The impact of sex differences on ischemic postconditioning during primary PCI in STEMI
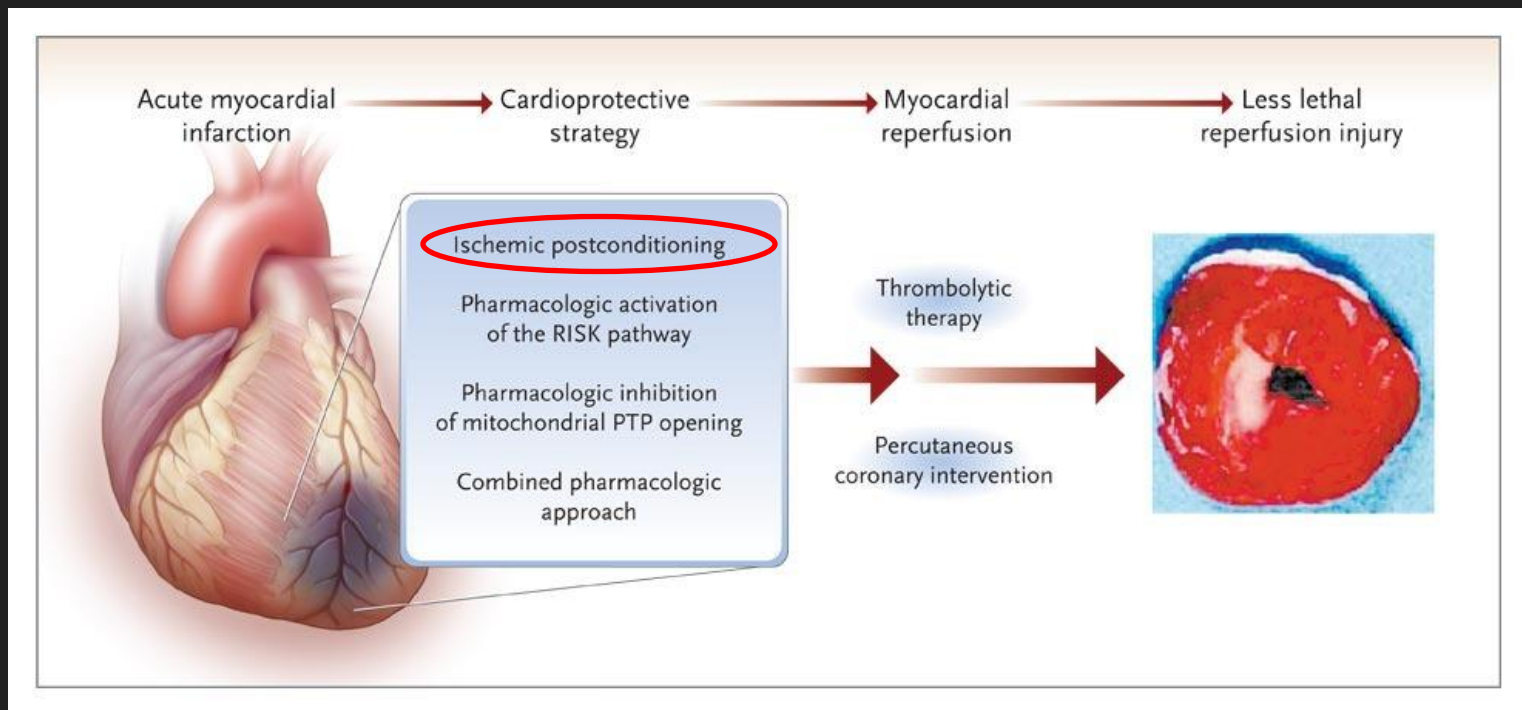
