Atrial Fibrillation and the Risk of Sudden Cardiac Death: Incidence, Impact, and Implications

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ABSTRACT

Background: Atrial fibrillation (AF) may be linked to increased sudden cardiac death (SCD) risk, but AF patients are often neglected in studies on ECG risk factors for SCD. We aimed to clarify the long-term SCD incidence in AF among patients undergoing coronary angiography.

Methods: SCD incidence was retrospectively assessed between 2007–2018 in patients with suspected or known coronary artery disease referred for elective angiography and in acute coronary syndrome (ACS) patients. Follow-up extended until December 31st, 2022. SCD (defined per AHA/ACC/HRS/ESC guidelines) and SCD-equivalent events occurring during follow-up were identified through in-depth review of medical records, including accounts of circumstances leading to deaths. History of AF was identified through review of medical records, while AF at baseline and during follow-up was detected using the GE HealthCare Marquette 12SL algorithm.

Results: 9,622 ACS and 11,799 elective patients were included, with 955 SCD events during follow-up. The 10-year SCD incidence among AF patients was 7.7% in ACS and 6.4% in elective patients, compared to 4.5% and 3.2% in those without AF. In competing risk models adjusted for baseline risk factors including left ventricular ejection fraction, AF was associated with SCD (ACS: subdistribution hazard 1.33 [1.05–1.67]; elective: 1.37 [1.10–1.71]), but this was no longer evident in the elective cohort after adjusting for incident heart failure hospitalizations, which AF preceded in 57.5% by an average of 1.4 years. Overall, 33% of SCD cases occurred in patients with known AF (paroxysmal, persistent or permanent), and 21% of SCD victims had AF on their last ECG.

Conclusions: A significant proportion of SCDs occur in AF patients but the risk appears mediated by heart failure hospitalizations rather than AF itself.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting millions of individuals worldwide. Its prevalence increases sharply with age and AF is often associated with comorbid conditions such as hypertension, coronary artery disease (CAD), and heart failure[1]. AF has traditionally been considered as a risk factor for thromboembolic events, particularly ischemic stroke. However, emerging evidence suggests that AF may affect the pathogenesis of sudden cardiac death (SCD)[2,3].

AF frequently coexists with left ventricular dysfunction[4], which increases the likelihood of fatal ventricular arrhythmias. Comorbid cardiovascular diseases liked to AF, including diabetes, vascular disease and prior myocardial infarction (MI) all increase the SCD risk[1,5]. SCD is the leading cause of death among patients with AF[1,4,5], highlighting the need to explore whether AF independently contributes to SCD risk. Alternatively, the elevated SCD risk observed in AF patients could simply reflect the presence of underlying cardiovascular diseases commonly associated with AF[6].

Studies investigating electrocardiographic (ECG) predictors and ECG-based risk scores for SCD have consistently excluded patients with AF[7–14], limiting the understanding of the SCD risk in these individuals. Given that CAD remains the primary cause of SCD, accounting for approximately 80% of cases[15], it is surprising that the role of AF in SCD risk among patients with CAD remains inadequately characterized. Thus, the purpose of this study was to clarify the long-term incidence of SCD in AF patients across a broad spectrum of CAD, including both patients undergoing coronary angiography for the assessment of suspected or known CAD, and those being evaluated for acute coronary syndrome (ACS).

METHODS

All consecutive patients undergoing coronary angiography for suspected chronic CAD, arrhythmia, cardiothoracic surgery evaluation, or ACS at TAYS Heart Hospital, Finland, between January 1st, 2007, and December 31st, 2018, were included. Heart Hospital is the sole provider of invasive cardiac care for 500,000 residents in Pirkanmaa and the only cardiothoracic surgery center in a broader area of approximately 1 million residents.

Only the first coronary angiography was included for patients who underwent multiple procedures. Patients with suspected ACS who did not receive coronary angiography were excluded, accounting for less than 8% of all ACS cases at Heart Hospital. Coronary syndrome classification followed ESC and AHA/ACC guidelines.

