



Supplementary material

**Prevalence and Prognosis of High-risk Myocardial Infarction Patient
Candidates to Extended Antiplatelet Therapy**

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Table 1 of the supplementary material.

Acute Myocardial Infarction Annual Incidence (x 100 000) and Mortality Rates (x 100) by Sex and Age Group in Spain

	45-54 y	55-64 y	65-74 y	75-84 y	> 84 y
Men					
Incidence	0.00190	0.00325	0.00548	0.01723	0.01723
Mortality 1 st y	0.04670	0.08115	0.13968	0.20222	0.26136
Mortality 2 nd -4 th y	0.01072	0.02711	0.04732	0.05693	0.06944
Women					
Incidence	0.00023	0.00082	0.00237	0.01238	0.01238
Mortality 1 st y	0.04762	0.09756	0.16851	0.21413	0.40503
Mortality 2 nd -4 th y	0.02749*	0.02749	0.04212	0.01818	0.06250

AMI, acute myocardial infarction.

Data obtained from the IBERICA and REGICOR population AMI Registries. IBERICA: incidence rates for the population aged 45-74 years. Rates were adjusted for clustering and AMI definition change.

REGICOR: incidence rates in population > 74 years and mortality rates. Incident rates in the population > 74 years were weighted for the observed differences in incidence rates between Girona and Spain in the 65-74 years age group in the IBERICA Study (1126 in men and 1263 in women). Due to the similarity of the population > 75 years and to the low sample size, the incidence was combined for age groups 75-84 years and > 84 years. * There were no patients in this group, so the incidence of the following age group was assumed.

Table 2 of the supplementary material.

Bleeding Risk in Acute Myocardial Infarction Patients During Hospital Admission and During the First Year After The Event in Patients From the REGICOR Registry From 2003-2009.

	In-hospital risk of bleeding (CRUSADE scale)		Risk of bleeding during the 1 st year post AMI (CARDIOCHUS scale)	
	Men	Women	Men	Women
45-54 y	4.00%	6.30%	1.54%	5.05%
55-64 y	5.20%	7.39%	3.24%	6.89%
65-74 y	7.52%	10.93%	7.25%	12.82%

First, the number of patients in each scale category was calculated and then this number was combined with the described risk for each category^{1,2} to obtain the expected risk in each group.

AMI, acute myocardial infarction.

Table 3 of the supplementary material

Prevalence of PEGASUS Main Characteristics in Stable Acute Myocardial Infarction Patients Aged > 49 Years in the 2003-2009 REGICOR Registry, When no Age Limit Was Established in the Recruitment

	Men (n = 1378)			Women (n = 439)		
	Diabetes	Previous AMI	CKD	Diabetes	Previous AMI	CKD
50-64 y	27.8%	9.2%	9.2%	33.1%	7.7%	14.6%
65-74 y	35.5%	17.4%	23.1%	35.7%	9.5%	30.3%
75-84 y	25.4%	19.0%	28.7%	40.6%	13.4%	38.6%
≥ 85 y	40.0%	26.3%	30.0%	45.0%	42.1%	75.0%
≥ 50 y	28.9%	14.5%	14.6%	40.4%	13.3%	33.5%

AMI, acute myocardial infarction; CKD, chronic kidney disease.

Table 4 of the supplementary material

Prevalence of > 0, > 1 and > 2 PEGASUS Characteristics in Stable Acute Myocardial Infarction Patients in the REGICOR Registry, 2007-2008, by Age Group

	55-64 y	65-74 y	75-84 y	>84 y
Men				
>0	37.3%	47.1%	56.1%	72.7%
>1	5.3%	15.2%	18.4%	27.3%
>2	1.0%	2.9%	3.5%	3.5%*
Women				
>0	38.1%	66.7%	60.3%	85.7%
>1	11.9%	11.8%	26.0%	57.1%
>2	4.8%	4.8%*	6.8%	19.0%

AMI, acute myocardial infarction.

* There were no patients in these groups so the prevalence of the previous age group was assumed.

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Incidence (x 100) of Events in Stable Acute Myocardial Infarction Patients With and Without PEGASUS
Criteria Obtained by Competing Risk Adjusted Survival Analysis

	Non-PEGASUS		PEGASUS	
	Estimate	95%CI	Estimate	95%CI
Annual incidence during the second year after the index AMI				
AMI	1.52	(0.68, 2.98)	2.62	(1.72, 3.81)
CV death	0.22	(0.02, 1.16)	0.76	(0.34, 1.52)
Non-CV death	0.43	(0.09, 1.47)	1.31	(0.72, 2.22)
All-cause death	0.64	(0.18, 1.77)	2.05	(1.28, 3.12)
Incidence during a median follow-up of 4.7 years after 1 year of stable disease				
AMI	6.38	(3.83, 9.79)	7.68	(5.88, 9.77)
CV death	0.96	(0.32, 2.33)	13.39	(6.96, 21.94)
Non-CV death	2.95	(1.25, 5.86)	9.67	(6.45, 13.65)
All-cause death	3.86	(1.94, 6.82)	22.95	(15.28, 31.57)

