Suppl. Material

Association between ranolazine, ischemic preconditioning and cardioprotection in patients undergoing scheduled percutaneous coronary intervention

Suppl. Table S1. Patients' data from electrocardiography, echocardiography and percutaneous coronary intervention

	Control group (1) *N=50; 33.3%* **N (%)**	Preconditioning group (2) *N=50; 33.3%* **N (%)**	Ranolizine group (3) *N=50; 33.3%* **N (%)**	**P**
Electrocardiography				
Sinus Rhythm	47 (94.0)	48 (96.0)	48 (96.0)	>0.999+
Atrial Fibrillation	2 (4.0)	2 (4.0)	2 (4.0)	>0.999+
Left Bundle Branch Block	1 (2.0)	5 (10.0)	2 (4.1)	0.226++
QRS Width, mean (SD)	98.8 (19.5)	113.5 (47.2)	101.2 (25.7)	0.062‡
QTc, mean (SD)	401.2 (22.6)[2,3]	419 (36.5)[1]	421.3 (23.0)[1]	**0.001‡**
ST Before PCI				
Normal	49 (98.0)	49 (98.0)	48 (96.0)	>0.999++
Depression	1 (2.0)	1 (2.0)	1 (2.0)	
Elevation	0 (0.0)	0 (0.0)	1 (2.0)	
(-) T waves	0 (0.0)	0 (0.0)	0 (0.0)	
ST after PCI				
Normal	32 (64.0)	38 (76.0)	41 (82.0)	0.061++
Depression	13 (26.0)	9 (18.0)	4 (8.0)	
Elevation	1 (2.0)	3 (6.0)	3 (6.0)	
(-) T waves	4 (8.0)	0 (0.0)	2 (4.0)	
Echocardiography				
LVEF, median (IQR)	55 (50 — 60)	55 (45 — 60)	55 (50 — 60)	0.593‡
LVEF>=50	40 (80.0)	32 (64.0)	38 (76.0)	0.170+
LVIDD, median (IQR)	52 (49 — 54)	51 (49 — 54)	50 (48 — 54)	0.350‡
LVIDS, median (IQR)	33 (31 — 37)	35 (31 — 40)	35 (31 — 39)	0.268‡
IVSd, median (IQR)	12 (11 — 13)	11 (10 — 12)	12 (9 — 13)	0.190‡
PWd, median (IQR)	11 (10 — 12)[3]	11 (10 — 12)[3]	10 (9 — 11)[1,2]	**0.002‡**
IVSs, median (IQR)	11 (10 — 12)[2]	12.6 (11.5 — 14)[1,3]	10 (9 — 11)[2]	**<0.001‡**
PWs, median (IQR)	-	18 (16 — 23)	11 (10 — 18)	0.071‡
E/A				

<1	33 (67.3)	32 (66.7)	25 (52.1)	0.218+
>1	16 (32.7)	16 (33.3)	23 (47.9)	
A (m/s), median (IQR)	0.8 (0.7 — 0.9)	0.7 (0.6 — 0.8)	0.8 (0.7 — 0.9)	0.073‡
Ao_root (mm), median (IQR)	32 (30 — 35)	33 (30 — 36)	31 (29 — 34)	0.318‡
AscAo (mm), median (IQR)	35 (32 — 39)	35 (33 — 38)	34 (32 — 36)	0.054‡
IVC (cm), median (IQR)	-	1.4 (1.4 — 1.4)	1.2 (1.2 — 1.2)	0.373‡
LAdiamParast (mm), median (IQR)	-	40.9 (35 — 42.5)	42 (42 — 45)	0.029‡
E/E', median (IQR)	15 (15 — 15)	8.7 (8 — 15)	7.1 (5.2 — 9)	0.360‡
TAPSE, median (IQR)	-	12 (2.1 — 19)	19.5 (19 — 20)	0.139‡
AV_Vmax (m/s), median (IQR)	1.3 (1.3 — 1.5)	1.3 (1.2 — 1.4)[3]	1.5 (1.3 — 1.7)[2]	**<0.001‡**
TR_Vmax(m/s), median (IQR)	-	2 (0.6 — 2.2)	2.2 (2 — 2.9)	0.131‡
PASP (mmHg), median (IQR)	-	24 (18.9 — 29)	19 (15 — 23)	0.217‡
PCI characteristics				
Previous PCI	25 (50.0)	21 (42.0)	29 (58.0)	0.278+
Access point				
Left upper limb	9 (18.0)	6 (12.2)	14 (28.0)	0.134+
Right upper limb	41 (82.0)	43 (87.8)	36 (72.0)	
Chest pain during PCI	27 (54.0)	19 (38.0)	25 (50.0)	0.249+
Complications	7 (14.6)	9 (18.0)	8 (16.0)	0.899+

