Supplementary material

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Differential Prognostic Impact on Mortality of Myocardial Infarction Compared With Bleeding Severity in Contemporary Acute Coronary Syndrome Patients

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SUPPLEMENTARY MATERIAL

Table 1 of the supplementary material

Adjusted Effect (HR) of Postdischarge MI and BARC Bleeding as a Whole, on Subsequent All-cause Mortality

	Adjusted HR (95%CI)	P
Posdischarge MI (time-varying exposure)	5.8 (3.7-9.8)	< .001
Posdischarge bleeding time-varying exposure)	5.1 (3.6-7.7)	< .001
Age ≥ 65 y	2.1 (1.4-3.1)	< .001
Female sex	0.9 (0.7-1.3)	.58
BMI, kg/m²	1.0 (0.98-1.1)	.83
Current smoking	1.2 (0.8-1.7)	.40
Hypertension	1.1 (0.8-1.7)	.48
Diabetes mellitus	1.1 (0.8-1.4)	.66
Dyslipidemia	0.7 (0.5-0.9)	.03
Prior CAD	1.2 (0.9-1.6)	.36
Prior vascular disease[a]	1.9 (1.4-2.6)	< .001
History of heart failure or LVEF < 40%	3.3 (2.4-4.3)	< .001
History of bleeding[b]	1.6(1.1-2.3)	.02

COPD	1.4 (1.02-2.0)	.04
Prior malignant disease	1.9 (1.3-2.9)	< .001
ACS presentation:		
Unstable angina	Ref.	Ref.
STEMI	1.3 (0.8-2.4)	.38
NSTEMI	1.9 (1.0-3.7)	.04
Serum creatinine (per 1 mg/dL increase)	1.5 (1.03-2.2)	.03
Hemoglobin (per 1 g/dL increase)	0.9 (0.8-0.9)	.001
Multivessel coronary disease	1.6 (1.2-2.2)	.003
In-hospital PCI	0.6 (0.4-0.9)	.005
In-hospital CABG	0.6 (0.3-1.2)	.19
DAPT at discharge:		
No DAPT	Ref.	Ref.
Aspirin plus prasugrel	1.0 (0.4-2.3)	.99
Aspirin plus ticagrelor	0.4 (0.2-1.0)	.05
Aspirin plus clopidogrel	1.2 (0.7-1.9)	.50
Oral anticoagulant at discharge	1.4 (1.0-1.9)	.07
Proton pump inhibitor at discharge	1.2 (0.9-1.6)	.08
Study center	0.8 (0.6-1.2)	.28

95%CI, 95% confidence interval; ACS, acute coronary syndrome; BARC, bleeding academic research consortium; BMI, body mass index; CAD, coronary artery disease; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; HR, hazard ratio; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

[a]Denots prior stroke or peripheral arterial disease.

[b]Denotes prior hospitalization for bleeding and/or in-hospital BARC type 2, BARC type 3, and BARC

type 4 bleeding.

Table 2 of the supplementary material

Adjusted Effect (HR) of Postdischarge MI and the Specific Type of BARC Bleeding (Bleeding Severity),

on Subsequent All-cause Mortality

	Adjusted HR (95%CI)	P
Posdischarge MI (time-varying exposure)	6.6 (4.2-10.5)	< .001
Postdischarge BARC 2 bleeding (time-varying exposure)	1.7 (1.2-3.1)	.009
Postdischarge BARC 3a bleeding (time-varying exposure)	3.3 (1.9-5.6)	<.001
Postdischarge BARC 3b bleeding (time-varying exposure)	7.2 (3.4-15.3)	< .001
Postdischarge BARC 3c bleeding (time-varying exposure)	26.5 (15.4-45.7)	< .001
Age ≥ 65 years	2.2 (1.5-3.3)	< .001
Female sex	0.9 (0.6-1.3)	.63
BMI, kg/m²	1.01 (0.98-1.04)	.38
Current smoking	1.3 (0.9-2.0)	.16
Hypertension	1.2 (0.8-1.8)	.36
Diabetes mellitus	1.1 (0.8-1.6)	.38
Dyslipidemia	0.8 (0.6-1.1)	.09
Prior CAD	1.2 (0.9-1.6)	.33
Prior vascular disease[a]	1.9 (1.3-2.6)	< .001
History of heart failure or LVEF < 40%	3.6 (2.7-4.8)	< .001
History of bleeding[b]	1.5 (1.0-2.2)	.05
COPD	1.6 (1.1-2.4)	.01
Prior malignant disease	2.1 (1.4-3.3)	.001
ACS presentation:		

