

Supplement

D. Venetsanos, E. Träff, D. Erlinge et al. **Prasugrel versus Ticagrelor in myocardial infarction patients undergoing percutaneous coronary intervention**

Figure S1. Flow chart

Appendix:

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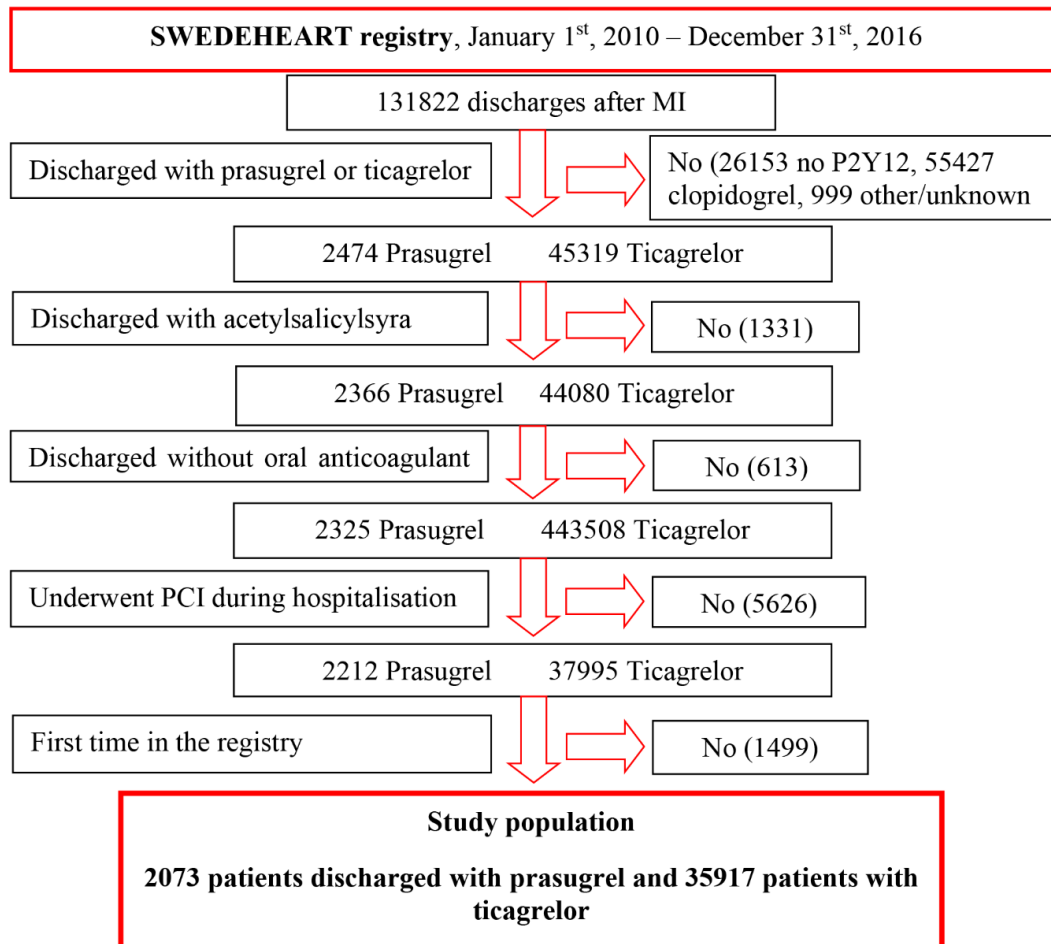
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Figure S2: Distribution of propensity score before (a) and after (b) inverse probability weighting

Figure S1. Flow chart

Appendix

Outcome definition

Major bleeding was defined as any rehospitalisation for a cerebral, gastrointestinal or urogenital bleeding or bleeding from the respiratory tract, identified by using the following International Classification of Diseases codes: I60, I61, I62, D629, D500, H356, H431, H450, H922, I850, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K625, K920, K921, K922, N421, N938, N939, N950, R041, R042, R048, R049, R210, R319, T810, N501A.

