

Supplemental material

Impact of known or new-onset atrial fibrillation on 2-year cardiovascular event rate in patients with acute coronary syndromes: results from the prospective EPICOR Registry

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**Supplemental Table 1. In-hospital management of index event; atrial fibrillation (AF) versus no AF, prior or new-onset:
unadjusted and adjusted values following multivariable logistic regression analysis**

	Prior AF Y / N (n = 497 / 9954)	Unadjusted		Adjusted ^b		New-onset AF Y / N (n = 382 / 10 165)	Unadjusted		Adjusted ^b		Any AF Y / N (n = 879 / 9565)	Unadjusted		Adjusted ^b	
		RR	p	RR	p		RR	p	RR	p		RR	p	RR	p
Fibrinolysis	16 (3.2) / 931 (9.4)	0.35	<0.001	0.65	0.13	33 (8.6) / 921 (9.1)	0.95	0.77	1.15	0.42	49 (5.6) / 896 (9.4)	0.60	<0.001	0.93	0.63
Antiplatelets															
Aspirin	434 (87.3) / 9404 (94.5)	0.92	<0.001	0.95	0.003	365 (95.5) / 9557 (94.0)	1.02	0.15	1.03	0.007	799 (90.9) / 9032 (94.4)	0.96	0.001	0.99	0.17
Clopidogrel	410 (82.5) / 8667 (87.1)	0.95	0.010	0.95	0.022	337 (88.2) / 8820 (86.8)	1.02	0.39	1.03	0.11	747 (85.0) / 8327 (87.1)	0.98	0.10	0.99	0.37
Prasugrel	13 (2.6) / 783 (7.9)	0.33	<0.001	0.61	0.074	15 (3.9) / 787 (7.7)	0.51	0.008	0.54	0.016	28 (3.2) / 765 (8.0)	0.40	<0.001	0.56	0.002
GP IIb/IIIa inhibitor	42 (8.5) / 1705 (17.1)	0.49	<0.001	0.79	0.11	67 (17.5) / 1691 (16.6)	1.05	0.64	1.07	0.51	109 (12.4) / 1638 (17.1)	0.72	<0.001	0.94	0.51
DAPT	383 (77.1) / 8950 (89.9)	0.86	<0.001	0.91	<0.001	340 (89.0) / 9067 (89.2)	1.00	0.91	1.02	0.27	723 (82.3) / 8603 (89.9)	0.91	<0.001	0.96	0.005
Aspirin+ clopidogrel	372 (74.8) / 8385 (84.2)	0.89	<0.001	0.91	<0.001	327 (85.6) / 8501 (83.6)	1.02	0.28	1.05	0.025	699 (79.5) / 8054 (84.2)	0.94	0.001	0.97	0.10
TAPT ^a	39 (7.8) / 1612 (16.2)	0.48	<0.001	0.81	0.17	64 (16.8) / 1598 (15.7)	1.07	0.58	1.10	0.36	103 (11.7) / 1548 (16.2)	0.72	0.001	0.97	0.76

Anticoagulants															
UFH	143 (28.8) / 3527 (35.4)	0.81	0.004	0.99	0.92	124 (32.5) / 3567 (35.1)	0.93	0.30	0.95	0.44	267 (30.4) / 3400 (35.5)	0.85	0.003	0.97	0.52
LMWH	219 (44.1) / 4713 (47.3)	0.93	0.16	0.91	0.061	230 (60.2) / 4744 (46.7)	1.29	<0.001	1.31	<0.001	449 (51.1) / 4483 (46.9)	1.09	0.013	1.08	0.025
Fondaparinux	45 (9.1) / 1051 (10.6)	0.86	0.29	0.64	0.003	53 (13.9) / 1049 (10.3)	1.34	0.024	1.22	0.13	98 (11.1) / 998 (10.4)	1.07	0.51	0.86	0.14
Bivalirudin	2 (0.4) / 162 (1.6)	0.25	0.049	0.31	0.095	3 (0.8) / 162 (1.6)	0.49	0.22	0.41	0.12	5 (0.6) / 159 (1.7)	0.34	0.018	0.35	0.016
Oral anticoagulants	167 (33.6) / 257 (2.6)	13.01	<0.001	8.94	<0.001	73 (19.1) / 358 (3.5)	5.42	<0.001	3.66	<0.001	240 (27.3) / 189 (2.0)	13.82	<0.001	10.50	<0.001
Warfarin / acenocoumarol	166 (33.4) / 255 (2.6)	13.04	<0.001	8.94	<0.001	73 (19.1) / 355 (3.5)	5.47	<0.001	3.69	<0.001	239 (27.2) / 187 (2.0)	13.91	<0.001	10.56	<0.001
Dabigatran	1 (0.2) / 2 (0.02)	10.01	0.060	-	-	0 (0.0) / 3 (0.03)	-	-	-	-	1 (0.1) / 2 (0.02)	5.44	0.17	-	-
Intervention															
PCI	245 (49.3) / 6586 (66.2)	0.75	<0.001	0.85	<0.001	213 (55.8) / 6674 (65.7)	0.85	<0.001	0.86	0.001	458 (52.1) / 6367 (66.6)	0.78	<0.001	0.85	<0.001
CABG	8 (1.6) / 256 (2.6)	0.63	0.19	0.37	0.005	49 (12.8) / 217 (2.1)	6.01	<0.001	4.39	<0.001	57 (6.5) / 205 (2.1)	3.03	<0.001	2.06	<0.001
Either	253 (50.9) / 6825 (68.6)	0.74	<0.001	0.82	<0.001	258 (67.5) / 6877 (67.7)	1.00	0.96	1.01	0.88	511 (58.1) / 6559 (68.6)	0.85	<0.001	0.90	<0.001

^aAspirin plus either clopidogrel or prasugrel, and a GP IIb/IIIa inhibitor.