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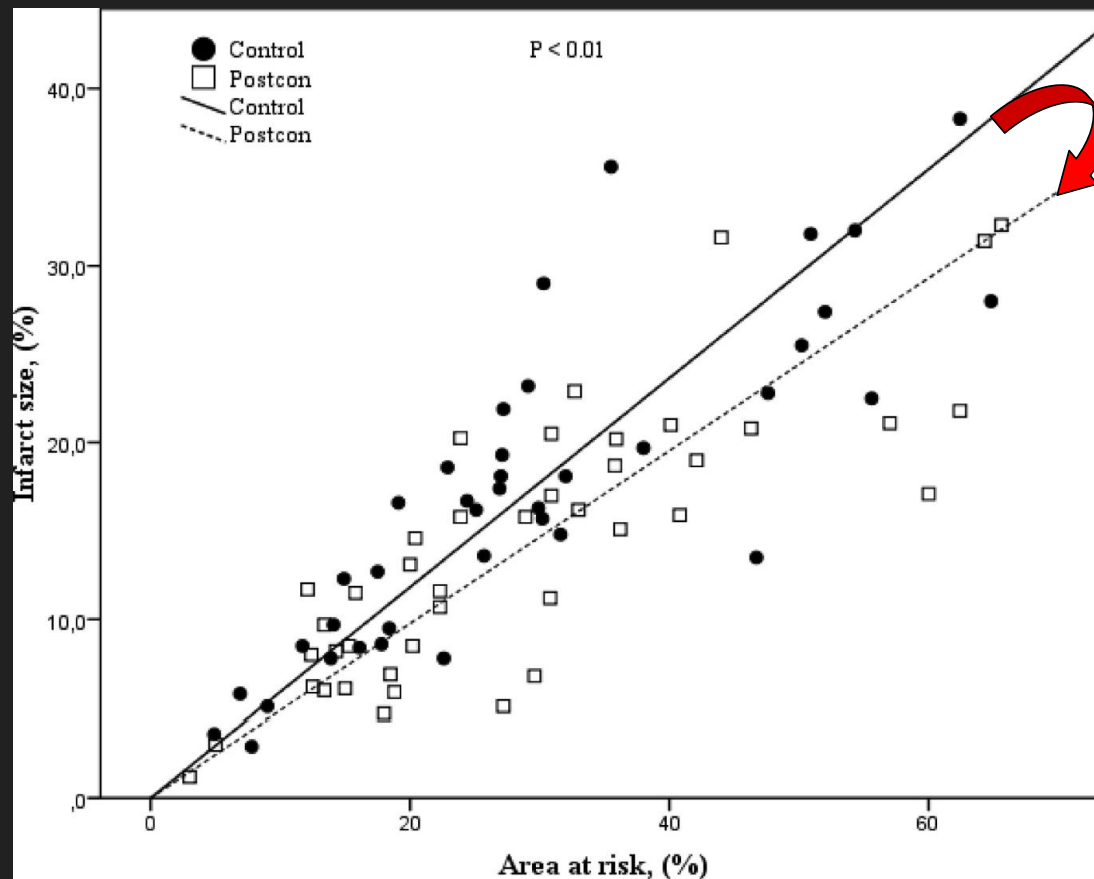
Ischemic postconditioning