Medical histories were obtained from the MADDEC database, which integrates retrospective data from all written and electronic hospital records. Diagnostic data, including echocardiography and angiography, were sourced from the prospectively maintained KARDIO registry. Missing data were supplemented through detailed review of health records (Supplementary Methods). A detailed description of the MADDEC study has been previously published[16].

Assessment of atrial fibrillation (primary exposure)

Baseline AF was defined as either a documented history of paroxysmal or persistent AF (in patients in sinus rhythm at baseline) or AF on the presenting ECG near the time of coronary angiography. History of AF was verified by review of electronic records from 2004 onwards (paper records were not used thereafter). All ECGs were collected in a regional electronic database (Fimlab Laboratoriot Oy), and GE HealthCare Marquette 12SL algorithm was used to identify AF. For the ACS cohort, baseline ECG was the one recorded within 30 days after angiography; for elective patients, the ECG taken before angiography was used.

Follow-up and Endpoints

Each patient was followed from initial angiography until death or December 31st, 2022. The primary endpoint was SCD, defined according to ESC and AHA/ACC/HRS guidelines[17,18], including true SCD events or situations where SCD would have occurred, unless successfully resuscitated.

SCD was specifically defined as: I) Unexpected and sudden natural death from a cardiac cause, occurring within one hour of symptom onset, or in patients found deceased within 24 hours of being asymptomatic[17,18]; II) An event that would have led to SCD (symptom onset <1 hour) but was prevented by successful cardiopulmonary resuscitation; and III) Episodes of rapid ventricular tachycardia and ventricular fibrillation resulting in hemodynamic collapse, but adequately treated with implantable cardioverter-defibrillator (ICD) therapy.

Endpoint data were gathered from written medical records, death certificates, and Statistics Finland. Statistics Finland offers comprehensive data on all deaths among Finnish citizens and permanent residents, including coverage for deaths occurring abroad[16].

In Finland, legislation mandates that the attending physician provide a written death certificate for all deaths, listing all diseases and circumstances surrounding the death, which is reviewed by a medico-legal expert before cause-of-death classification and may lead to further investigation[19]. If the cause of death cannot be determined through clinical information and post-mortem inspection, a medical autopsy is mandated by Finnish law. In cases of sudden or unexpected death, or fatalities occurring within one month of a medical procedure, a medico-legal autopsy is required. A significant proportion (21%) of all deaths undergo autopsy in Finland[19]. Successfully resuscitated patients were identified via comprehensive review of all medical records. Suspected SCD cases were individually assessed using previously defined methods to identify those most likely to have been caused by SCD. For ICD patients, records and device data (EGM, therapy type, event descriptions) were reviewed to verify life-threatening arrhythmias with hemodynamic collapse. If multiple endpoints occurred, the first was used for analysis.

Deaths of cardiac origin that were non-sudden or expected were not classified as SCDs. Similarly, deaths were not categorized as SCDs if the patient had prolonged cardiac symptoms during hospitalization, very poor functional capacity, severe dementia, or was receiving palliative care[20]. If the circumstances surrounding the death or the timeline were unclear or imprecise, the death was not considered an SCD.

Statistical Analysis

Fine-Gray subdistribution hazard models (SDH) were used for survival analysis, treating other-cause death as a competing risk. Adjustments included age, sex, diabetes, CAD severity, prior MI, serum creatinine, and left ventricular ejection fraction (LVEF), based on clinical judgment and prior evidence[4,5]. Analyses were stratified by baseline AF status: history of paroxysmal or persistent AF with sinus rhythm, and AF present in ECG. Results were reported separately for ACS and elective cohorts and combined via fixed-effects inverse variance meta-analysis if no heterogeneity was found (I^2 $p > 0.05$). Subgroup analyses by age (<70 vs. ≥70) and other clinically relevant variables assessed whether the AF–SCD association varied across potentially higher-risk groups. Additional sensitivity analyses were adjusted for hypertension, coronary syndrome type (chronic coronary syndrome/UAP/NSTEMI/STEMI), and ventricular fibrillation/tachycardia during hospitalization. Finally, AF and incident heart failure hospitalizations, revascularizations, and ICD implantations were modelled as time-varying covariates (Supplementary Methods). ECG records were screened to determine the proportion of SCDs occurring in patients with AF during follow-up.