^bMultivariable logistic regression adjusting for: age, LVEF, EQ-5D score, serum creatinine, blood glucose ≥ 160 mg/dL, chronic obstructive pulmonary disease, male gender,

diagnosis (STEMI vs. NSTEMI-ACS), PCI or CABG, haemoglobin <13 g/dL, peripheral vascular disease, on diuretics at discharge, and region (Eastern Europe, Latin America, Northern Europe, Southern Europe).

CABG: coronary artery bypass graft; DAPT: dual antiplatelet therapy; GP: glycoprotein; LMWH: low molecular weight heparin; NSTEMI-ACS: non-ST-segment elevation acute coronary syndromes; PCI: percutaneous coronary intervention; RR: relative risk; STEMI: ST-segment elevation myocardial infarction; TAPT: triple antiplatelet therapy; UFH: unfractionated heparin; Y / N: yes / no.

Supplemental Table 2. Other in-hospital cardiovascular and bleeding complications: unadjusted and adjusted values following multivariable logistic regression analysis

	Prior AF Y (n = 497) / N (n = 9954)	<i>Unadjusted</i>		<i>Adjusted*</i>		New-onset AF Y (n = 382) / N (n = 10,165)	<i>Unadjusted</i>		<i>Adjusted*</i>		Any AF Y (n = 879) / N (n = 9565)	<i>Unadjusted</i>		<i>Adjusted*</i>	
		<i>RR</i>	<i>p</i>	<i>RR</i>	<i>p</i>		<i>RR</i>	<i>p</i>	<i>RR</i>	<i>p</i>		<i>RR</i>	<i>p</i>	<i>RR</i>	<i>p</i>
None	358 (73.2) / 8195 (83.1)	1.59	<0.001	1.22	0.034	235 (63.0) / 8390 (83.3)	2.21	<0.001	1.69	<0.001	593 (68.8) / 7964 (83.9)	1.94	<0.001	1.49	<0.001
Any of the following	131 (26.8) / 1666 (16.9)					138 (37.0) / 1688 (16.7)					269 (31.2) / 1527 (16.1)				
MI/recurrent ischaemia	33 (6.7) / 554 (5.6)	1.19	0.31	0.75	0.23	34 (9.1) / 565 (5.6)	1.63	0.004	1.97	<0.001	67 (7.7) / 519 (5.5)	1.41	0.005	1.26	0.13
Cardiogenic shock	5 (1.0) / 99 (1.0)	1.01	0.97	0.21	0.13	15 (3.9) / 93 (0.9)	4.29	<0.001	2.40	0.023	20 (2.3) / 83 (0.9)	2.63	<0.001	1.23	0.58
Heart failure	71 (14.4) / 528 (5.3)	2.70	<0.001	1.67	0.001	69 (18.1) / 547 (5.4)	3.35	<0.001	2.11	<0.001	140 (16.0) / 460 (4.8)	3.32	<0.001	2.05	<0.001
Any other arrhythmia	28 (5.7) / 500 (5.0)	1.13	0.53	1.32	0.21	50 (13.2) / 486 (4.8)	2.76	<0.001	1.92	0.001	78 (8.9) / 450 (4.7)	1.90	<0.001	1.70	0.001
Stroke	1 (0.2) / 26 (0.3)	0.77	0.80	–	–	5 (1.3) / 22 (0.2)	6.04	<0.001	3.36	0.11	6 (0.7) / 21 (0.2)	3.11	0.014	1.37	0.65
Bleeding	22 (4.4) / 321 (3.2)	1.37	0.14	1.04	0.88	29 (7.6) / 313 (3.1)	2.46	<0.001	1.80	0.012	51 (5.8) / 291 (3.0)	1.91	<0.001	1.42	0.066

*Multivariable logistic regression adjusting for: age, LVEF, EQ-5D score, serum creatinine, blood glucose ≥ 160 mg/dL, chronic obstructive pulmonary disease, male gender, diagnosis (STEMI vs. NSTEMI-ACS), PCI or CABG, haemoglobin < 13 g/dL, peripheral vascular disease, on diuretics at discharge, and region (Eastern Europe, Latin America, Northern Europe, Southern Europe).

AF: atrial fibrillation; CABG: coronary artery bypass graft; EQ-5D: EuroQol 5 dimensions, LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTEMI-ACS: non-ST-segment elevation acute coronary syndromes; PCI: percutaneous coronary intervention; RR: relative risk; STEMI: ST-elevation myocardial infarction.

