



Supplementary material

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

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

<i>COPD</i>	1.4 (1.02-2.0)	.04
<i>Prior malignant disease</i>	1.9 (1.3-2.9)	< .001
<i>ACS presentation:</i>		
Unstable angina	Ref.	Ref.
STEMI	1.3 (0.8-2.4)	.38
NSTEMI	1.9 (1.0-3.7)	.04
<i>Serum creatinine (per 1 mg/dL increase)</i>	1.5 (1.03-2.2)	.03
<i>Hemoglobin (per 1 g/dL increase)</i>	0.9 (0.8-0.9)	.001
<i>Multivessel coronary disease</i>	1.6 (1.2-2.2)	.003
<i>In-hospital PCI</i>	0.6 (0.4-0.9)	.005
<i>In-hospital CABG</i>	0.6 (0.3-1.2)	.19
<i>DAPT at discharge:</i>		
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
<i>Oral anticoagulant at discharge</i>	1.4 (1.0-1.9)	.07
<i>Proton pump inhibitor at discharge</i>	1.2 (0.9-1.6)	.08
<i>Study center</i>	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.

^aDenots prior stroke or peripheral arterial disease.

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

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

^aDenote prior stroke or peripheral arterial disease.

^bDenotes 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.

^aAdjusted 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.

^bAttributable mortality was calculated using the following formula: number of deaths among patients with the attribute (MI or bleeding) \times [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	<i>P</i>
Demographic and past medical history			
<i>Age, y</i>	67 [57-77]	66.4 [56-77]	.08
<i>BMI, kg/m²</i>	27.9 [25.4-31.1]	27.7 [25.2-30.0]	.83
<i>Female</i>	1064 (25.2)	57 (28.2)	.31
<i>Current smoking</i>	1404 (33.2)	70 (34.7)	.80
<i>Hypertension</i>	2779 (65.7)	132 (65.3)	.93
<i>Diabetes mellitus</i>	1343 (31.8)	61 (30.2)	.79
<i>Dyslipidemia</i>	2800 (66.2)	132 (65.3)	.83
<i>Prior CAD</i>	1225 (29.0)	57 (28.2)	.90
<i>Prior vascular disease^a</i>	584 (13.8)	23 (11.4)	.74
<i>Congestive heart failure</i>	166 (3.9)	6 (3.0)	.91
<i>Prior hospitalization for bleeding</i>	108 (2.6)	3 (1.5)	.91
<i>COPD</i>	439 (10.4)	18 (8.9)	.84
<i>History of malignant disease</i>	330 (7.8)	13 (6.4)	.86
At hospital admission			
<i>ACS type:</i>			
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
<i>Killip II-IV</i>	663 (15.7)	26 (12.9)	.70
<i>Serum creatinine, mg/dL</i>	0.9 [0.8-1.1]	0.89 [0.76-0.97]	.06
<i>Hemoglobin, g/dL</i>	14.1 [12.9-15.2]	14.3 [13.1-15.5]	.47
<i>LVEF < 40%</i>	449 (10.6)	21 (10.4)	.98
In-hospital management and complications			
<i>Multivessel coronary disease</i>	1998 (47.3)	93 (45.1)	.68
<i>PCI</i>	3110 (73.5)	152 (75.2)	.64
<i>CABG</i>	232 (5.5)	9 (4.5)	.90
<i>Drug-eluting stent</i>	2447 (57.9)	118 (58.4)	.91
<i>Bare-metal stent</i>	697 (16.5)	32 (15.8)	.92
<i>In-hospital bleeding^b</i>	433 (10.2)	21 (10.4)	.98
Treatment at discharge			
<i>DAPT</i>	3588 (84.8)	176 (87.1)	.41
<i>Aspirin</i>	4008 (95.9)	194 (96.0)	.95
<i>Clopidogrel</i>	2597 (62.3)	121 (59.9)	.59
<i>Ticagrelor</i>	659 (15.8)	36 (17.8)	.75
<i>Prasugrel</i>	391 (9.4)	19 (9.4)	1
<i>Oral anticoagulant</i>	479 (11.3)	18 (8.9)	.75
<i>Proton pump inhibitor</i>	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