RESULTS

Between January 1st, 2007, and December 31st, 2018, a total of 31,188 coronary angiographies were performed for 22,697 patients, some of whom underwent multiple procedures. Of these, 1,276 patients with incomplete ECG data were excluded. The final study population included 11,799 elective patients referred for angiography and 9,622 patients presenting with ACS (Supplementary Figure 1). CAD was diagnosed on coronary angiography in 88.4% (n=8,504) of ACS cohort and in 55.1% (n=6,503) of elective cohort. In ACS cohort, 95% of the baseline ECGs were taken within 7 days of the procedure, while median time from ECG to angiography was six days (90% of all ECG taken before or at the day of angiography).

Overall, 1,684 patients (17.5%) in the ACS cohort and in 3,104 patients (26.3%) in the elective cohort had AF (documented history of AF or AF present in their ECG at baseline). The prevalence of AF in baseline ECG was lower compared to the overall AF prevalence in both cohorts: 7.2% (n=692) in ACS and 11.5% (n=1,358) in elective cohort. AF was associated with a higher prevalence of traditional cardiovascular risk factors at baseline (Table 1).

No patients were lost to follow-up in this study (death certificate was available for all deceased patients), and the autopsy rate for fatal SCD in ACS cohort was 55%. Follow-up times were 7.6 years (interquartile range [IQR] 4.7-11.9) in ACS cohort and 8.5 years (5.4-11.9) in elective cohort, during which 486 (5.1%) and 469 (4.0%) incident SCDs occurred in ACS and elective cohorts, respectively. Appropriate ICD shocks for rapid ventricular tachycardia or ventricular fibrillation leading to hemodynamic collapse accounted for 64 cases (13.2%) and 71 cases (15.1%) of all SCD events in the ACS and elective cohorts, respectively (Table 2).

Atrial fibrillation and the incidence of sudden cardiac death

The unadjusted cumulative incidences of SCD at ten years were 7.7% in ACS cohort and 6.4% in elective cohort among patients with AF, whereas the corresponding incidence of SCD in patients with no AF at baseline were 4.5% in ACS cohort and 3.2% in elective cohort (Figure 1) after accounting for competing events due to other (non-SCD) deaths. Table 3 shows adjusted

SDH for SCD according to AF status in both cohorts and meta-analysis. Briefly, the age- and sex-adjusted SDH for SCD was 1.71-fold higher (95% confidence interval 1.46–1.99, p<0.001) in AF patients compared to those without AF. This association remained significant regardless of adjustments for other baseline risk factors and even additionally with LVEF. However, the association was attenuated when LVEF was added to the model (SDH 1.35; 1.15–1.59; p<0.001). In additional sensitivity analyses, further adjustment for hypertension, coronary syndrome type, and ventricular fibrillation/tachycardia during hospitalization yielded similar results (Supplementary Table 1). Patients with AF also exhibited higher overall long-term mortality (Supplementary Figure 2).

When stratified by AF type, the results showed that AF recorded on ECG at baseline was a stronger risk factor for SCD than only a history of AF in patients in sinus rhythm at baseline (SDH 1.97; 1.47–2.67 vs. SDH 1.51; 1.27–1.80; Table 4).

Subgroup analyses

Subgroup analyses adjusted for age and sex suggested a stronger AF–SCD association in patients under 70 years and those without angiographic stenosis (p<0.01 for both; Figure 2).