○ Short periods of coronary occlusion at the onset of reperfusion, has been shown to protect the heart against the ischemia/reperfusion injury

Positive?

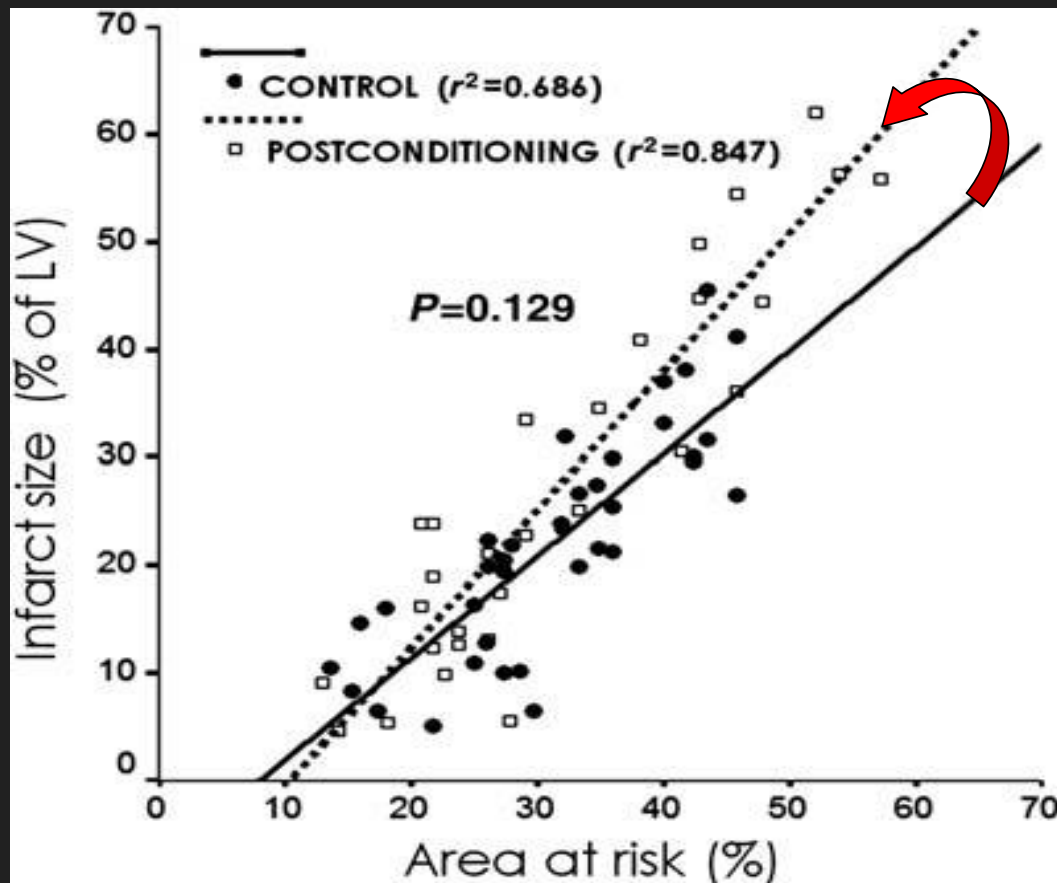- Ischemic postconditioning reduces myocardial infarct size in 18% of STEMI

Circ Cardiovasc Interv. 2010;3:34-41.

Negative?

○ Ischemic postconditioning does not reduce infarct size and might have a potential harmful effect

European Heart Journal. 2012;33:103–112.

POST study

Interventional Cardiology

Ischemic Postconditioning During Primary Percutaneous Coronary Intervention

The Effects of Postconditioning on Myocardial Reperfusion in Patients With ST-Segment Elevation Myocardial Infarction (POST) Randomized Trial

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Background—Ischemic postconditioning has been reported to reduce infarct size in patients with ST-segment–elevation myocardial infarction. However, cardioprotective effects of postconditioning have not been demonstrated in a large-scale trial.

Methods and Results—We performed a multicenter, prospective, randomized, open-label, blinded end-point trial. A total of 700 patients undergoing primary percutaneous coronary intervention (PCI) for ST-segment–elevation myocardial infarction within 12 hours after symptom onset were randomly assigned to the postconditioning group or to the conventional primary PCI group in a 1:1 ratio. Postconditioning was performed immediately after restoration of coronary flow as follows: The angioplasty balloon was positioned at the culprit lesion and inflated 4 times for 1 minute with low-pressure (<6 atm) inflations, each separated by 1 minute of deflation. The primary end point was complete ST-segment resolution (percentage resolution of ST-segment elevation >70%) measured at 30 minutes after PCI. Complete ST-segment resolution occurred in 40.5% of patients in the postconditioning group and 41.5% of patients in the conventional PCI group (absolute difference, −1.0%; 95% confidence interval, −8.4 to 6.4; *P*=0.79). The rate of myocardial blush grade of 0 or 1 and the rate of major adverse cardiac events (a composite of death, myocardial infarction, severe heart failure, or stent thrombosis) at 30 days did not differ significantly between the postconditioning group and the conventional PCI group (17.2% versus 22.4% [*P*=0.20] and 4.3% versus 3.7% [*P*=0.70], respectively).