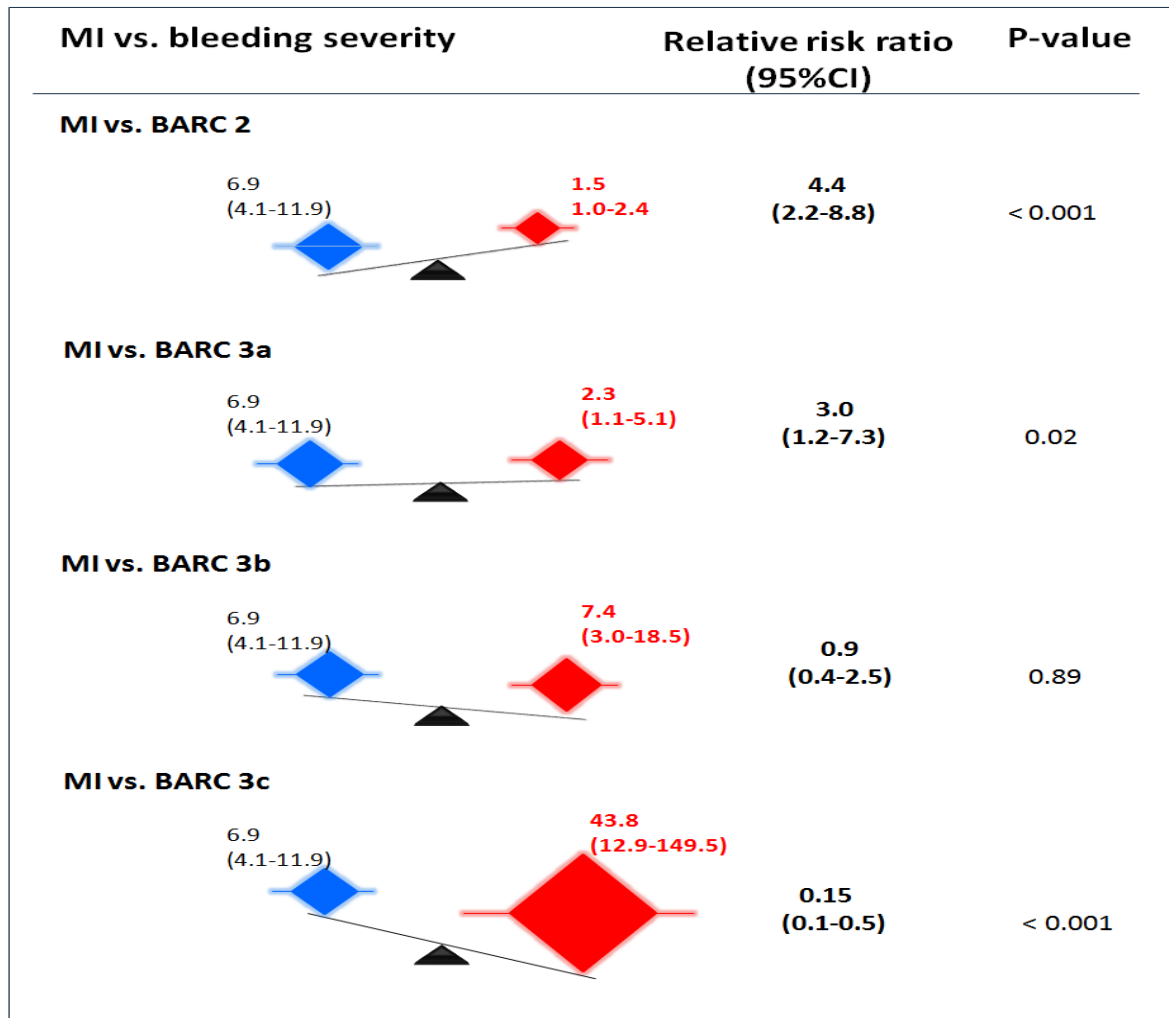
fraction; MI, myocardial infarction; NSTEMI, non–ST-elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

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

^aDenotes prior stroke or peripheral arterial disease.