+Pearson's chi-square test; ++Fisher's exact test; ‡ANOVA; ‡‡Kruskal-Wallis test

1,2,3 significant differences after Bonferroni correction

Abbreviations: LVEF, Left Ventricular Ejection Fraction; LVIDD, Left Ventricular Internal Diameter in Diastole; LVIDS, Left Ventricular Internal Diameter in Systole; IVSd, Interventricular septum diameter in diastole; IVSs, Interventricular septum diameter in systole; PWd, Posterior wall diameter in diastole; PWs, Posterior wall diameter in systole; Ao_root, Aortic root; AscAo, Ascending aorta; IVC, Inferior Vena Cava; LAdiamParast, Left Atrial diameter parasternal view; PCI, Percutaneous Coronary Intervention; TAPSE, Tricuspid Annular Plane Systolic Excursion; AV, Aortic valve; TR, Tricuspid regurgitation; PASP, Pulmonary Artery Systolic Pressure; DES, Drug Eluting Stent; PCI, Percutaneous Coronary Intervention.

Suppl. Table S2. Patients' medical treatment

	Control group (1)	Preconditioning group (2)	Ranolizine group (3)	P
	N=50; 33.3%	*N=50; 33.3%*	*N=50; 33.3%*	
	N (%)	**N (%)**	**N (%)**	
Nitrates during PCI	1 (2.0) [3]	6 (12.0) [3]	48 (96.0) [1,2]	**<0.001+**
Nitrates after PCI	8 (16.0)	7 (14.0)	13 (26.0)	0.256+
Nitrates before PCI	49 (98.0) [3]	50 (100.0) [3]	8 (16.0) [1,2]	**<0.001+**
Ezetimibe	5 (10.0)	5 (10.0)	10 (20.4)	0.216+
Fenofibrate	2 (4.0)	1 (2.0)	1 (2.0)	>0.999++
Calcium Chanel Blockers	10 (20.0)	17 (34.0)	18 (36.7)	0.149+
Ivabradine	2 (4.0)	3 (6.0)	2 (4.1)	>0.999++
Digitalis	0 (0.0)	1 (2.0)	0 (0.0)	>0.999++
Sacubitril/Valsartan	0 (0.0)	1 (2.0)	0 (0.0)	>0.999++
Angiotensin-converting enzyme inhibitors	17 (34.0)	11 (22.0)	13 (26.5)	0.398+
Angiotensin receptor blockers	20 (40.0)	23 (46.0)	26 (53.1)	0.427+
B-Blocker	33 (67.3)	36 (72.0)	41 (83.7)	0.162+
Mineralocorticoid receptor antagonist	2 (4.0)	3 (6.0)	4 (8.2)	0.640++
Diuretics	11 (22.0)[2]	24 (48.0) [1]	19 (38.0)	**0.024+**
Furosemide	4 (8.0)	8 (16.0)	8 (16.0)	0.397+
Hydrochlorothiazide	8 (16.0)	15 (30.0)	13 (26.0)	0.240+
Indapamide	1 (2.0)	1 (2.0)	1 (2.0)	>0.999++

+Pearson's chi-square test; ++Fisher's exact test;