Conclusion—Ischemic postconditioning did not improve myocardial reperfusion in patients with ST-segment–elevation myocardial infarction undergoing primary PCI with current standard practice.

Background
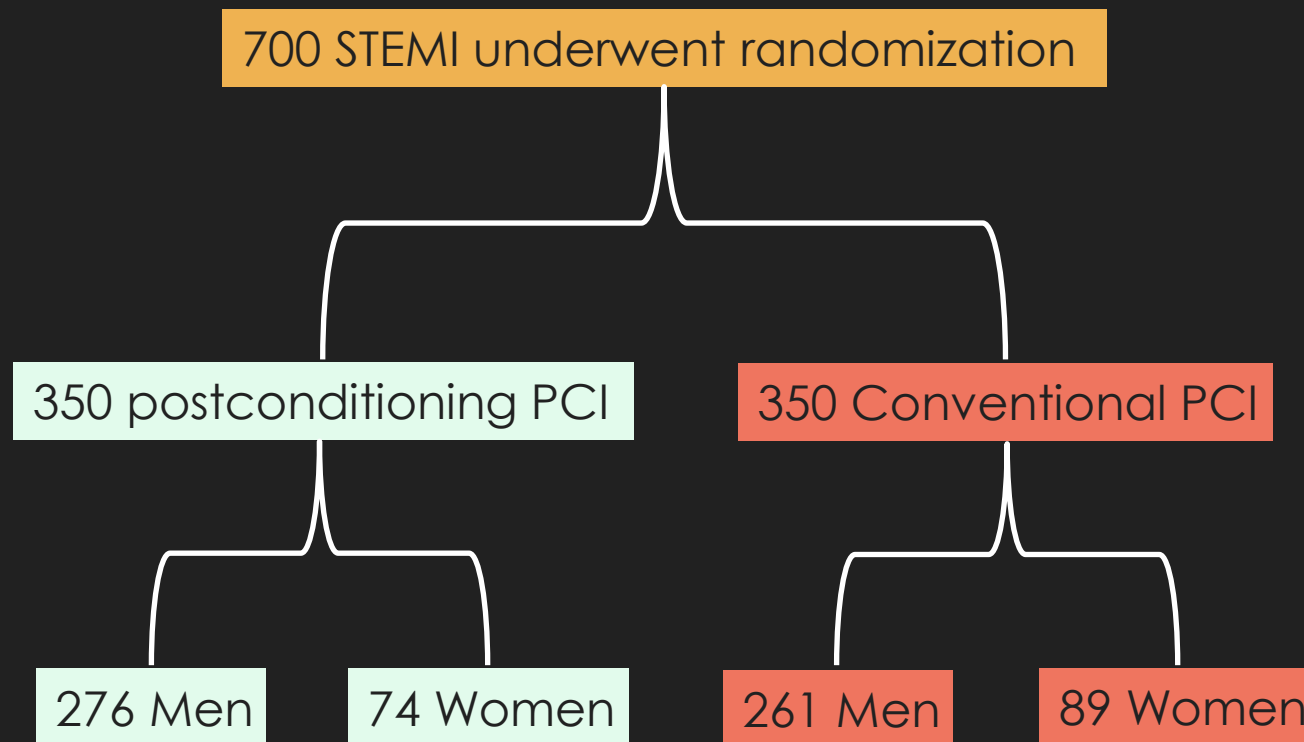## Sex difference on postconditioning

- Cardioprotection from ischemic postconditioning may be influenced by gender, however data have not been conclusive.

