Title: Post-hoc analyses of randomized clinical trial for the effect of clopidogrel added to aspirin on kidney function

Authors: [1]Jesse C Ikeme; [2]Pablo E Pergola, PhD, MD; [1]Rebecca Scherzer, PhD; [1]Michael G Shlipak, MD, MPH; [3]Oscar R Benavente, MD; [1]Carmen A Peralta, MD, MAS

Affiliations: [1]The Kidney Health Research Collaborative at University of California San Francisco and San Francisco VA Medical Center, San Francisco, CA; [2]University of Texas Health Science Center at San Antonio, San Antonio, TX; [3]University of British Columbia, Vancouver, Canada

Contact

Carmen A. Peralta, MD, MAS

University of California San Francisco

4150 Clement St, 111A1

San Francisco, CA 94121

Tel: 415-221-4810 (x3678)

Fax: 415-379-5573

E-mail: (carmenalicia.peralta@ucsf.edu)

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Table S1: Baseline demographic and clinical characteristics of SPS3 participants, stratified by inclusion/exclusion status

Parameter	Included (n = 2611)	Excluded (n = 409)	P-value
Dual antiplatelet arm	1303 (50%)	214 (52%)	0.36
Intensive blood pressure target arm	1302 (50%)	199 (49%)	0.65
Age	62 (55, 71)	61 (54, 71)	0.21
Male	1655 (63%)	247 (60%)	0.24
Race			<.0001
Hispanic	835 (32%)	81 (20%)	
Non-Hispanic White	1300 (50%)	238 (58%)	
Black	413 (16%)	79 (19%)	
Other/multiple	63 (2%)	11 (3%)	
Education			0.14
0-4 years	273 (10%)	45 (11%)	
5-8 years	424 (16%)	48 (12%)	
9-12 years	983 (38%)	163 (40%)	
Any college	931 (36%)	153 (37%)	
Country			<.0001
Argentina	43 (2%)	2 (0%)	
Canada	242 (9%)	41 (10%)	
Chile	117 (4%)	10 (2%)	
Ecuador	162 (6%)	9 (2%)	
Mexico	147 (6%)	18 (4%)	
Peru	178 (7%)	8 (2%)	
Spain	290 (11%)	76 (19%)	
United States	1432 (55%)	245 (60%)	
Diabetes	949 (36%)	157 (38%)	0.43
Body mass index (kg/m^2)	28 (25, 32)	28 (25, 32)	0.89
Smoking			0.0008
Never	1035 (40%)	161 (39%)	
Former	1069 (41%)	138 (34%)	
Current	507 (19%)	110 (27%)	
History of myocardial infarction	137 (5%)	23 (6%)	0.75
History of Angina	143 (5%)	25 (6%)	0.60
History Ischemic Disease	271 (10%)	46 (11%)	0.59
History of coronary artery bypass graft	112 (4%)	23 (6%)	0.22
History of congestive heart failure	12 (<1%)	2 (<1%)	0.94
History of chronic obstructive pulmonary disease	71 (3%)	15 (4%)	0.28
History of hyperlipidemia	1291 (49%)	180 (44%)	0.041
Systolic blood pressure (mmHg)	141 (129, 154)	141 (129, 157)	0.33

Diastolic blood pressure (mmHg)	78 (71, 85)	78 (71, 85)	0.47
Antihypertensive use:			0.63
Diuretics	951 (36%)	144 (35%)	
Potassium supplements	93 (4%)	15 (4%)	0.91
Beta blockers	641 (25%)	109 (27%)	0.36
Calcium channel blockers	665 (25%)	111 (27%)	0.47
Angiotensin converting enzyme inhibitors	1374 (53%)	204 (50%)	0.30
Angiotensin receptor blockers	428 (16%)	54 (13%)	0.10
Miscellaneous blood pressure meds	177 (7%)	44 (11%)	0.0041
Number of antihypertensive meds:			0.84
0	398 (15%)	65 (16%)	
1	911 (35%)	146 (36%)	
2	746 (29%)	108 (26%)	
3+	556 (21%)	90 (22%)	
Alcohol use			0.74
0-6 drinks/week	2281 (87%)	353 (86%)	
7-13 drinks/week	165 (6%)	30 (7%)	
14+ drinks/week	165 (6%)	26 (6%)	
Prior lacunar stroke	259 (10%)	49 (12%)	0.19
Hypertension at randomization by SPS3 definition	2339 (90%)	370 (90%)	0.59
Statin use	1786 (68%)	295 (72%)	0.13
Low-density lipoprotein (mg/dL)	110 (84, 138)	110 (86, 136)	0.77
Fasting blood glucose (mg/dL)	105 (93, 136)	106 (94, 139)	0.52
eGFR	81 (67, 94)	81 (67, 97)	0.39
eGFR < 60	401 (15%)	73 (18%)	0.20