Supplemental Table 3. Multivariable analysis for mortality – prior AF

	HR	95% CI	p-value
Multivariable analysis	1.48	1.14, 1.90	0.003
Age (per 10 years)	1.56	1.44, 1.69	<0.00001
LVEF			
<40%	1.84	1.46, 2.31	<0.00001
<30%	3.32	2.50, 4.41	
EQ-5D score (per unit)	1.15	1.10, 1.21	<0.00001
Serum creatinine (per unit ≥ 1.2 mg /dL)	1.25	1.15, 1.36	<0.00001
Other cardiac complications in hospital	1.30	1.08, 1.57	0.007
Blood glucose ≥ 160 mg/dL	1.42	1.19, 1.71	0.0001
Chronic obstructive pulmonary disease	1.69	1.34, 2.14	<0.0001
Male sex	1.48	1.23, 1.80	<0.0001
Diagnosis			
NSTE-ACS	1.00	-	0.56
STEMI	0.95	0.79, 1.13	
PCI or CABG	0.62	0.52, 0.73	<0.00001
Haemoglobin <13 mg/dL	1.52	1.25, 1.85	<0.0001
Peripheral vascular disease	1.34	1.03, 1.76	0.031
On diuretics at discharge	1.47	1.22, 1.78	<0.0001
Region			
Eastern Europe	1.00	-	<0.00001
Latin America	1.22	0.97, 1.52	
Northern Europe	0.54	0.43, 0.68	
Southern Europe	0.68	0.53, 0.87	

AF: atrial fibrillation; CABG: coronary artery bypass graft; CI: confidence interval; EQ-5D: EuroQol 5 dimensions; HR: hazard ratio; LVEF: left ventricular ejection fraction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction.

Supplemental Table 4. Multivariable analysis for mortality – new-onset AF

	HR	95% CI	p-value
Multivariable analysis	1.03	0.73, 1.44	0.88
Age (per 10 years)	1.58	1.46, 1.71	<0.00001
LVEF			
<40%	1.78	1.40, 2.26	<0.00001
<30%	3.30	2.49, 4.37	
EQ-5D score (per unit)	1.15	1.10, 1.21	<0.00001
Serum creatinine (per unit ≥ 1.2 mg /dL)	1.25	1.15, 1.35	<0.00001
Other cardiac complications in hospital	1.34	1.11, 1.62	0.002
Blood glucose ≥ 160 mg/dL	1.41	1.17, 1.69	0.0003
Chronic obstructive pulmonary disease	1.68	1.33, 2.13	<0.0001
Male sex	1.48	1.22, 1.79	<0.0001
Diagnosis			
NSTE-ACS	1.00	-	0.51
STEMI	0.94	0.79, 1.13	
PCI or CABG	0.61	0.51, 0.72	<0.00001
Haemoglobin <13 mg/dL	1.54	1.28, 1.86	<0.00001
Peripheral vascular disease	1.35	1.04, 1.74	0.025
On diuretics at discharge	1.53	1.27, 1.85	<0.00001
Region			
Eastern Europe	1.00	-	<0.00001
Latin America	1.19	0.95, 1.49	
Northern Europe	0.55	0.43, 0.69	
Southern Europe	0.68	0.53, 0.87	

AF: atrial fibrillation; CABG: coronary artery bypass graft; CI: confidence interval; EQ-5D: EuroQol 5 dimensions; HR: hazard ratio; LVEF: left ventricular ejection fraction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction.

Supplemental Table 5. Multivariable analysis for mortality – any AF

	HR	95% CI	p-value
Multivariable analysis	1.32	1.06, 1.64	0.013
Age (per 10 years)	1.56	1.44, 1.69	<0.00001
LVEF			
<40%	1.82	1.43, 2.32	<0.00001
<30%	3.25	2.45, 4.31	
EQ-5D score (per unit)	1.15	1.10, 1.21	<0.00001
Serum creatinine (per unit ≥ 1.2 mg /dL)	1.25	1.15, 1.35	<0.00001
Other cardiac complications in hospital	1.29	1.07, 1.56	0.008
Blood glucose ≥ 160 mg/dL	1.32	1.20, 1.74	<0.0001
Chronic obstructive pulmonary disease	1.70	1.35, 2.15	<0.00001
Male sex	1.48	1.22, 1.79	<0.0001
Diagnosis			
NSTE-ACS	1.00	–	0.47
STEMI	0.94	0.78, 1.12	
PCI or CABG	0.62	0.52, 0.73	<0.00001
Haemoglobin <13 mg/dL	1.53	1.27, 1.85	<0.00001
Peripheral vascular disease	1.33	1.02, 1.72	0.032
On diuretics at discharge	1.48	1.23, 1.79	<0.0001
Region			
Eastern Europe	1.00	–	<0.00001
Latin America	1.22	0.97, 1.51	
Northern Europe	0.54	0.42, 0.68	
Southern Europe	0.67	0.53, 0.86	

AF: atrial fibrillation; CABG: coronary artery bypass graft; CI: confidence interval; EQ-5D: EuroQol 5 dimensions; HR: hazard ratio; LVEF: left ventricular ejection fraction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PCI: percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

Supplemental Table 6. Multivariable analysis for composite endpoint of death, non-fatal MI and stroke – prior AF