Unstable angina	Ref.	Ref.
STEMI	1.4 (0.8-2.6)	.32
NSTEMI	2.1 (1.0-4.1)	.04
Serum creatinine (per 1 mg/dL increase)	1.6 (1.0-2.4)	.03
Hemoglobin (per 1 g/dL increase)	0.9 (0.8-1.0)	.001
Multivessel coronary disease	1.6 (1.2-2.2)	.004
In-hospital PCI	0.6 (0.4-0.9)	.01
In-hospital CABG	0.6 (0.3-1.3)	.18
DAPT at discharge:		
No DAPT	Ref.	Ref.
Aspirin plus prasugrel	1.1 (0.4-2.6)	.86
Aspirin plus ticagrelor	0.4 (0.2-1.1)	.07
Aspirin plus clopidogrel	1.1 (0.7-1.8)	.73
Oral anticoagulant at discharge	1.5 (1.0-2.2)	.03
Proton pump inhibitor at discharge	1.2 (0.9-1.6)	.18
Study center	0.8 (0.6-1.1)	.14

95%CI, 95% confidence interval; ACS, acute coronary syndrome; BARC, bleeding academic research consortium; BMI, body mass index; CAD, coronary artery disease; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; HR, hazard ratio; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

[a]Denote prior stroke or peripheral arterial disease.

[b]Denotes prior hospitalization for bleeding and/or in-hospital BARC type 2, BARC type 3, and BARC type 4 bleeding.

Table 3 of the supplementary material

Crude Mortality Rate by Postdischarge MI and Bleeding Status, and Their Adjusted Effect (HR) on Subsequent All-cause Mortality, Among the 3588 Patients Discharged With DAPT

	Nº of patients	Death, n	Crude mortality rate (per 100 person-years) (95%CI)	Adjusted HR (95%CI)[a]	Attributable mortality[b] No. (%)
Neither event	2971	173	3.2 (2.8-3.7)	---	---
MI	189	39	29.5 (22.1-40.5)	5.7 (3.6-9.3)	32 (12.0)
Bleeding	428	58	22.3 (17.1-29.1)	5.4 (3.6-8.1)	47 (17.5)

95%CI, 95% confidence interval; ACS, acute coronary syndrome; BARC, bleeding academic research consortium; BMI, body mass index; CAD, coronary artery disease; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; HR, hazard ratio; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

[a]Adjusted for: age ≥65 years, female sex, body mass index (kg/m^2), current smoking, hypertension, dyslipidemia, diabetes mellitus, prior coronary artery disease, history of congestive heart failure or LVEF < 40%, prior vascular disease, history of bleeding, malignant disease, COPD, ACS type, baseline serum creatinine (mg/dL) and hemoglobin (g/dL) values, multivessel coronary disease, in-hospital PCI, in-hospital CABG, treatment at discharge, and study center.

[b]Attributable mortality was calculated using the following formula: number of deaths among patients with the attribute (MI or bleeding) x [adjusted HR-1]/adjusted HR.

Table 4 of the supplementary material

Comparison of the Baseline and Clinical Characteristics of Patients With Data on Follow-up vs

Patients Lost to Follow-up

	With data on follow-up n = 4229	Lost to follow-up n = 202	P
Demographic and past medical history			
Age, y	67 [57-77]	66.4 [56-77]	.08
BMI, kg/m^2	27.9 [25.4-31.1]	27.7 [25.2-30.0]	.83
Female	1064 (25.2)	57 (28.2)	.31
Current smoking	1404 (33.2)	70 (34.7)	.80
Hypertension	2779 (65.7)	132 (65.3)	.93
Diabetes mellitus	1343 (31.8)	61 (30.2)	.79
Dyslipidemia	2800 (66.2)	132 (65.3)	.83
Prior CAD	1225 (29.0)	57 (28.2)	.90
Prior vascular disease[a]	584 (13.8)	23 (11.4)	.74
Congestive heart failure	166 (3.9)	6 (3.0)	.91
Prior hospitalization for bleeding	108 (2.6)	3 (1.5)	.91
COPD	439 (10.4)	18 (8.9)	.84
History of malignant disease	330 (7.8)	13 (6.4)	.86
At hospital admission			
ACS type:			
Unstable angina	310 (7.3)	13 (6.4)	.90
NSTEMI	2297 (54.3)	109 (54.0)	.95