Data presented as median (interquartile range) or number (%). Abbreviations: SPS3 = Secondary prevention of small subcortical strokes, eGFR = estimated glomerular filtration rate.

Table S2: Association of antiplatelet arm with annual change in eGFR by systolic blood pressure target, time after randomization and baseline eGFR, without measures collected after June 19, 2011.

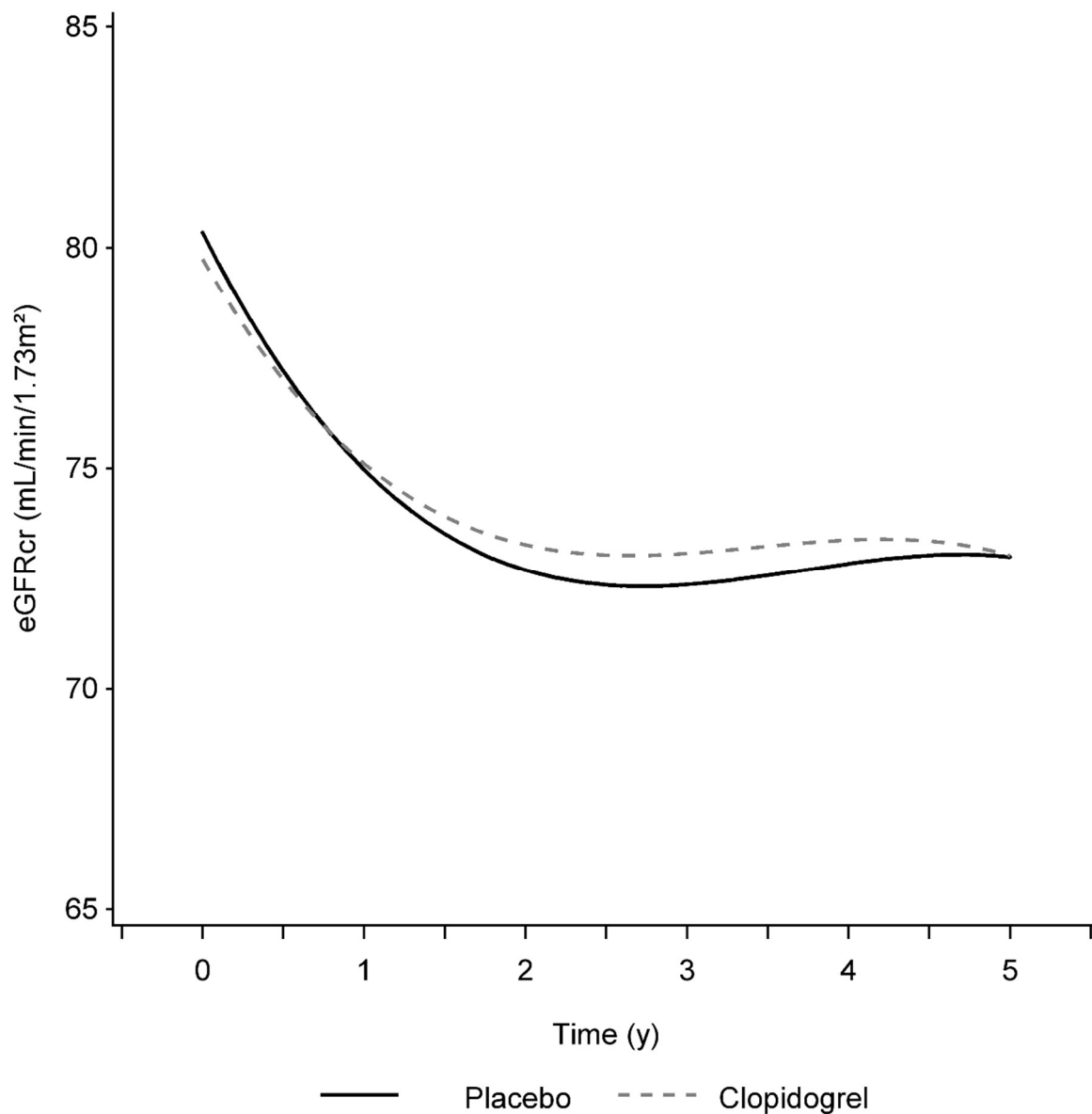| Year(s)	Annualized change in eGFR, mL/min/m2 (95% confidence interval)		Difference (95% confidence interval)	p-value
	Clopidogrel plus aspirin	Placebo plus aspirin		
Years 0-5	-1.34 (-1.58, -1.10)	-1.47 (-1.70, -1.25)	0.13 (-0.20, 0.46)	0.45
Year 0-1	-4.6 (-5.3, -4.0)	-5.4 (-6.0, -4.7)	0.74 (-0.21, 1.68)	0.13
Years 1-5	-0.52 (-0.82, -0.22)	-0.49 (-0.78, -0.21)	-0.025 (-0.44, 0.39)	0.90
Systolic blood pressure target <130 mmHg	-1.59 (-1.92, -1.25)	-1.62 (-1.95, -1.29)	0.035 (-0.44, 0.51)	0.88
Systolic blood pressure target 130-150 mmHg	-1.08 (-1.43, -0.74)	-1.32 (-1.63, -1.01)	0.23 (-0.22, 0.69)	0.32
eGFR <60 ml/min/1.73m^2	-0.60 (-1.12, -0.081)	-0.83 (-1.38, -0.29)	0.23 (-0.52, 0.99)	0.55
eGFR >60 ml/min/1.73m^2	-1.48 (-1.76, -1.21)	-1.60 (-1.84, -1.35)	0.11 (-0.26, 0.48)	0.55