Statistical analysis

Covariates that were included in multivariable analysis and in individual propensity score calculation were selected based on investigators clinical experience. The following covariates were included: age, gender, smoking status, history of diabetes mellitus, hypertension, hyperlipidemia, previous myocardial infarction (MI), previous percutaneous coronary intervention (PCI), previous coronary artery by-pass grafting, previous stroke, previous congestive heart failure, known renal insufficiency, chronic obstructive pulmonary disease, peripheral artery disease, previous cancer, a history of bleeding, cardiopulmonary resuscitation before admission, Killip class >1, anaemia on admission, estimated glomerular filtration rate <60 ml/min/1.72m² on admission, treatment with aspirin on arrival, P2Y₁₂ receptor inhibitors on arrival, statins on arrival, multivessel disease, PCI with stent, PCI-access site, use of continuous positive airway pressure, administration of inotropic agents, iv diuretics during the index hospitalisation, medication at discharge including beta blockers, statins, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, diuretics and antidiabetic treatment (no, po drugs or insulin) and MI type (ST segment elevation MI vs non-ST segment elevation MI).

Based on the individual PS, we calculated the stabilised inverse probability of treatment weights (IPTW). To obtain a similar number in the two treatment arms after inverse probability weighting, the weights were stabilized. Stabilization (multiplying the weight by the probability of being exposed for those exposed and the probability of being unexposed for those unexposed), results in a pseudo-population with similar percentage of patients exposed/un-exposed in each level of the covariates as the overall percentage in the study population. Stabilization does not affect the point estimates but reduces the variability of the weights.

Goodness of fit of the logistic regression, used to calculate the individual propensity score was assessed using Hosmer-Lemeshow test (0.11). The c-index was 0.73. Plots of PS after weighting for IPTW showed an

excellence balance between the two treatment groups. Finally, in a sensitivity analysis, truncation of PS score at 1st centile was performed and similar results were obtained (data not shown).

All 5 imputed data bases were used in the IPTW cox regression and multivariable cox regressions models to obtain the 5 completed data estimates of coefficients.

Table S1. Missing values

Baseline characteristics	N missing	Clinical characteristics on arrival	N missing	Percutaneous Coronary Intervention	N missing
Age, years	0	CPR outside hospital	425	Access site- radial artery	127
Body weight	472	Thrombolysis before admission	233	Multivessel disease	208
Sex	0	Atrial Fibrillation on arrival	313	PCI with stent	158
Smoking	1031	Heart rate	208	Medication during PCI	
Previous MI	0	Systolic blood pressure	208	Aspirin	0
History of Diabetes Mellitus	0	Killip Class	596	P2Y12 receptor inhibitors	0
History of Hypertension	130	Laboratory data index		Unfractionated heparin	14
History of Hyperlipidaemia	443	Estimated GFR	1649	GP IIb/IIIa receptor inhibitor	23
Previous PCI	137	Anaemia	2220	During the index hospitalisation	
Previous CABG	0	Crusade bleeding score	2874	CPAP	31
Previous stroke	0	Medication on arrival		New onset AF	12
History of CHF	977	Oral Anticoagulant	422	Iv diuretics	25
History of Renal failure - on dialysis	0	Aspirin	431	Inotropic drug	29
History of COPD	0	P2Y12 receptor inhibitors	427	LMWH /fondaparinux	60
History of PAD	0	Statins	443	Medication at discharge	
History of Dementia	0	Beta blockers	567	Aspirin	0
History of Cancer	0	ACE-I/ARB	503	Beta blockers	3
Previous Bleeding	0	Anti-Diabetic medications	376	ACE-I/ARB	0
Clinical characteristics on arrival		Diuretics	504	Statins	2
Infarct type	4			Anti-diabetic medications	1
Abbreviations (in order of appearance): MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; CPR, cardiopulmonary resuscitation; GFR, estimated glomerular filtration rate; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; Infarct type, ST segment elevation myocardial infarction or non ST segment elevation myocardial infarction; CPR, cardiopulmonary resuscitation; GFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention; CPAP, continuous positive airway pressure;					

Table S2. P2Y12 receptor inhibitors and acetylsalicylic acid dispensed prescriptions during follow-up (6 to 12 months, from discharge)

Patients, n 37990	Dispensed prescriptions 6-12 months after the index procedure			
	No or other	Ticagrelor	Prasugrel	Clopidogrel
Ticagrelor group	4048 (11.3)	28838 (80.3)	282 (0.8)	2749 (7.7)
Prasugrel group	232 (11.2)	59 (2.8)	1647 (79.5)	135 (6.5)
Among patients who survived the first year after discharge				
Ticagrelor group	3223 (9.2)	28646 (82.2)	281 (0.8)	2711 (7.8)
Prasugrel group	190 (9.4)	59 (2.9)	1641 (81.0)	135 (6.7)
Acetylsalicylic acid				
	Yes		No	
Ticagrelor group	33412 (93.0)		2505 (7.0)	
Prasugrel group	1945 (93.8)		128 (6.2)	