AMI, acute myocardial infarction; CI, confidence interval; CV, cardiovascular

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Harrell's C for the Cox Proportional Hazards Regression Models at 4.7 Years of Median Follow-up

Outcome at 4.7 years of median follow-up↓	Harrell's C Model1 (SE)	Harrell's C Model2 (SE)	Harrell's C Model3 (SE)	Harrell's C Model4 (SE)
AMI	0.529 (0.027)	0.629 (0.035)	0.646 (0.037)	0.654 (0.037)
CV death	0.637 (0.028)	0.732 (0.037)	0.746 (0.039)	0.759 (0.040)
Non-CV death	0.604 (0.03)	0.700 (0.041)	0.729 (0.042)	0.734 (0.043)
All-cause death	0.622 (0.021)	0.712 (0.028)	0.717 (0.029)	0.727 (0.029)
AMI/All-cause death	0.579 (0.017)	0.644 (0.023)	0.645 (0.024)	0.655 (0.024)

Model 1: outcome~PEGASUS; Model 2: outcome~PEGASUS + age + hypertension + smoking + heart failure

Model 3: as model 2 plus ST elevation + reperfusion + arrhythmia + maximum Killip class

Model 4: as model 3 plus beta-blockers and lipid-lowering drugs at discharge

SE, standard error.

Table 7 of the supplementary material

Hazard Ratio of Outcomes During a 4.7 Years of Median Follow-up of Stable PEGASUS Acute Myocardial Infarction Patients Including Multivessel Coronary Heart Disease in the PEGASUS Definition

	Model 1	Model 2	Model 3	Model 4
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
AMI	1.16 (0.69, 1.94)	1.22 (0.63, 2.36)	1.11 (0.49, 2.56)	1.12 (0.49, 2.56)
CV death	8.92 (2.81, 28.32)*	4.29 (1.22, 15.07)*	2.73 (0.71, 10.42)	2.81 (0.73, 10.74)
Non-CV death	3.69 (1.59, 8.54)*	1.72 (0.63, 4.73)	1.32 (0.37, 4.76)	1.19 (0.33, 4.33)
All-cause death	5.43 (2.76, 10.67)*	2.58 (1.19, 5.58)*	1.91 (0.76, 4.79)	1.83 (0.73, 4.60)
AMI/All-cause death	2.22 (1.49, 3.32)*	1.41 (0.85, 2.34)	1.29 (0.70, 2.39)	1.26 (0.68, 2.34)

AMI, acute myocardial infarction; CHD, coronary heart disease; CI, confidence interval; CV, cardiovascular; HR, hazard ratio.

Models: 1=Crude HR; 2=Adjusted for age, hypertension, smoking, heart failure; 3 = As model 2 plus ST elevation, reperfusion, arrhythmia, maximum Killip class; 4=As model 3 plus beta-blockers and lipid-lowering drugs at discharge. * $P < .05$

Table 8 of the supplementary material

Estimated Annual Number of Acute Myocardial Infarction Patients \geq 50 Years, Stable and Without Bleeding Events at 1-year Follow-up, in Spain in 2014.

	Hospitalized AMI patients n (95%CI)	Stable AMI patients at 1 year n (95%CI)	Stable AMI patients without severe bleeding n (95%CI)
50-64 y	11831 (11620; 12046)	11021 (10017; 11229)	10077 (9882; 10276)
65-74 y	13157 (12934; 13384)	11192 (10987; 11401)	9301 (9114; 9492)
75-84 y	25544 (25233; 25859)	20234 (19957; 20515)	16583 (16332; 16837)
> 84 y	9996 (9802; 10194)	6560 (6403; 6721)	5350 (5209; 5495)
\geq 50 y	60528 (60047; 61012)	49007 (48575; 49442)	41311 (40914; 41711)

AMI, acute myocardial infarction; CI, confidence interval.

Table 9 of the supplementary material

Estimated Annual Number of Acute Myocardial Infarction Patients \geq 50 Years, by Number of PEGASUS Criteria, in Spain in 2014

	\geq 1 PEGASUS characteristic n (95%CI)	\geq 2 PEGASUS characteristics n (95%CI)	3 PEGASUS characteristics n (95%CI)
50-64 y	3746 (3628; 3868)	627 (580; 678)	171 (147; 199)
65-74 y	4943 (4807; 5083)	1310 (1241; 1383)	336 (302; 374)
75-84 y	9582 (9392; 9776)	3576 (3461; 3695)	793 (740; 850)
> 84 y	4223 (4098; 4352)	2239 (2148; 2334)	584 (538; 633)
\geq 50 y	22493 (22200; 22788)	7752 (7581; 7926)	1885 (1802; 1972)

AMI, acute myocardial infarction; CI, confidence interval.

*PEGASUS criteria: diabetes, previous AMI and chronic disease.