- One study demonstrated that ischemic postconditioning reduced infarct size in only female hearts after 10 minutes of ischemia [1].

- However another showed that ischemic postconditioning exerted cardioprotection in male rats only after 25 min ischemia [2].

- In view of the conflicting data on the influence of gender on the benefits of postconditioning, we performed a post hoc subanalysis of the POST study to evaluate the impact of sex differences on postconditioning.

[1] Basic Res Cardiol 104:390-402
[2] J Surg Res 134:342-347

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Methods

700 STEMI underwent randomization

350 postconditioning PCI

350 Conventional PCI

276 Men

74 Women

261 Men

89 Women

Primary endpoint: MACE (composite of death, MI, severe HF, stent thrombosis or TVR at 1 year after PCI

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Baseline characteristics

	Postconditioning			Conventional		
	Men (n = 276)	Women (n = 74)	p Value	Men (n = 261)	Women (n = 89)	p Value
Age, y	57.1 ± 11.5	69.7 ± 8.0	<0.001	56.7 ± 11.3	69.0 ± 10.1	<0.001
Body mass index, Kg/m^2	24.5 ± 3.2	22.9 ± 3.1	<0.001	24.7 ± 3.0	23.4 ± 3.1	<0.001
Diabetes mellitus	65 (23.8)	19 (26.0)	0.695	69 (26.6)	18 (20.7)	0.268
Hypertension	116 (42.3)	45 (61.6)	0.003	104 (40.0)	55 (61.8)	<0.001
Dyslipidemia	108 (39.6)	31 (43.1)	0.591	124 (47.5)	35 (39.8)	0.208
Current smoking	178 (64.7)	6 (8.3)	<0.001	169 (65.3)	13 (14.6)	<0.001
Previous myocardial infarction	10 (3.7)	0	0.225	8 (3.1)	1 (1.1)	0.457
Previous revascularization	17 (6.2)	3 (4.2)	0.776	11 (4.2)	5 (5.6)	0.566
Cerebrovascular disease	8 (2.9)	2 (2.8)	>0.999	10 (3.9)	6 (6.7)	0.254
Chronic renal failure	3 (1.1)	1 (1.4)	>0.999	2 (0.8)	0	>0.999
Ejection fraction	50.4 ± 10.5	48.6 ± 12.0	0.241	50.4 ± 11.6	49.4 ± 11.7	0.490

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Angiographic findings and procedural results

	Postconditioning			Conventional		
	Men (n = 276)	Women (n = 74)	p Value	Men (n = 261)	Women (n = 89)	p Value
Diseased vessels			0.503			0.078
1	153 (55.4)	36 (48.6)		129 (49.4)	36 (40.4)	
2	77 (27.9)	22 (29.7)		87 (33.3)	28 (31.5)	
3	46 (16.7)	16 (21.6)		45 (17.2)	25 (28.1)	
Infarct-related artery			0.783			0.126
Left anterior descending	126 (45.7)	37 (50.0)		116 (44.4)	41 (46.1)	
Left circumflex	30 (10.9)	8 (10.8)		35 (13.4)	5 (5.6)	
Right coronary artery	120 (43.5)	29 (39.2)		110 (42.1)	43 (48.3)	
TIMI 0/1 before PCI	269 (97.5)	73 (98.6)	0.640	249 (95.4)	85 (95.5)	0.263
Symptom-to-reperfusion time, median (IQR),min	185 (120-344)	229 (145-383)	0.044	181 (120-313)	232 (137-393)	0.025
Door-to-reperfusion time, median (IQR),min	51 (42-73)	58 (42-73)	0.324	56 (45-73)	55 (42-77)	0.936
Thrombus aspiration	121 (43.8)	37 (50.0)	0.344	129 (49.4)	49 (55.1)	0.359
Direct stenting	29 (10.5)	9 (12.2)	0.684	39 (14.9)	10 (11.2)	0.384
Glycoprotein IIb/IIIa inhibitor	70 (25.4)	11 (14.9)	0.057	58 (22.2)	22 (24.7)	0.628
Stent implantation	267 (96.7)	70 (94.6)	0.485	256 (98.1)	86 (96.6)	0.424
Type of stent						
Drug-eluting stent	225 (84.3)	65 (92.9)	0.065	215 (84.0)	79 (91.9)	0.069
Total stent length	27.6 ± 11.6	30.6 ± 12.1	0.060	28.3 ± 12.8	30.1 ± 12.1	0.255
Stent diameter	3.3 ± 0.5	3.1 ± 0.4	<0.001	3.3 ± 0.5	3.1 ± 0.5	0.024
TIMI 3 after PCI	255 (92.7)	66 (89.2)	0.874	232 (89.6)	74 (83.2)	0.514
Syntax score	15.0 ± 8.8	15.0 ± 9.2	0.985	15.2 ± 8.5	16.5 ± 9.8	0.197
Residual Syntax score after PCI	3.6 ± 6.5	4.3 ± 6.9	0.406	3.6 ± 5.8	4.4 ± 6.5	0.256
Peak creatine kinase-MB	233.7 ± 168.9	224.1 ± 182.5	0.670	233.7 ± 214.5	216.2 ± 170.8	0.487
ST-segment resolution, >70%	105 (39.0)	33 (45.8)	0.344	98 (39.4)	41 (47.7)	0.205