	HR	95% CI	p-value
Multivariable analysis	1.46	1.16, 1.83	0.001
Age (per 10 years)	1.37	1.28, 1.47	<0.00001
LVEF			
<40%	1.71	1.40, 2.10	<0.00001
<30%	2.98	2.30, 3.85	
EQ-5D score (per unit)	1.12	1.07, 1.17	<0.00001
Serum creatinine (per unit ≥ 1.2 mg /dL)	1.22	1.13, 1.31	<0.00001
Other cardiac complications in hospital	1.29	1.09, 1.52	0.003
Blood glucose ≥ 160 mg/dL	1.36	1.17, 1.58	<0.0001
Chronic obstructive pulmonary disease	1.70	1.38, 2.09	<0.00001
Male sex	1.35	1.14, 1.59	0.0004
Diagnosis			
NSTE-ACS	1.00	-	0.049
STEMI	0.86	0.74, 1.00	
PCI or CABG	0.68	0.59, 0.79	<0.00001
Haemoglobin <13 mg/dL	1.43	1.20, 1.71	<0.0001
Peripheral vascular disease	1.42	1.13, 1.78	0.002
On diuretics at discharge	1.44	1.22, 1.69	<0.0001
Region			
Eastern Europe	1.00	-	<0.00001
Latin America	1.06	0.87, 1.29	
Northern Europe	0.63	0.52, 0.77	
Southern Europe	0.70	0.57, 0.86	

AF: atrial fibrillation; CABG: coronary artery bypass graft; CI: confidence interval; EQ-5D: EuroQol 5 dimensions; HR: hazard ratio; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTE-ACS: non-ST-segment

elevation acute coronary syndrome; PCI: percutaneous coronary intervention: STEMI, ST-elevation myocardial infarction.

Supplemental Table 7. Multivariable analysis for composite endpoint of death, non-fatal MI and stroke – new-onset AF

	HR	95% CI	<i>p</i>-value
Multivariable analysis	0.98	0.73, 1.33	0.92
Age (per 10 years)	1.39	1.30, 1.49	<0.00001
LVEF			
<40%	1.72	1.38, 2.14	<0.00001
<30%	2.95	2.25, 3.88	
EQ-5D score (per unit)	1.12	1.07, 1.17	<0.00001
Serum creatinine (per unit ≥ 1.2 mg /dL)	1.22	1.13, 1.31	<0.00001
Other cardiac complications in hospital	1.31	1.11, 1.55	0.002
Blood glucose ≥ 160 mg/dL	1.37	1.17, 1.60	<0.0001
Chronic obstructive pulmonary disease	1.68	1.37, 2.07	<0.00001
Male sex	1.32	1.12, 1.56	0.0008
Diagnosis			
NSTE-ACS	1.00	-	0.035
STEMI	0.85	0.73, 0.99	
PCI or CABG	0.67	0.58, 0.78	<0.00001
Haemoglobin <13 mg/dL	1.39	1.18, 1.64	<0.0001
Peripheral vascular disease	1.47	1.17, 1.85	0.001
On diuretics at discharge	1.47	1.25, 1.73	<0.00001
Region			
Eastern Europe	1.00	-	<0.00001
Latin America	1.04	0.86, 1.26	
Northern Europe	0.64	0.53, 0.78	
Southern Europe	0.70	0.57, 0.86	

AF: atrial fibrillation; CABG: coronary artery bypass graft; CI: confidence interval; EQ-5D: EuroQol 5 dimensions; HR: hazard ratio; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTE-ACS: non-ST-segment

elevation acute coronary syndrome; PCI: percutaneous coronary intervention: STEMI, ST-elevation myocardial infarction.

Supplemental Table 8. Multivariable analysis for composite endpoint of death, non-fatal MI and stroke – any AF

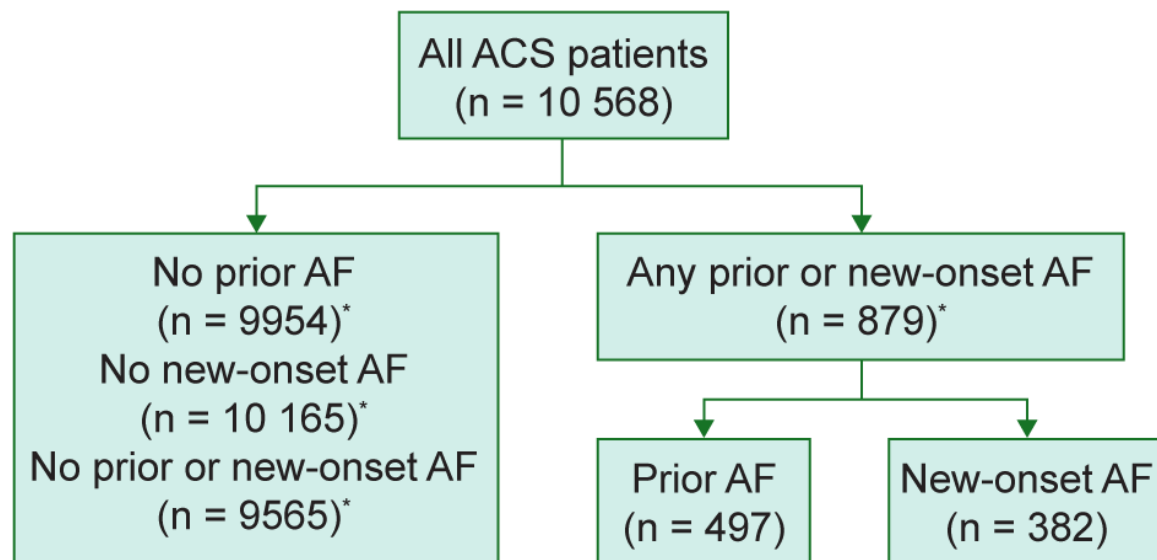
	HR	95% CI	<i>p</i> -value
Multivariable analysis	1.28	1.06, 1.56	0.012
Age (per 10 years)	1.37	1.28, 1.47	<0.00001
LVEF			
<40%	1.71	1.39, 2.09	<0.00001
<30%	2.94	2.25, 3.83	
EQ-5D score (per unit)	1.12	1.07, 1.17	<0.00001
Serum creatinine (per unit ≥ 1.2 mg /dL)	1.21	1.12, 1.30	<0.00001
Other cardiac complications in hospital	1.28	1.08, 1.51	0.004
Blood glucose ≥ 160 mg/dL	1.35	1.14, 1.60	0.0004
Chronic obstructive pulmonary disease	1.69	1.38, 2.08	<0.00001
Male sex	1.34	1.13, 1.58	0.0005
Diagnosis			
NSTE-ACS	1.00	-	0.037
STEMI	0.85	0.73, 0.99	
PCI or CABG	0.68	0.59, 0.79	<0.00001
Haemoglobin <13 mg/dL	1.42	1.21, 1.68	<0.0001
Peripheral vascular disease	1.46	1.16, 1.83	0.001
On diuretics at discharge	1.44	1.23, 1.70	<0.00001
Region			
Eastern Europe	1.00	-	<0.00001
Latin America	1.06	0.87, 1.28	
Northern Europe	0.63	0.52, 0.76	
Southern Europe	0.69	0.56, 0.85	

