. Therefore, there is lack of data, for example, on smoking habits, alcohol use, height, or weight.

The patients with MI have been recognized particularly from the Finnish special care register (HILMO), which has a long history of high quality and is well validated; thus, the diagnosis of MI should be reliably registered.[23] A particular strength of our study is the use of comprehensive nationwide data of all patients recorded with AF in Finland, encompassing a large and unselected patient population. Earlier studies often have focused on index cohorts of patients with MI, but our index cohort consists of patients with new-onset AF, which gives a new viewpoint to the investigation of the relation between AF and MI.

In conclusion, the diagnoses of AF and MI accumulated close to one another. The 1-year survival of patients with concomitant AF and MI varied, depending on the temporal relation between the disease onsets. The worst outcome was found in patients with MI diagnosed after the new-onset AF. Our study emphasizes the recognition of this frail and high-risk group of patients with AF and MI.

Declaration of Competing Interest

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Authors' Contributions

Elin Karlsson: conceptualization, method, investigation, data curation, formal analysis, writing − original draft, visualization. Tuomas Kiviniemi: conceptualization, method, writing − review & editing, supervision, visualization. Olli Halminen: conceptualization, method, investigation, data curation, writing − review & editing. Ossi Lehtonen: conceptualization, method, investigation, data curation, writing − review & editing. Konsta Teppo: conceptualization, method, writing − review & editing. Jari Haukka: conceptualization, method, data curation, writing − review & editing, supervision. Pirjo Mustonen: conceptualization, method, writing − review & editing, supervision. Jukka Putaala: conceptualization, method, Writing − review & editing, supervision. Miika Linna: conceptualization, method, writing − review & editing, supervision. Juha Hartikainen: conceptualization, method, writing − review & editing, supervision. K.E. Juhani Airaksinen: conceptualization, method, writing − review & editing, supervision. Mika Lehto: conceptualization, method, visualization, writing − review & editing, supervision, project administration, funding acquisition.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.10.071.

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