Table S3. Covariate balance between treatment groups, presented as mean standardised difference (MSD), before and after weighting for inverse probability of treatment weights

	Before IPTW			After IPTW		
	Prasugrel	Ticagrelor	MSD	Prasugrel	Ticagrelor	MSD
Age, mean	62.2	66.5	39.5	65.4	66.2	7.8
Female sex	0.21	0.27	13.9	0.27	0.27	0.0
Previous/current smokers	0.68	0.62	11.2	0.62	0.63	1.1
Previous MI	0.24	0.18	13.3	0.21	0.18	5.3
History of Diabetes Mellitus	0.24	0.21	6.6	0.24	0.22	4.4
History of Hypertension	0.49	0.52	5.9	0.53	0.52	2.0
History of Hyperlipidaemia	0.30	0.25	10.7	0.27	0.25	4.7
Previous PCI	0.22	0.15	18.1	0.18	0.16	6.4
Previous CABG	0.05	0.06	0.3	0.06	0.06	0.6
Previous stroke	0.04	0.06	3.1	0.08	0.06	9.3
History of CHF	0.04	0.04	3.1	0.05	0.04	3.0
History of renal failure	0.02	0.02	0.6	0.02	0.02	3.0
History of COPD	0.04	0.05	5.1	0.05	0.05	0.8
History of PAD	0.03	0.03	0.7	0.03	0.03	0.5
History of Cancer	0.01	0.02	5.7	0.02	0.02	3.8
Previous Bleeding	0.03	0.04	3.5	0.04	0.04	2.8
Killip Class II-IV	0.05	0.05	0.1	0.05	0.05	2.1
CPR outside hospital	0.03	0.02	7.1	0.03	0.02	8.0
Estimated GFR ≤ 60 ml/min/1.73 ²	0.13	0.16	8.4	0.16	0.16	0.1
Anaemia	0.21	0.20	2.1	0.20	0.20	0.1
Aspirin on arrival	0.30	0.28	4.6	0.31	0.29	5.1
P2Y12 on arrival	0.10	0.04	24.9	0.04	0.04	1.5
Statins on arrival	0.30	0.25	10.5	0.28	0.26	4.4
Multivessel disease	0.52	0.49	5.0	0.52	0.50	4.0
PCI with stent	0.93	0.93	1.7	0.93	0.93	1.3
Radial access site	0.66	0.81	34.9	0.81	0.80	1.1
CPAP during hospitalisation	0.02	0.03	0.3	0.03	0.03	1.8
Inotropic drugs	0.05	0.03	13.1	0.03	0.03	2.0
Beta blocker at discharge	0.92	0.91	4.5	0.91	0.91	2.1
ACE-I/ARB at discharge	0.89	0.86	8.1	0.85	0.86	4.8
Statin at discharge	0.98	0.97	0.9	0.97	0.97	2.5
Anti-diabetic medication at discharge	0.20	0.17	7.3	0.20	0.18	4.5
Diuretics at discharge	0.18	0.16	4.3	0.17	0.16	2.2
Infarct Type-STEMI	0.73	0.46	56.1	0.50	0.48	3.9
Figures present proportion, if not otherwise stated. Abbreviations (in order of appearance): SD, standardised difference; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; CPR, cardiopulmonary resuscitation; GFR, estimated glomerular filtration rate; ICD, implantable cardiac defibrillator; CPAP,						

continuous positive airway pressure; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; STEMI, ST elevation myocardial infarction