AF: atrial fibrillation; CABG: coronary artery bypass graft; CI: confidence interval; EQ-5D: EuroQol 5 dimensions; HR: hazard ratio; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTE-ACS: non-ST-segment

elevation acute coronary syndrome; PCI: percutaneous coronary intervention: STEMI, ST-elevation myocardial infarction.

Supplemental Figure 1. Flow chart

Of 10,568 ACS patients enrolled in EPICOR, 497 had known prior AF at baseline, 382 had new-onset AF during the index event, and 9565 had no prior or new-onset AF.

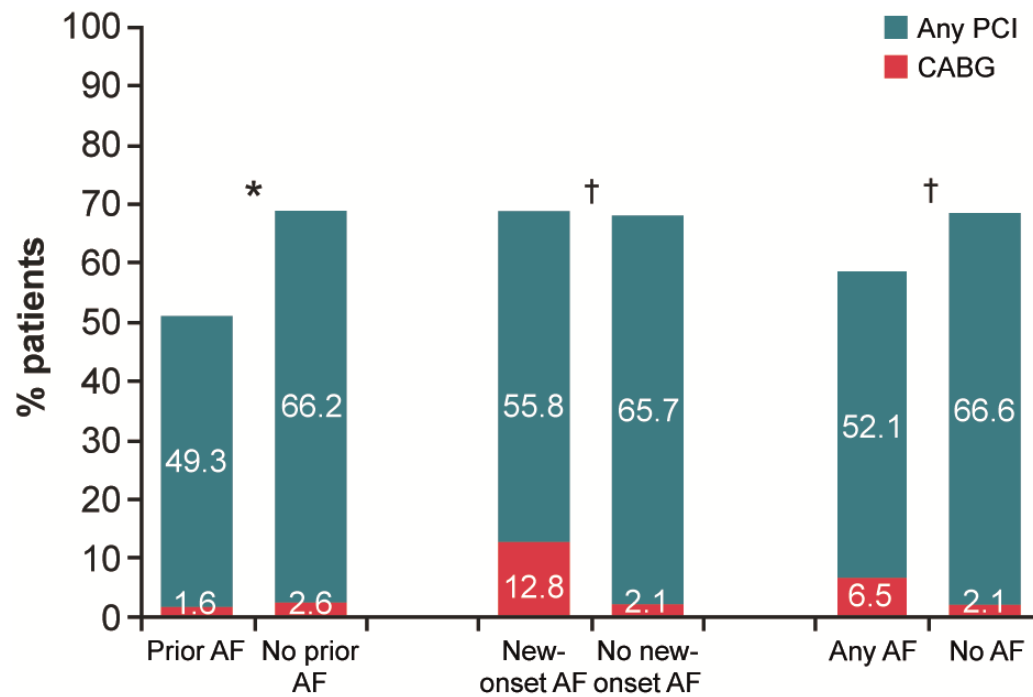


ACS: acute coronary syndromes; AF: atrial fibrillation.

*Patients with any data for prior or new-onset in-hospital AF. Data were missing for 134 patients overall (117 patients for prior AF and 21 patients for new-onset AF, including 4 patients missing data for both categories of AF).

Supplement Figure 2. Proportion of patients undergoing revascularization for index event

Patients with any AF were significantly less frequently managed with PCI than those without AF, whereas patients with new-onset AF were more likely to undergo CABG.