Clinical outcomes at 1-year between men and women for each group

	Total			Postconditioning			Conventional		
	Men (n = 537)	Women (n = 163)	p Value	Men (n = 276)	Women (n = 74)	p Value	Men (n = 261)	Women (n = 89)	p Value
Death	19 (3.5)	13 (8.0)	0.018	10 (3.6)	8 (10.8)	0.032	9 (3.4)	5 (5.6)	0.359
Cardiac death	15 (2.8)	13 (8.0)	0.003	8 (2.9)	8 (10.8)	0.008	7 (2.7)	5 (5.6)	0.191
Myocardial infarction	3 (0.6)	2 (1.2)	0.331	3 (1.1)	1 (1.4)	>0.999	0	1 (1.1)	0.254
Severe heart failure	12 (2.2)	6 (3.7)	0.394	6 (2.2)	3 (4.1)	0.406	6 (2.3)	3 (3.4)	0.698
Stent thrombosis	11 (2.0)	6 (3.7)	0.248	6 (2.2)	4 (5.4)	0.229	5 (1.9)	2 (2.2)	>0.999
Target vessel revascularization	10 (1.9)	4 (2.5)	0.749	5 (1.8)	2 (2.7)	0.642	5 (1.9)	2 (2.2)	>0.999
Major adverse cardiac event*	29 (5.4)	16 (9.8)	0.044	15 (5.4)	9 (12.2)	0.042	14 (5.4)	7 (7.9)	0.391

*Major adverse cardiac event: a composite of death, MI, severe heart failure, and stent thrombosis, TVR

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Comparison of treatment group in men and women