Table S4. Propensity matched cohort

	Ticagrelor	Prasugrel	p-value
Number of patients	2071	2071	
Demographics			
Age, years, mean \pm SD	62.2 (11.0)	62.3 (10.1)	0.29
Female sex	434 (21.0)	435 (21.0)	0.97
Previous/current smoker	1389 (67.1)	1400 (67.5)	0.72
Medical History			
Previous MI	441 (21.3)	486 (23.5)	0.10
History of Diabetes Mellitus	455 (22.0)	500 (24.1)	0.10
History of Hypertension	1023 (49.4)	1012 (48.9)	0.73
History of Hyperlipidaemia	589 (28.4)	617 (29.8)	0.34
Previous PCI	434 (21.0)	456 (22.0)	0.41
Previous CABG	98 (4.7)	114 (5.5)	0.26
Previous stroke	89 (4.3)	90 (4.3)	0.94
History of CHF	80 (3.9)	93 (4.5)	0.31
History of COPD	100 (4.8)	88 (4.2)	0.37
History of PAD	59 (2.8)	71 (3.4)	0.29
History of Cancer*	27 (1.3)	28 (1.4)	0.89
Previous Bleeding	66 (3.2)	63 (3.0)	0.79
Clinical characteristics on arrival			
Killip Class II-IV	102 (4.9)	107 (5.2)	0.72
CPR outside hospital	77 (3.7)	68 (3.3)	0.45
Estimated GFR \leq 60 ml/min/1.73 ²	250 (12.1)	273 (13.2)	0.28
Anaemia	419 (20.2)	431 (20.8)	0.64
Crusade bleeding score	20 (14- 27)	20 (14- 27)	0.32
1-20	1082 (52.2)	1062 (51.3)	0.54
21-30	658 (31.8)	654 (31.6)	
31-40	229 (11.1)	232 (11.2)	
\geq 41	102 (4.9)	123 (5.9)	
Medications on arrival			
Aspirin	584 (28.2)	628 (30.3)	0.13
P2Y ₁₂ receptor inhibitors	176 (8.6)	203 (9.8)	0.17
Statins	595 (28.7)	620 (29.9)	0.39
Percutaneous Coronary Intervention			
Multivessel disease	1042 (50.3)	1076 (52.0)	0.29
PCI with stent	1939 (93.6)	1920 (92.7)	0.24
Transradial access	1383 (66.8)	1361 (65.7)	0.13
During the index hospitalisation			
CPAP	64 (3.1)	51 (2.5)	0.22
Inotropic drug	104 (5.0)	104 (5.0)	1.00
Medication at discharge			
Beta blockers	1915 (92.5)	1906 (92.0)	0.60
ACE-I/ARB	1836 (88.7)	1842 (88.9)	0.77
Statins	2013 (97.2)	2022 (97.6)	0.38
Anti-diabetic medications	375 (18.1)	407 (19.7)	0.20
Diuretics	343 (16.6)	366 (17.7)	0.34
Infarct type			
ST-segment elevation MI	1537 (74.2)	1507 (72.8)	0.29
Non-ST-segment elevation MI	534 (25.8)	564 (27.2)	
Results are presented as numbers and percentages unless otherwise indicated. Abbreviations (in order of appearance): SD, standard deviation; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; CPR, cardiopulmonary resuscitation; GFR, estimated glomerular filtration rate; ICD, implantable cardiac defibrillator; CPAP, continuous positive airway pressure; ACE-I, angiotensin-converting			

enzyme inhibitor; ARB, angiotensin receptor blocker; *Any cancer diagnosis the last 5 years; ** Were administrated 24 hours before or during PCI

Table S5. One-year outcomes before and after multivariable Cox regression, including calendar year

	Prasugrel	Ticagrelor	
Patients, n	2073	35917	
	Events, n (%)		HR (95% CI)
MACCE			
Crude	127 (6.1)	2196 (6.1)	1.00 (0.84- 1.20)
MV analysis including calendar year			1.08 (0.89- 1.32)
NACCE			
Crude	174 (8.4)	3130 (8.7)	0.96 (0.82- 1.12)
MV analysis including calendar year			1.07 (0.90- 1.27)
All-cause mortality			
Crude	48 (2.3)	1056 (2.9)	0.79 (0.59- 1.05)
MV analysis including calendar year			0.95 (0.69- 1.30)
Myocardial infarction			
Crude	85 (4.1)	1123 (3.2)	1.32 (1.06- 1.64)
MV analysis including calendar year			1.15 (0.90- 1.48)
Stroke			
Crude	18 (0.9)	385 (1.1)	0.81 (0.50- 1.30)
MV analysis including calendar year			0.84 (0.50- 1.40)
Major bleeding			
Crude	51 (2.5)	1124 (3.2)	0.78 (0.59- 1.03)
MV analysis including calendar year			0.98 (0.72- 1.33)
Major adverse cardiac and cerebrovascular events (MACCE) including all-cause death, myocardial infarction, or stroke (ischemic and haemorrhagic); Net adverse cardiac and cerebrovascular events (NACCE) including MACCE and major bleeding during follow up. Hazard ratios (HR) with 95% confidence intervals were derived from Cox regression analysis. In the unadjusted model (crude) only treatment was included as covariate. In the multivariable model (MV) 34 additional covariates and calendar year were included.			