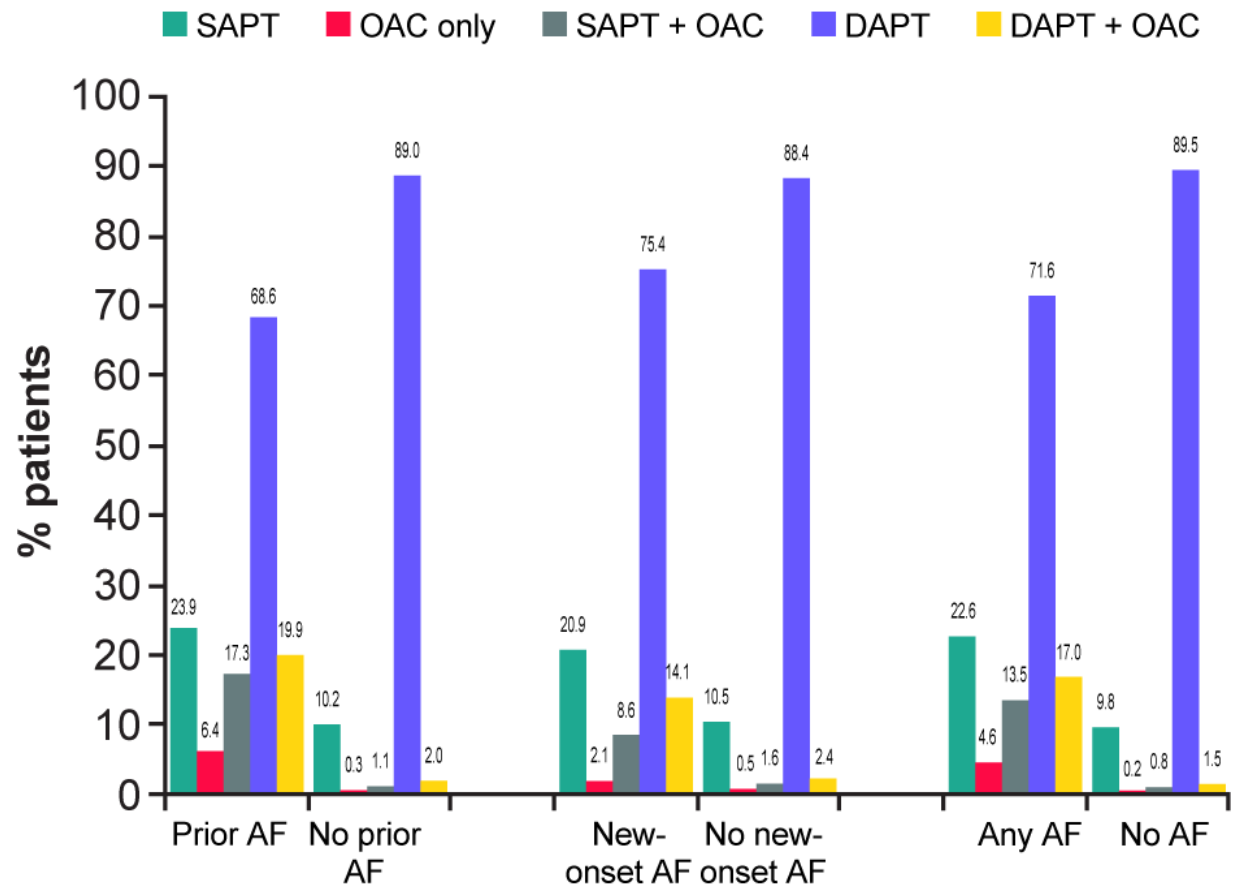
* $p < 0.001$ AF versus no AF for PCI, and $p = 0.18$ AF versus no AF for CABG

† $p < 0.001$ AF versus no AF for PCI and CABG

AF: atrial fibrillation; CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention.