1,2,3 significant differences after Bonferroni correction

Suppl. Table S3. Changes in SGOT, LDH, CRP, CPK and CK-MB by group

	Control group (1)		Preconditioning group (2)		Ranolizine group (3)		P++
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
SGOT							
Before PCI	19.4 (4.87)	20 (16 — 22)	20.62 (6.01)	19 (17 — 24)	21.34 (5.79)	20 (17 — 26)	0.270
4 hours	23.06 (6.21)	22 (18 — 26)	25.55 (10.95)	22 (18 — 30)	25.84 (8.78)	23 (20 — 30)	0.304
10 hours	28.72 (15.29)	23.5 (21 — 31)	31.84 (20.39)	24 (20 — 35)	30.46 (10.79)	28.5 (22 — 39)	0.352
24 hours	27.06 (14.48)	22 (19 — 29)	30.59 (19.47)	22 (18 — 34)	28.96 (14.22)	28 (18 — 34)	0.643
P+	<0.001		<0.001		<0.001		
LDH							
Before PCI	141.56 (36.05)	138.5 (128 — 158)[3]	157.38 (28.19)	150.5 (139 — 180)	160.52 (29.28)	153 (138 — 177)[1]	**0.027**
4 hours	159.54 (40.59)	156 (134 — 188)[2]	182.64 (43.11)	175 (148 — 207)[1]	176.08 (39.31)	164.5 (149 — 192)	**0.027**
10 hours	173.03 (49.9)	164.5 (138 — 205)	201.49 (114.73)	174 (159 — 215)	191.7 (62.9)	179.5 (160 — 199)	0.084
24 hours	162.54 (43.71)	158.5 (136 — 192)	173.22 (54.32)	160 (142 — 202)	171.1 (31.67)	169.5 (150 — 185)	0.318
P+	<0.001		<0.001		<0.001		
CRP							
Before PCI	1.52 (1.24)	1.12 (0.64 — 2.1)	2.15 (2.15)	1.29 (0.67 — 3.2)	1.9 (2.19)	1.3 (0.65 — 2.21)	0.410
4 hours	2.13 (1.64)	1.83 (0.86 — 2.94)	3.07 (3.01)	1.92 (1.14 — 3.81)	2.38 (2.23)	1.62 (1.04 — 2.9)	0.185
10 hours	2.55 (1.59)	2.19 (1.22 — 3.65)	4.14 (4.66)	2.53 (1.77 — 5.58)	3.26 (3.35)	2.31 (1.39 — 3.65)	0.246
24 hours	3.14 (1.9)	2.66 (1.63 — 4.32)	5.5 (7.48)	3.61 (2.39 — 5.04)	3.64 (3.13)	2.95 (1.91 — 3.99)	0.183
P+	<0.001		<0.001		<0.001		
CPK							
Before PCI	79.24 (34.69)	81 (51 — 95)	94.38 (58.89)	79 (54 — 107)[3]	69.25 (29.77)	63.5 (52 — 81)[2]	**0.024**
4 hours	99.5 (45.95)	94 (62 — 121)	116.45 (66.84)	102 (71 — 137)[3]	86.47 (48.84)	73.5 (61 — 97)[2]	**0.025**
10 hours	142.08 (105.15)	111.5 (87 — 165)[3]	141.41 (84.97)	117 (85 — 177)[3]	102.81 (61.38)	85.5 (70 — 108)[1,2]	**0.012**
24 hours	130.5 (88.23)	105 (69 — 160)	148.14 (120.4)	108 (81 — 180)	115.12 (123.42)	82.5 (71 — 109)	0.068
P+	<0.001		<0.001		<0.001		
CK-MB							
Before PCI	0.93 (3.2)	0.5 (0.2 — 0.7)	0.83 (0.96)	0.6 (0.4 — 0.8)	0.54 (0.73)	0.4 (0.3 — 0.6)	0.133

4 hours	1.53 (2.52)	0.85 (0.5 − 1.4)	1.88 (2.25)	1 (0.7 − 2.4)	1.39 (2.55)	0.8 (0.5 − 0.9)	0.104
10 hours	6.46 (10.99)	1.7 (0.8 − 6.7)[3]	5.7 (11.51)	1.7 (0.9 − 6)	2.59 (4.54)	1.1 (0.8 − 1.9)[1]	**0.047**
24 hours	5.18 (7.93)	1.55 (0.9 − 5.9)	4.91 (8.55)	1.8 (0.9 − 5.9)	3.8 (10.46)	0.95 (0.7 − 2.1)	0.123
P+	<0.001		<0.001		<0.001		

+p-value for time comparisons (after logarithmic transformation)

++p-value for group comparisons (after logarithmic transformation)

1,2,3 significant differences after Bonferroni correction

Abbreviations: SGOT, serum glutamic-oxaloacetic transaminase; LDH, Lactate Dehydrogenase; CRP, C reactive Protein; CPK, Creatinine Phosphokinase.

Suppl. Table S4. Multiple linear regression results for changes in troponin in a stepwise method

		β+	SE++	P
Group	Control (reference)			
	Preconditioning	-0.008	0.038	0.839
	Ranolazine	-0.073	0.037	**0.050**
Gender	Men (reference)			
	Women	0.142	0.038	**<0,001**
Change SGOT (from pre-PCI until 24 hours)		0.009	0.002	**<0.001**
Change CK-MB (from pre-PCI until 24 hours)		0.013	0.003	**<0.001**

Note. Regression was conducted after logarithmic transformation of the dependent variable

+regression coefficient ++Standard Error