In patients <70 years, AF was linked to 2.32-fold higher SCD risk (SDH 1.85–2.92; p<0.001; adjusted for age, sex, diabetes, prior MI, creatinine, and CAD severity). This remained significant after further LVEF adjustment (SDH 1.75; 1.38–2.21; p<0.001). In patients ≥70 years, the association was borderline significant before (SDH 1.29; 1.06–1.58; p=0.013) and non-significant after LVEF adjustment (SDH 1.13; 0.92–1.40; p=0.239).

Among patients without significant stenosis in coronary angiography, AF was associated with 2.54-fold higher risk (SDH 1.80–3.59, p<0.001), remaining significant after LVEF adjustment (SDH 2.00; 1.40–2.85, p<0.001). In those with at least one significant stenosis, the adjusted association was weaker but remained significant both before (SDH 1.47; 1.24–1.76, p<0.001) and after LVEF adjustment (SDH 1.25; 1.04–1.50, p=0.016).

The proportion of AF patients among SCD victims

Over 500,000 ECGs were recorded for both cohorts, with a median of 17 ECGs per patient (IQR 9-29 ECGs). Of all patients who ultimately suffered an SCD (n=955) in the combined study population, one third had AF in ECG at baseline or had been previously diagnosed with AF (n=315/955) (Table 5). In last available ECG taken during follow-up before SCD, 20.8% of patients were in AF (n=199/955) and when analysing all ECGs accrued over the follow-up, 43.1% of SCD victims had AF recorded at least once before in their ECG (n=412/955). The number of AF patients among SCD victims are depicted in Table 5.

Relevance of heart failure hospitalizations

Analyses treating AF as a time-varying covariate (median time to AF 1.3 years, IQR 3.6) yielded results consistent with baseline models (Table 6).

In patients with angiography-confirmed CAD at baseline (n=15,007), most (84.3%, n=664/788) SCDs occurred in those who did not undergo any subsequent revascularization beyond the first three months of follow-up. Furthermore, among 6,435 patients without CAD at index angiography, only 4,5% (n=290) developed CAD and underwent revascularization – only eleven of these suffered SCD (0.17% of patients without CAD at index angiography). When incident revascularizations were included as time-varying covariates, AF remained independently associated with SCD risk (Table 6).

When both baseline and incident ICD implantations were included in the model as time-varying covariates, AF remained independently associated with SCD (Table 6).

Follow-up data on hospitalizations for heart failure were obtainable for the elective cohort. 2,446 (20.7%) patients (1,411 [16.2%] without AF, and 1,035 [33.3%] AF patients) were hospitalized for heart failure at a median of 3.5 years from baseline (IQR 4.6). In 57.5% of cases, AF preceded heart failure hospitalization, on average 1.4 years earlier (Supplementary Figure 3). When both AF and heart failure hospitalizations were treated as time-varying

covariates, AF was no longer associated with SCD (hazard ratio 1.11 [0.85-1.44], p=0.449; Table 6).

DISCUSSION

In this large, consecutive cohort of 21,421 patients who underwent coronary angiography either electively or in the setting of ACS, we made three key observations concerning AF and SCD. First, patients with AF at baseline (paroxysmal, persistent, or permanent) accounted for one-third of all SCD cases, and in one-fifth of SCD victims, the last ECG prior to death showed AF. Second, after adjustment for risk factors present at baseline, AF appeared as an independent risk factor for SCD, and AF documented on baseline ECG seemed to identify a higher-risk group compared to those with only a history of AF but sinus rhythm at baseline. Third, however, after accounting for heart failure hospitalizations during follow-up, AF was no longer independently associated with SCD risk, having preceded heart failure hospitalization in 57.5% of cases by an average of 1.4 years.