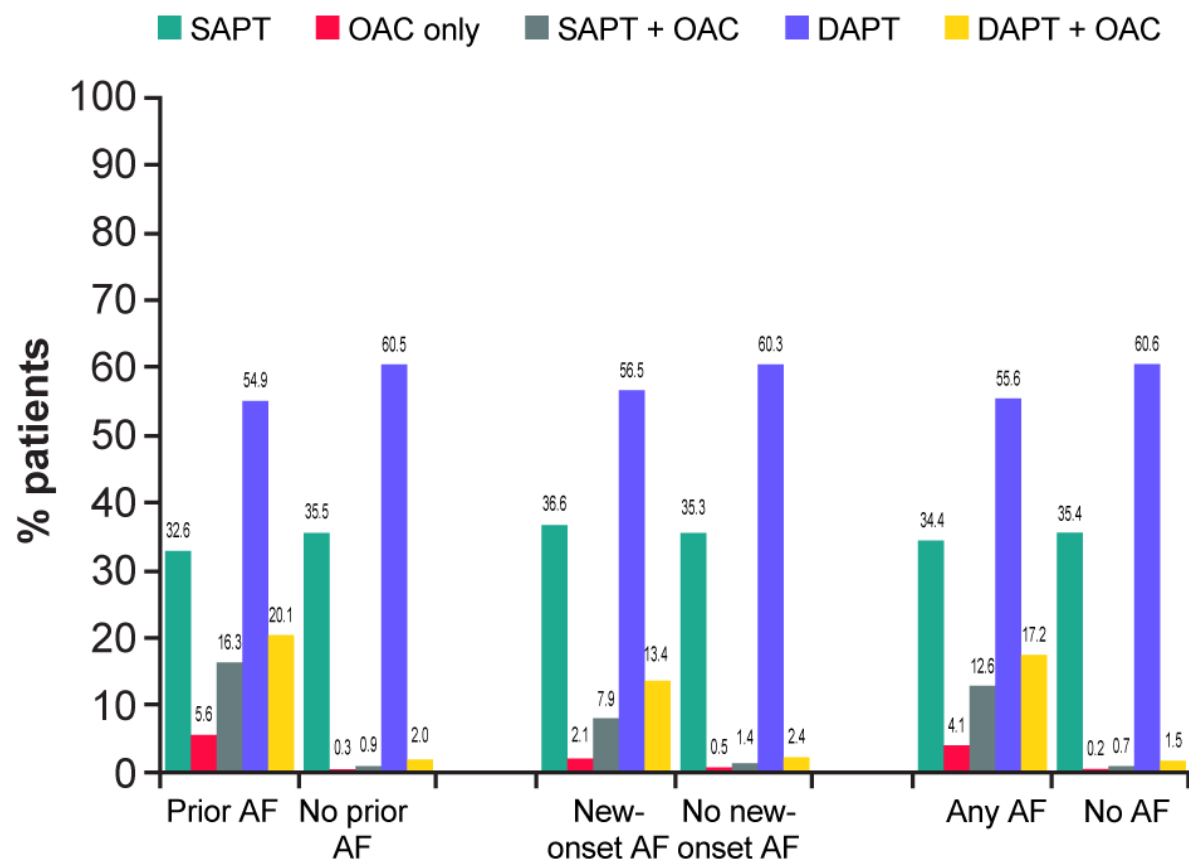
Supplemental Figure 3. Oral antithrombotic medication: A) at discharge, and B) at end of follow-up

(A)



$p < 0.001$ for antiplatelets and anticoagulants for AF versus no AF across all the categories

(B)



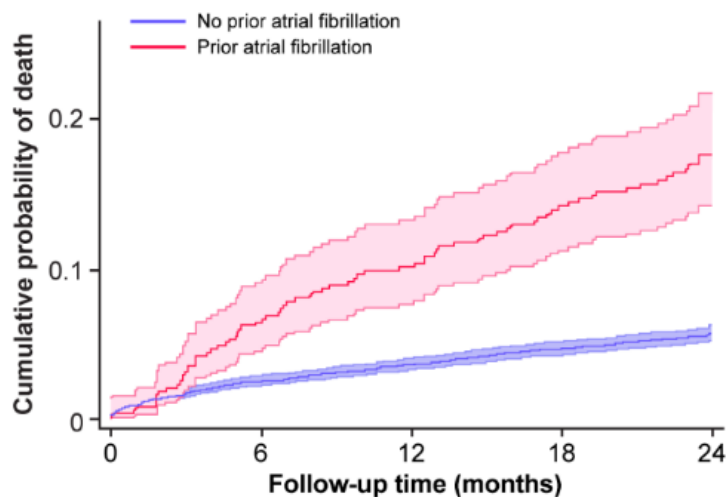
$p < 0.001$ for antiplatelets and anticoagulants for AF versus no AF across all the categories, except for antiplatelets for new-onset versus no new-onset AF, $p = 0.051$

AF: atrial fibrillation; DAPT: dual antiplatelet therapy; OAC: oral anticoagulant; SAPT: single antiplatelet therapy.

Supplemental Figure 4. Kaplan–Meier plots for (A) death and (B) the composite of death/non-fatal myocardial infarction (MI)/stroke

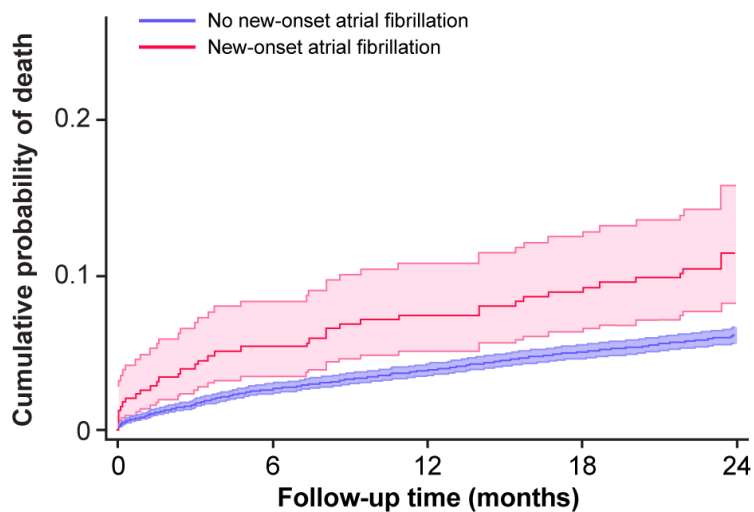
(A)

Prior versus no prior atrial fibrillation (AF)