STEMI	1622 (38.4)	80 (39.6)	.83
Killip II-IV	663 (15.7)	26 (12.9)	.70
Serum creatinine, mg/dL	0.9 [0.8-1.1]	0.89 [0.76-0.97]	.06
Hemoglobin, g/dL	14.1 [12.9-15.2]	14.3 [13.1-15.5]	.47
LVEF < 40%	449 (10.6)	21 (10.4)	.98
In-hospital management and complications			
Multivessel coronary disease	1998 (47.3)	93 (45.1)	.68
PCI	3110 (73.5)	152 (75.2)	.64
CABG	232 (5.5)	9 (4.5)	.90
Drug-eluting stent	2447 (57.9)	118 (58.4)	.91
Bare-metal stent	697 (16.5)	32 (15.8)	.92
In-hospital bleeding[b]	433 (10.2)	21 (10.4)	.98
Treatment at discharge			
DAPT	3588 (84.8)	176 (87.1)	.41
Aspirin	4008 (95.9)	194 (96.0)	.95
Clopidogrel	2597 (62.3)	121 (59.9)	.59
Ticagrelor	659 (15.8)	36 (17.8)	.75
Prasugrel	391 (9.4)	19 (9.4)	1
Oral anticoagulant	479 (11.3)	18 (8.9)	.75
Proton pump inhibitor	3847 (91)	186 (92.1)	.61

ACS, acute coronary syndrome; BARC, bleeding academic research consortium; BMI, body mass index; CAD, coronary artery disease; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; HR, hazard ratio; LVEF, left ventricular ejection

fraction; MI, myocardial infarction; NSTEMI, non–ST-elevation acute myocardial infarction; PCI,

percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

Data are expressed as No. (%) or median [interquartile range].

[a]Denotes prior stroke or peripheral arterial disease.

[b]Denotes in-hospital BARC type 2, BARC type 3, and BARC type 4 bleeding.

Figure 1 of the supplementary material. Differential impact of postdischarge myocardial infarction vs bleeding severity on subsequent mortality among the 3588 patients discharged with DAPT.
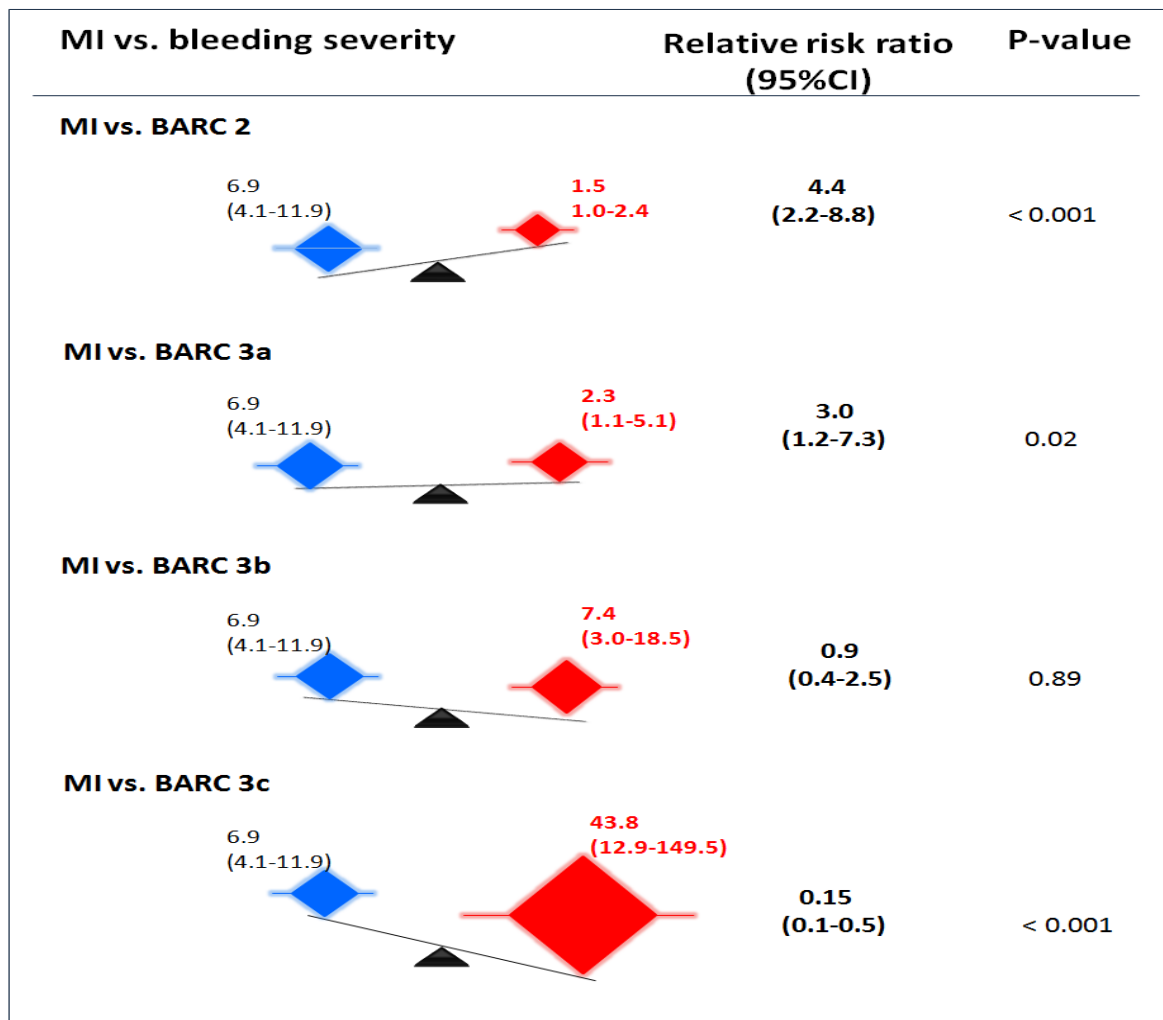
MI and bleeding are represented in blue and red, respectively.