Preliminary data has suggested that AF could play a role in both initiating ventricular arrhythmias and contributing to the formation of a substrate that predisposes to SCD[21]. AF may share genetic architecture with ventricular fibrillation[22]. Patients with AF were associated with adverse ventricular remodeling, characterized by diffuse ventricular fibrosis, compared to those with sinus rhythm[23]. High ventricular rates during supraventricular tachycardias have been found to shorten the ventricular refractory period[21], facilitating the onset of ventricular arrhythmias[24]. Grönefeld et. al observed a high frequency of short-long-short sequences preceding ventricular tachyarrhythmias in patients with AF[25], emphasizing the risk of SCD associated with an irregular ventricular response.

Given that AF and SCD share common risk factors, it has been suggested that common underlying pathophysiological processes might drive both outcomes[6], or that AF could be associated with subclinical CAD predisposing to adverse outcomes[26]. Of interest, after adjusting for risk factors present at baseline, AF was associated with SCD even in the absence of obstructive CAD and remained a robust predictor of SCD regardless of whether baseline

LVEF was >50% or <50%. Thus, SCD risk in this patient population cannot rely solely on baseline systolic function.

The recent PROFID analysis found that even a broad set of baseline clinical variables failed to meaningfully enhance SCD risk prediction[27]. The timing of non-invasive risk marker assessment may be critical[28]. Indeed, in our study, AF was no longer associated with SCD once hospitalizations for heart failure during follow-up were taken into account, thereby calling into question the predictive value of baseline risk factors alone in assessing SCD risk. Consistently, a case-control study of the Oregon-SUDS population reported that AF was no longer an independent predictor of SCD after adjustment for a prior diagnosis of heart failure[6]. Post-hoc analyses of major novel anticoagulant trials have concluded that heart failure is the strongest predictor of SCD in the AF population[1,4,5], and in our study, AF preceded hospitalization for heart failure in 57.5% of cases—on average 1.4 years earlier—although the causal direction of this relationship remains difficult to establish. Whether AF merely reflects an underlying susceptibility to heart failure or whether early intervention could mitigate downstream risk remains uncertain. Notably, early rhythm control in EAST-AFNET 4[29] and catheter ablation[30] in selected AF patients reduced heart failure events and mortality—findings that raise the possibility of indirectly reducing SCD risk through optimal AF management. Given that AF often occurs 17 months before heart failure hospitalization in most patients, this may provide a valuable time window for effective prevention and intervention.

Research on ECG markers and risk scores for SCD has frequently omitted individuals with AF[7–14]. In the Oregon-SUDS case-control analysis AF patients accounted for 27.4% (179/652) of SCD cases[6]. We observed that patients with AF at baseline accounted for 25.3% and 40.9% of all SCD cases in our ACS and elective cohorts, respectively (315/955 of all SCD cases). Ultimately, 43.1% of all SCD victims had at least one prior ECG recording of AF before their demise (n=412/955). This finding emphasizes the need for more inclusive research and perhaps a re-evaluation of existing risk prediction models to better account for the fact that AF patients represent a significant proportion of SCD cases.

Key strengths of this study include a large cohort with comprehensive patient data, encompassing both angiographically excluded CAD and a broad spectrum of CAD patients, long-term follow-up resulting in a high number of observed SCD events, and accurate SCD classification based on death certificates and high rate of medico-legal autopsies (55% of SCD cases in ACS cohort), as required by Finnish law. We adhered to strict SCD criteria, excluding cases that were not deemed unexpected and of cardiac origin, including those with prolonged cardiac symptoms, deteriorating health conditions, or vague event descriptions. Additionally, we had no loss to follow-up. Therefore, the quality of the endpoint data can be considered high.

Limitations of this analysis should be considered. Our findings are derived from a largely Caucasian cohort in Finland, where the healthcare system is highly centralized. This may limit the generalizability of the results to other populations. Second, a retrospective study cannot assess causality. However, we believe this does not diminish the main conclusion of our research, which emphasizes that patients with AF constitute a significant proportion of SCD cases, underscoring the need for targeted preventive strategies in this population.