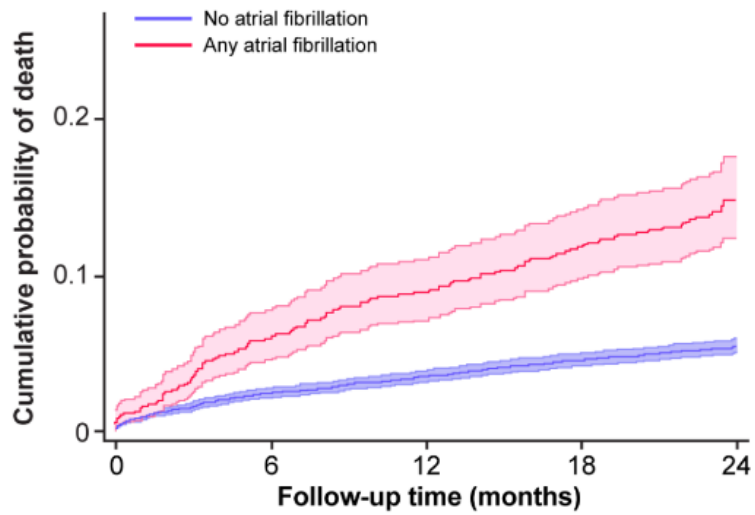
$p < 0.0001$ at 2 years

New-onset versus no new-onset AF



$p < 0.0001$ at 2 years

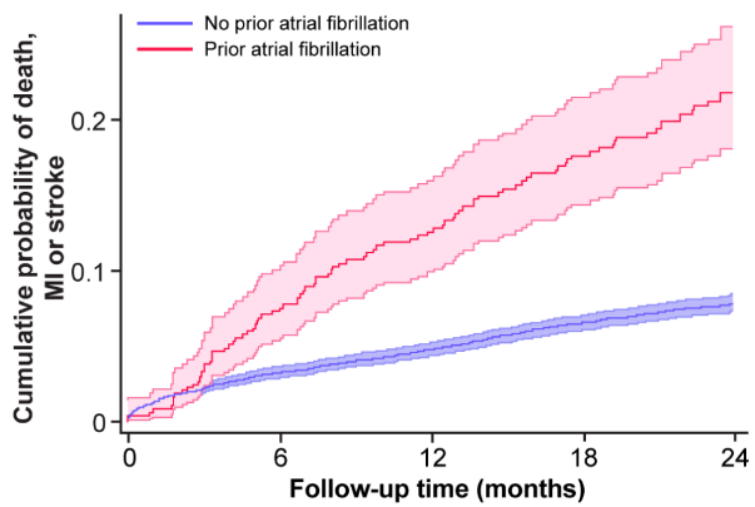
Any versus no AF



$p < 0.0001$ at 2 years

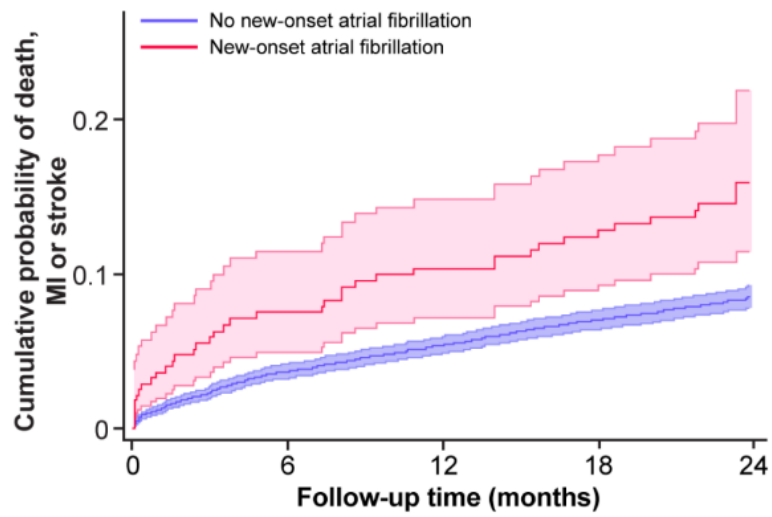
(B)

Prior versus no prior AF



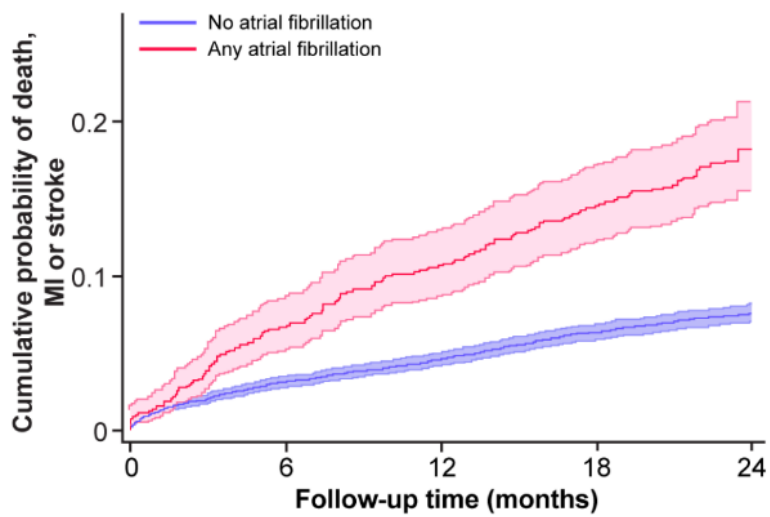
$p < 0.0001$ at 2 years

New-onset versus no new-onset AF



$p < 0.0001$ at 2 years

Any versus no AF



$p < 0.0001$ at 2 years