Estimated within-group changes and between-group differences and p-values from generalized estimating equation models including inverse probability weighting to account for loss to follow-up. Estimated glomerular filtration rate = eGFR.

Table S3: Association of antiplatelet arm with rapid decline in eGFR by time after randomization, BP arm, and by baseline eGFR, without measures collected after June 19, 2011.

Group	Event rate, n (%)		Hazard ratio (95% confidence interval)	p-value
	Aspirin plus clopidogrel	Aspirin plus placebo		
Years 0-5	240/1303 (18%)	269/1308 (21%)	0.91 (0.77, 1.09)	0.30
Year 0-1	101/1303 (7.8%)	117/1308 (8.9%)	0.85 (0.65, 1.11)	0.24
Years 1-5	139/1303 (11%)	152/1308 (12%)	0.98 (0.77, 1.24)	0.84
Systolic blood pressure target <130 mmHg	131/650 (20%)	152/652 (23%)	0.87 (0.69, 1.10)	0.24
Systolic blood pressure target 130-150 mmHg	109/653 (17%)	117/656 (18%)	0.97 (0.75, 1.25)	0.80
eGFR <60 ml/min/1.73 m^2	40/210 (19%)	41/191 (21%)	0.99 (0.64, 1.53)	0.96
eGFR >60 ml/min/1.73 m^2	200/1093 (18%)	228/1117 (20%)	0.90 (0.75, 1.09)	0.27

Hazard ratios and p-values from interval censored proportional hazards models including inverse probability weighting to account for loss to follow-up. Estimated glomerular filtration rate = eGFR.

Figure S1: Association of antiplatelet treatment with eGFRcr trajectory during follow-up among SPS3 participants, without measures collected after June 19, 2011.

Estimates from generalized estimating equation model with inverse probability of censoring weighting to account for study dropout. Median follow-up was 3.0 years. Creatinine-based estimated glomerular filtration rate = eGFRcr.