CONCLUSIONS

Although AF was associated with SCD after adjustment for baseline risk factors, this association was no longer evident after accounting for incident heart failure hospitalizations during follow-up. This highlights the importance of longitudinal risk assessment and questions the adequacy of baseline characteristics alone in predicting SCD risk. Yet, patients with AF at baseline accounted for 33.0% of all observed SCD cases, and 43.1% of SCD victims had a history of AF recorded at least once in their ECG during the follow-up. Therefore, patients with AF should not be excluded from studies investigating risk factors for SCD.

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ETHICS STATEMENTS

Patient consent for publication

Not applicable.

Ethics approval

This study adhered to the ethical principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments. The scientific monitoring board of the Pirkanmaa Hospital District approved the study design. Given its retrospective nature, obtaining patient consent was not required. Ethical approval was provided by the district's scientific monitoring committee.

PATIENT AND PUBLIC INVOLVEMENT

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

DATA AVAILABILITY STATEMENT

The anonymized data from this study are available upon request, provided that justified reasons are given.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Atrial fibrillation (AF) may be linked to an increased risk of sudden cardiac death (SCD), but studies have lacked data on the full spectrum of coronary artery disease (CAD) and on patients with angiographically excluded CAD.

WHAT THIS STUDY ADDS

AF patients accounted for one-third of all SCD events. AF was independently associated with SCD after adjustment for baseline risk factors, regardless of CAD status, but lost significance once incident heart failure hospitalizations were considered – events that AF preceded in 57.5% of cases by an average of 1.4 years.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

Our findings emphasize the need for preventive strategies, particularly addressing heart failure risk, in this patient group. As AF patients contribute to substantial amount of SCD cases, they should not be excluded from ECG risk prediction models.

Table 1. General characteristics of patients undergoing coronary angiography for acute coronary syndrome (ACS cohort) or for suspected coronary artery disease in elective setting (elective cohort).

	ACS cohort (n= 9,622)			Elective cohort (n=11,799)		
	No AF (n=7,938)	AF (n=1,684)	P-value	No AF (n=8,695)	AF (n=3,104)	P-value
Age	66.7 SD 11.9	74.5 SD 9.3	<0.001	65.7 SD 10.8	70.6 SD 9.6	<0.001
eGFR	81.6 SD 20.2	69.0 SD 21.9	<0.001	84.0 SD 22.9	76.6 SD 22.8	<0.001
LVEF	52% SD 11.5	49% SD 12.9	<0.001	57% SD 12.4	51% SD 14.2	<0.001
Men	67.4% (5353)	64.9% (1093)	0.045	58.9% (5120)	65.8% (2042)	<0.001
Diabetes	22.6% (1784)	33.1% (552)	<0.001	26.9% (2329)	29.1% (900)	0.019
History of stroke	6.4% (509)	14.3% (241)	<0.001	5.8% (502)	9.4% (293)	<0.001
Hypertensive	57.6% (4532)	70.3% (1174)	<0.001	67.3% (5837)	70.9% (2198)	<0.001
History of MI	13.4% (1062)	20.1% (338)	<0.001	10.3% (896)	13.4% (414)	<0.001
VHD	4.9% (391)	13.1% (220)	<0.001	15.1% (1309)	32.5% (1008)	<0.001
PAD	6.3% (499)	10.7% (180)	<0.001	4.5% (393)	6.4% (197)	<0.001
Previous CABG	6.0% (479)	9.4% (159)	<0.001	7.8% (681)	13.8% (427)	<0.001
Previous PCI	8.4% (670)	10.0% (168)	0.042	8.8% (766)	7.9% (245)	0.117
CAD Severity			<0.001			<0.001
0-VD	11.9% (941)	10.5% (177)		43.6% (3793)	48.4% (1503)	
1-VD	40.4% (3210)	33.9% (571)		23.0% (2004)	19.9% (617)	
2-VD	26.5% (2103)	26.1% (440)		18.3% (1589)	16.8% (521)	
3-VD	21.2% (1684)	29.4% (496)		15.1% (1309)	14.9% (463)	
LM stenosis	7.5% (596)	13.1% (220)	<0.001	6.7% (583)	6.5% (203)	0.752