Table 10 of the supplementary material

Estimated Number of Patients Older Than 50 Years With Stable Coronary Artery Disease After Previous (1-3 Years) Acute Myocardial Infarction, in Spain in 2014.

	Men		Women	
	n	95%CI	n	95%CI
50-64 y	29 518	(29 183; 29 856)	6 457	(6 301; 6 616)
65-74 y	24 171	(23 868; 24 477)	11 655	(11 445; 11 868)
75-84 y	45 370	(44 954; 45 789)	48 863	(48 431; 49 298)
> 84 y	11 528	(11 319; 11740)	13 927	(13 697; 14 160)
≥ 50 y	110 589	(109 939; 111 242)	80 902	(80 346; 81 461)

CI, confidence interval

Table 11 of the supplementary material

Crude Incidence (x 100) of Events in Stable Acute Myocardial Infarction Patients With and Without PEGASUS Criteria, at 3 Years After the Index Acute Myocardial Infarction

	Non-PEGASUS (n = 470)	PEGASUS (n = 936)
AMI	3.1	4.4
CV death	0.4*	3.2
Non-CV death	0.6*	3.1
All-cause death	1.1*	6.4
AMI/All-cause death	4.4*	10.5

AMI, acute myocardial infarction; CV, cardiovascular. * $P < .05$

Table 12 of the supplementary material

Hazard Ratio of Outcomes at 2 Years In PEGASUS vs non-PEGASUS Patients.

	Model 1	Model 2	Model 3	Model 4
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)
AMI	1.80 (0.78, 4.17)	2.48 (0.89, 6.94) [†]	2.52 (0.90, 7.05) [†]	2.37 (0.83, 6.76)
CV death	6.10 (0.79, 46.89) [†]	4.61 (0.50, 42.66)	4.45 (0.48, 41.44)	4.36 (0.47, 40.39)
Non-CV death	3.56 (0.81, 15.67) [†]	2.25 (0.38, 13.19)	1.82 (0.30, 10.81)	1.73 (0.29, 10.35)
All-cause death	4.41 (1.33, 14.56) [*]	3.07 (0.78, 11.99)	2.70 (0.68, 10.62)	2.63 (0.67, 10.35)
AMI/All-cause death	2.34 (1.18, 4.64) [*]	2.26 (0.97, 5.23) [†]	2.15 (0.92, 5.00) [†]	2.03 (0.86, 4.76)

AMI, acute myocardial infarction; CI, confidence interval; CV, cardiovascular; HR, hazard ratio.

Models: 1 = crude HR, 2 = adjusted for age, hypertension, heart failure, 3= as model 2 plus reperfusion and beta-blocker therapy during hospitalization, 4 = as model 3 plus antiplatelet therapy at discharge.

^{*} $P < .05$; [†] $P < .1$

Table 13 of the supplementary material

Analysis of Outcome Predictors in the Follow-up of PEGASUS Patients

	AMI	CV death	Non-CV death	All-cause death	AMI/All-cause death
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)
Age		1.05 (1.00, 1.10)	1.05 (0.99, 1.12)	1.06 (1.02, 1.10)*	1.04 (1.01, 1.07)*
Diabetes		1.73 (0.98, 3.05)			1.43 (0.99, 2.05)†
Previous AMI	2.17 (1.18, 4.00)*	1.76 (0.94, 3.29)		1.61 (0.99, 2.61)*	2.05 (1.39, 3.03)*
eGFR		0.98 (0.97, 0.99)*		0.99 (0.98, 0.99)*	0.99 (0.98, 0.99)*
Hypertension	2.77 (1.24, 6.19)*				
Smoking				1.39 (0.84, 2.27)	
Heart failure		2.82 (1.52, 4.60)*	2.30 (1.15, 4.60)*	2.11 (1.39, 3.21)*	1.59 (1.10, 2.30)*
Arrhythmia	0.52 (0.22, 1.23)				
Beta-blockers at discharge			0.40 (0.20, 0.81)*	0.53 (0.35, 0.81)*	0.60 (0.42, 0.87)*

AMI, acute myocardial infarction; ; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction.

Model building strategy:

- 1) Inclusion of all variables that showed an association with the outcome on bivariate analysis ($P < .25$)
- 2) Exclusion of the variables (one-by-one) that reduced the likelihood ($P > 0.1$) until further reduction was not possible ($P < .1$)
- 3) Reconsideration of all excluded variables (one-by-one) ($P < .1$)

* $P < .05$

REFERENCES

1. Subherwal S, Bach RG, Chen AY, Gage BF, Rao SV, Newby LK, et al. Baseline risk of major bleeding in non-ST-segment elevation myocardial infarction: the CRUSADE bleeding score. *Circulation*. 2009;119:1873–82.
2. Raposeiras S, Abu-Assi E, Alvarez B, Gonzalez MC, Mazon-Ramos P, Virgós A, et al. Prediction of bleeding admission in the first year after acute coronary syndrome and prognostic impact: the cardiochus bleeding risk score [abstract]. *J Am Coll Cardiol*. 2014;63(Suppl12):A32.