95%CI, 95% confidence interval; BARC, bleeding academic research consortium; DAPT, dual antiplatelet therapy; MI, myocardial infarction.

Figure 2 of the supplementary material. Time-association pattern of the impact of postdischarge myocardial infarction vs bleeding on subsequent mortality during follow-up among the 3588 patients discharged with dual antiplatelet therapy.
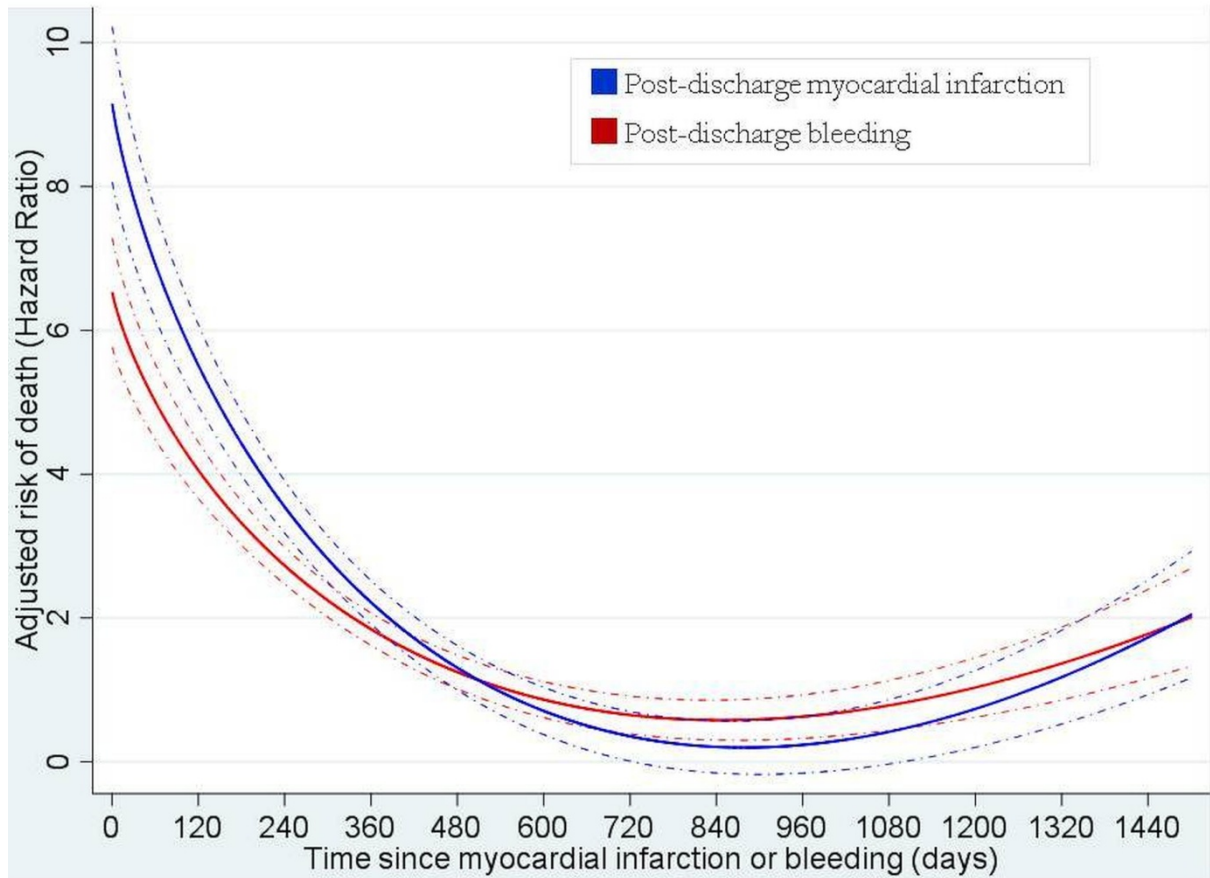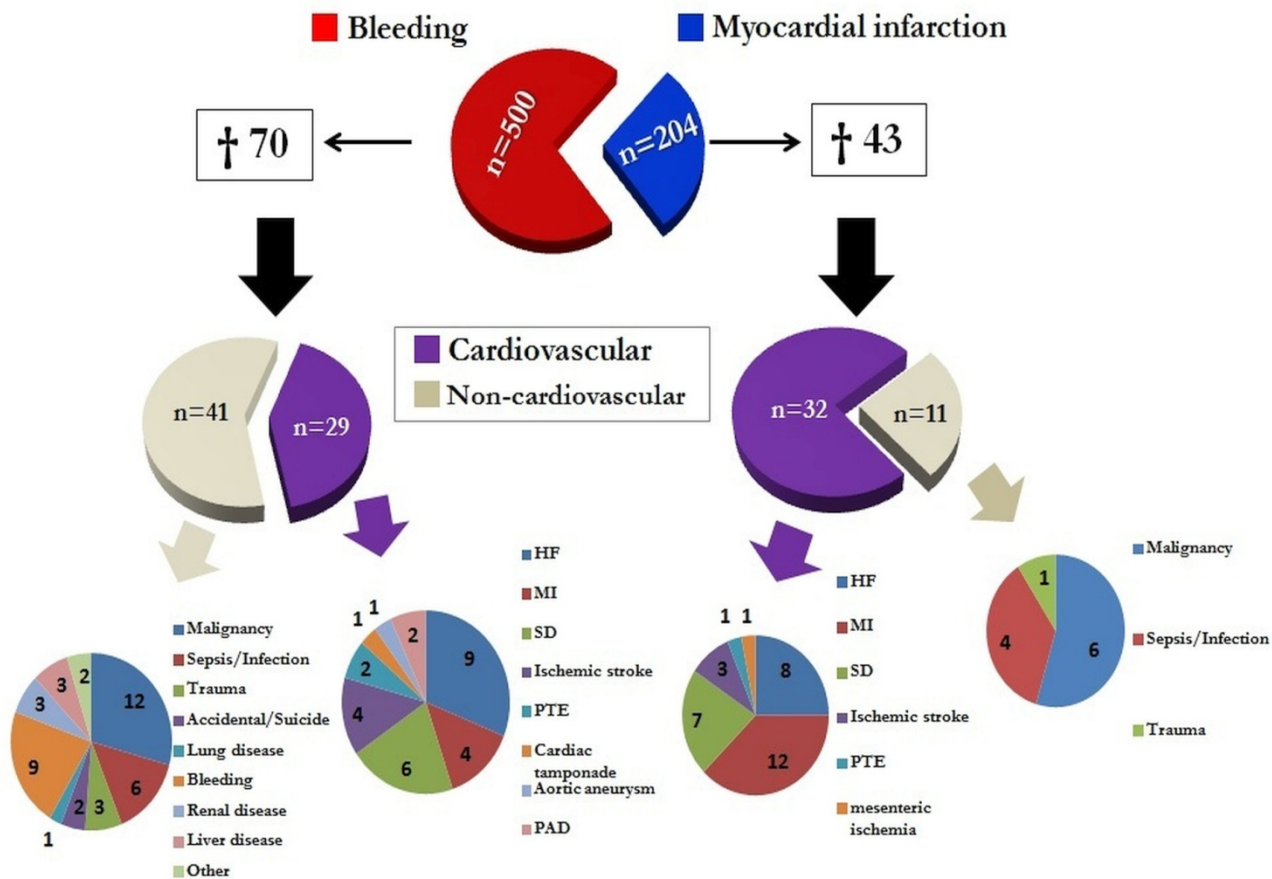
Figure 3 of the supplementary material. Specific cause of death among patients with an MI or a bleeding event during follow-up.

HF, heart failure; MI, myocardial infarction; PAD, peripheral arterial disease; PTE, pulmonary thromboembolism; SD, sudden death.