Abbreviations: AF, Atrial Fibrillation; eGFR, estimated glomerular filtration rate (ml/min/1.73m^2); LVEF, Left Ventricular Ejection Fraction; MI, Myocardial infarction; VHD, Valvular heart disease; PAD, Peripheral heart disease; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CAD, coronary artery disease; VD, vessel disease; coronary artery disease LM, left main.

Table 2. Sudden cardiac death (SCD) events in patients undergoing coronary angiography for acute coronary syndrome (ACS) or for suspected or known coronary artery disease (elective cohort).

	ACS cohort (n= 9,622)		Elective cohort (n=11,799)	
	No AF (n=7,938)	AF (n=1,684)	No AF (n=8,695)	AF (n=3,104)
SCD or equivalent event, n (% of all SCDs)	363 (100%)	123 (100%)	277 (100%)	192 (100%)
Fatal SCD*	294 (81.0%)	99 (80.5%)	212 (76.5%)	139 (72.4%)
Aborted SCD†	18 (5.0%)	5 (4.1%)	32 (11.6%)	13 (6.8%)
Adequate ICD therapy	46 (12.7%)	18 (14.6%)	33 (11.9%)	38 (19.8%)
Fatal SCD* with adequate ICD therapy	5 (1.4%)	1 (0.8%)	0	2 (1.0%)

*Death within one week of SCD event
†Survived over one week after SCD event

Table 3. Fine–Gray subdistribution hazard (SDH) estimates for sudden cardiac death risk associated with atrial fibrillation (paroxysmal, persistent or permanent) in patients undergoing coronary angiography for acute coronary syndrome (ACS) or for suspected or known coronary artery disease (elective cohort).

	ACS cohort		Elective cohort		INTERNAL META-ANALYSIS	
	SDH	95% CI	SDH	95% CI	SDH	95% CI (p-value)
MODEL						
1	1.61	1.29-2.00	1.80	1.48-2.18	1.71	1.46-1.99 (<0.001)
2	1.49	1.19-1.86*	1.81	1.46-2.24†	1.58	1.36-1.84 (<0.001)
3	1.33	1.05-1.67‡	1.37	1.10-1.71§	1.35	1.15-1.59 (0.002)

MODEL 1: Age and Sex adjusted
MODEL 2: Adjusted with Age, Sex, Diabetes, CAD severity, History of Myocardial Infarction, Creatinine
MODEL 3: Adjusted with Age, Sex, Diabetes, CAD severity, History of Myocardial Infarction, Creatinine and Left Ventricular Ejection Fraction.

*9,512 patients in analysis
†9,814 patients in analysis
‡8,818 patients in analysis
§9,665 patients in analysis

Table 4. Fine–Gray subdistribution hazard (SDH) estimates for sudden cardiac death risk associated with a documented history of paroxysmal or persistent AF (in patients with sinus rhythm at baseline ECG) or with atrial fibrillation on baseline ECG in patients undergoing coronary angiography for acute coronary syndrome (ACS) or for suspected or known coronary artery disease (elective cohort).