^bDenotes 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.

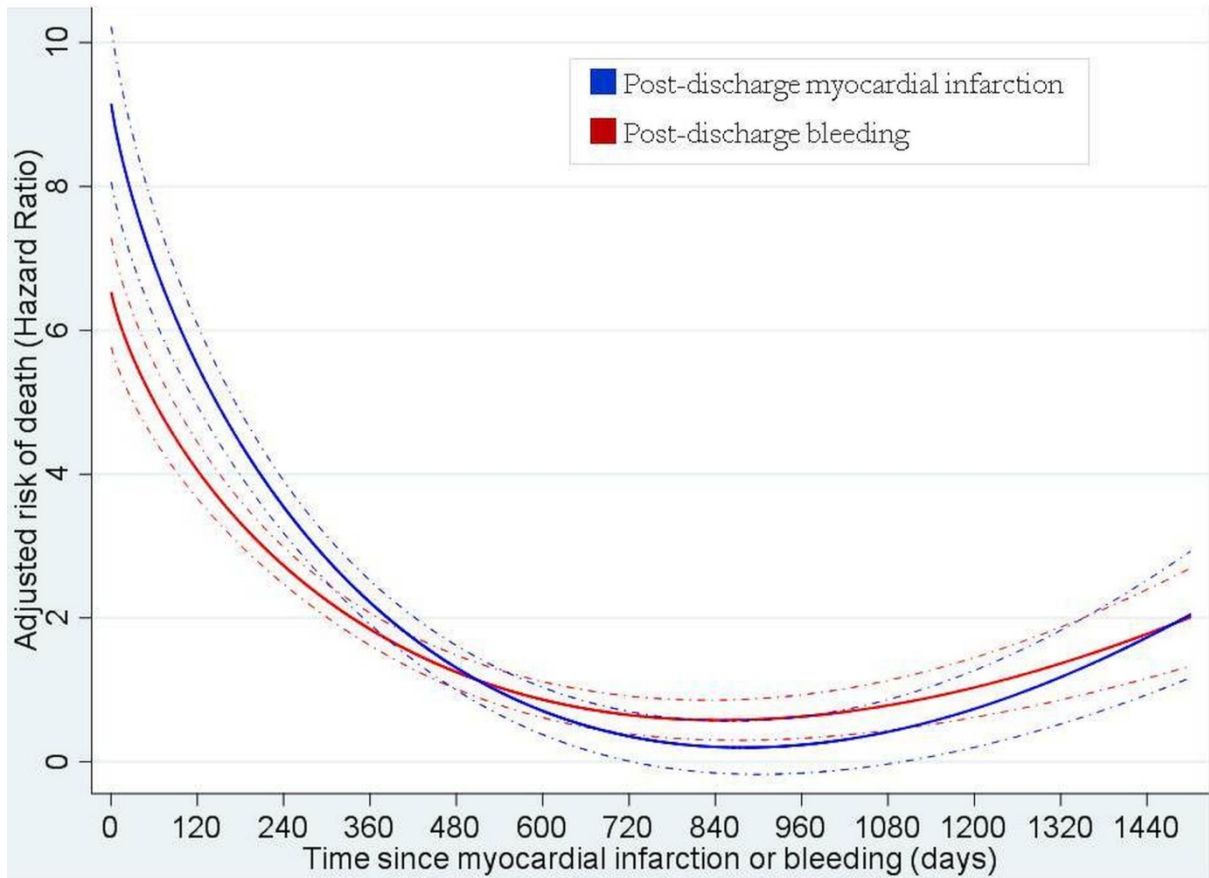
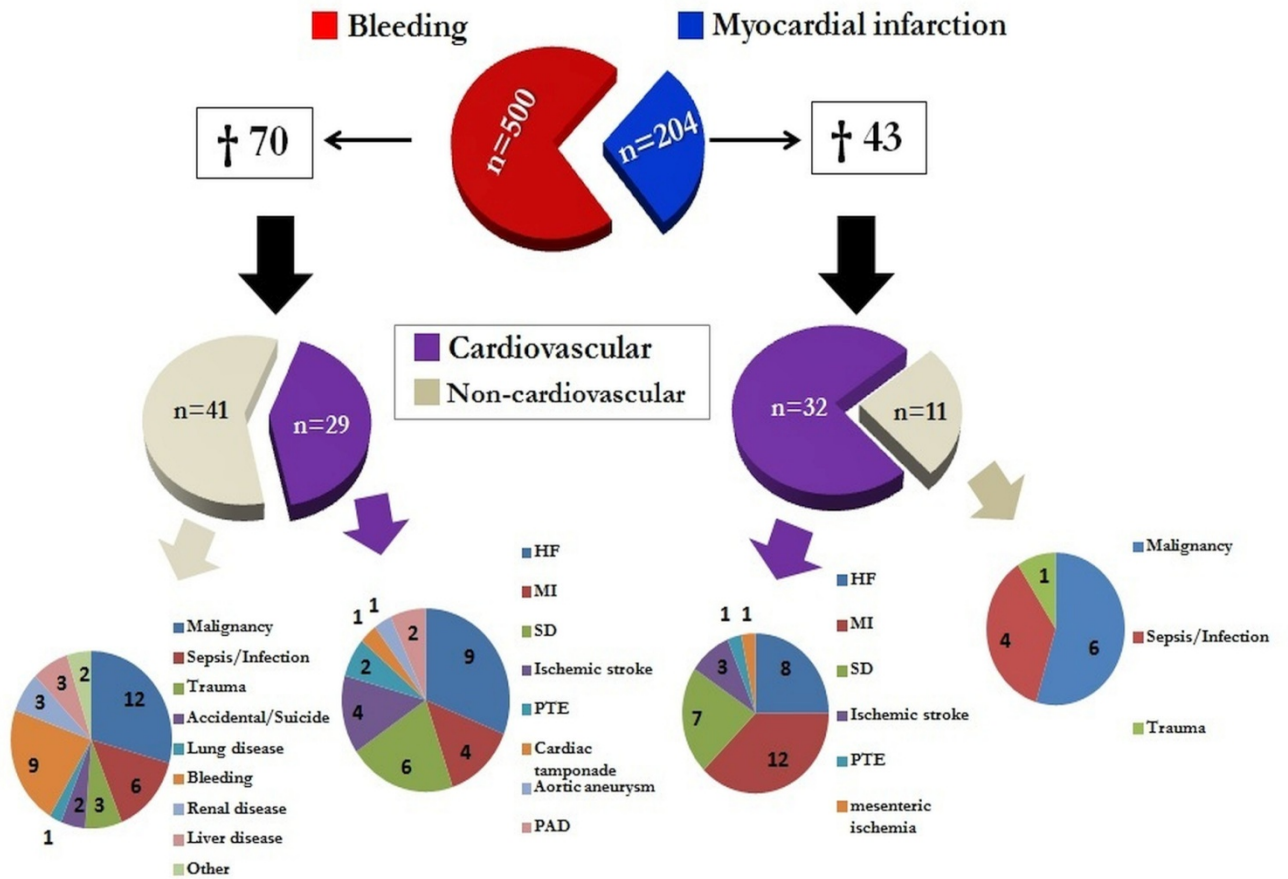


Figure 3 of the supplementary material. Specific cause of death among patients with an MI or a bleeding event during follow-up.



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