	ACS cohort		Elective cohort		INTERNAL META-ANALYSIS	
	SDH	95% CI	SDH	95% CI	SDH	95% CI (p-value)
Only history of AF						
MODEL						
1	1.59	1.23-2.05	1.44	1.12-1.85	1.51	1.27-1.80 (<0.001)
2	1.46	1.13-1.89	1.40	1.07-1.85	1.43	1.19-1.79 (<0.001)
3	1.33	1.02-1.74	1.12	0.84-1.49	1.23	1.01-1.49 (0.039)
Currently in AF						
MODEL						
1	1.64	1.18-2.28	2.23	1.78-2.86	1.97	1.47-2.67 (<0.001)
2	1.54	1.11-2.14	2.38	1.84-3.09	1.94	1.27.2.97 (0.002)
3	1.31	0.93-1.86	1.80	1.39-2.35	1.57	1.15-2.14 (0.004)

MODEL 1: Age and Sex adjusted
MODEL 2: Adjusted with Age, Sex, Diabetes, CAD severity, History of MI, Creatinine
MODEL 3: Adjusted with Age, Sex, Diabetes, CAD severity, History of MI, Creatinine and Left Ventricular Ejection Fraction.

Table 5. The proportion of patients with atrial fibrillation (AF) among sudden cardiac death (SCD) victims in patients undergoing coronary angiography for acute coronary syndrome (ACS) or for suspected or known coronary artery disease (elective cohort).

	ACS cohort	Elective cohort	ALL
	SCDs (486)	SCDs (469)	SCDs (955)
AF at baseline	25.3% (123)	40.9% (192)	33.0% (315)
History of AF but currently in sinus rhythm	9.1% (44)	18.3% (86)	13.6% (130)
Patients in AF at baseline	16.3% (79)	22.6% (106)	19.4% (185)
AF in last ECG before the end of follow-up	17.9% (87)	27.6% (112)	20.8% (199)
AF in any ECG recording during follow-up	37.0% (180)	49.5% (232)	43.1% (412)

Table 6. Cox proportional hazard estimates for sudden cardiac death risk associated with atrial fibrillation in patients undergoing coronary angiography for acute coronary syndrome (ACS) or for suspected or known coronary artery disease (elective cohort). Atrial fibrillation, incident revascularizations, incident ICD implantations, and incident heart failure hospitalizations were modelled as time-varying covariates.

	ACS cohort			Elective cohort		
	HR	95% CI	P-value	HR	95% CI	P-value
MODEL						
1	2.21	1.77-2.76	<0.001	1.95	1.58-2.41	<0.001
2	1.99	1.59-2.50	<0.001	1.64	1.28-2.10	<0.001
3	1.89	1.50-2.37	<0.001	1.44	1.13-1.84	0.003
4	1.98	1.59-2.47	<0.001	1.61	1.27-2.04	<0.001
5	1.84	1.48-2.29	<0.001	1.42	1.12-1.80	0.005
6*				1.11	0.86-1.42	0.449

MODEL 1: Age and Sex adjusted
MODEL 2: Adjusted with Age, Sex, Diabetes, Coronary Syndrome type (chronic coronary syndrome/UAP/NSTEMI/STEMI), History of Myocardial Infarction, Creatinine.
MODEL 3: Adjusted with Age, Sex, Diabetes, Coronary Syndrome type (chronic coronary syndrome/UAP/NSTEMI/STEMI), History of Myocardial Infarction, Creatinine and Left Ventricular Ejection Fraction.
MODEL 4: Adjusted with Age, Sex, Diabetes, Coronary Syndrome type (chronic coronary syndrome/UAP/NSTEMI/STEMI), History of Myocardial Infarction, Creatinine, and incident revascularizations (as time-varying covariate).
MODEL 5: Adjusted with Age, Sex, Diabetes, Coronary Syndrome type (chronic coronary syndrome/UAP/NSTEMI/STEMI), History of Myocardial Infarction, Creatinine, Left Ventricular Ejection Fraction, and baseline and incident ICD implantations (as time-varying covariate).
MODEL 6: Adjusted with Age, Sex, Diabetes, Coronary Syndrome type (chronic coronary syndrome/UAP/NSTEMI/STEMI), History of Myocardial Infarction, Creatinine, and incident heart failure hospitalizations (as time-varying covariate).

*Data on incident heart failure hospitalizations were available for the elective cohort.

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