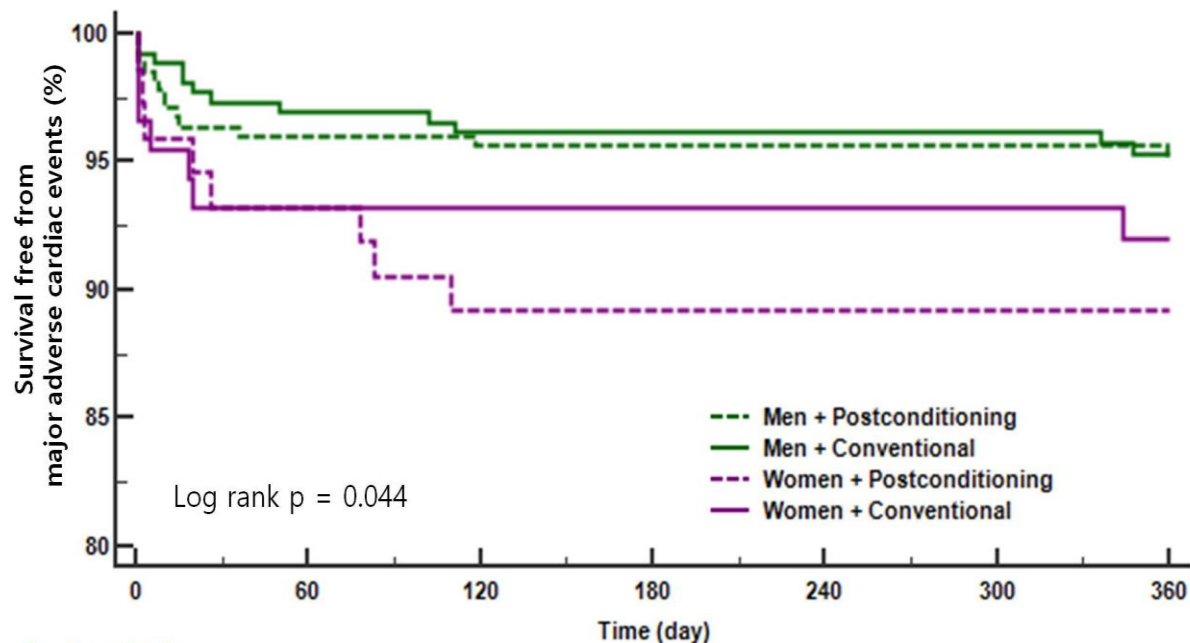|	Men			Women		
	Postconditioning (n = 276)	Conventional (n = 261)	p-value	Postconditioning (n = 74)	Conventional (n = 89)	p-value
Death	10 (3.6)	9 (3.4)	0.913	8 (10.8)	5 (5.6)	0.223
Cardiac death	8 (2.9)	7 (2.7)	0.879	8 (10.8)	5 (5.6)	0.223
Myocardial infarction	3 (1.1)	0	0.249	1 (1.4)	1 (1.1)	>0.999
Severe heart failure	6 (2.2)	6 (2.2)	0.922	3 (4.1)	3 (4.1)	>0.999
Stent thrombosis	6 (2.2)	5 (1.9)	0.833	4 (5.4)	2 (2.2)	0.412
Target vessel revascularization	5 (1.8)	5 (1.9)	>0.999	2 (2.7)	2 (2.2)	>0.999
Major adverse cardiac event	4 (1.4)	8 (3.1)	0.205	2 (2.7)	2 (2.2)	>0.999

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Adjusted comparison in postconditioning group

	Postconditioning		Unadjsted		Adjusted*	
	Men (n = 276)	Women (n = 74)	HR (95% CI)	p Value	HR (95% CI)	p Value
Death	10 (3.6)	8 (10.8)	3.00 (1.18-7.61)	0.021	2.30 (0.48-11.1)	0.301
Cardiac death	8 (2.9)	8 (10.8)	3.75 (1.41-9.99)	0.008	2.59 (0.51-13.2)	0.253
Myocardial infarction	3 (1.1)	1 (1.4)	1.32 (0.14-12.8)	0.809	0.46(0.03-7.81)	0.587
Severe heart failure	6 (2.2)	3 (4.1)	1.91 (0.48-7.65)	0.359	4.78 (0.23-98.9)	0.312
Stent thrombosis	6 (2.2)	4 (5.4)	2.46 (0.69-8.72)	0.164	1.52 (0.27-8.52)	0.637
Target vessel revascularization	5 (1.8)	2 (2.7)	1.58 (0.31-8.14)	0.585	1.72 (0.18-16.7)	0.640
Major adverse cardiac event	15 (5.4)	9 (12.2)	2.28 (1.00-5.21)	0.051	2.67 (0.68-10.5)	0.158

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ST-segment resolution after PCI
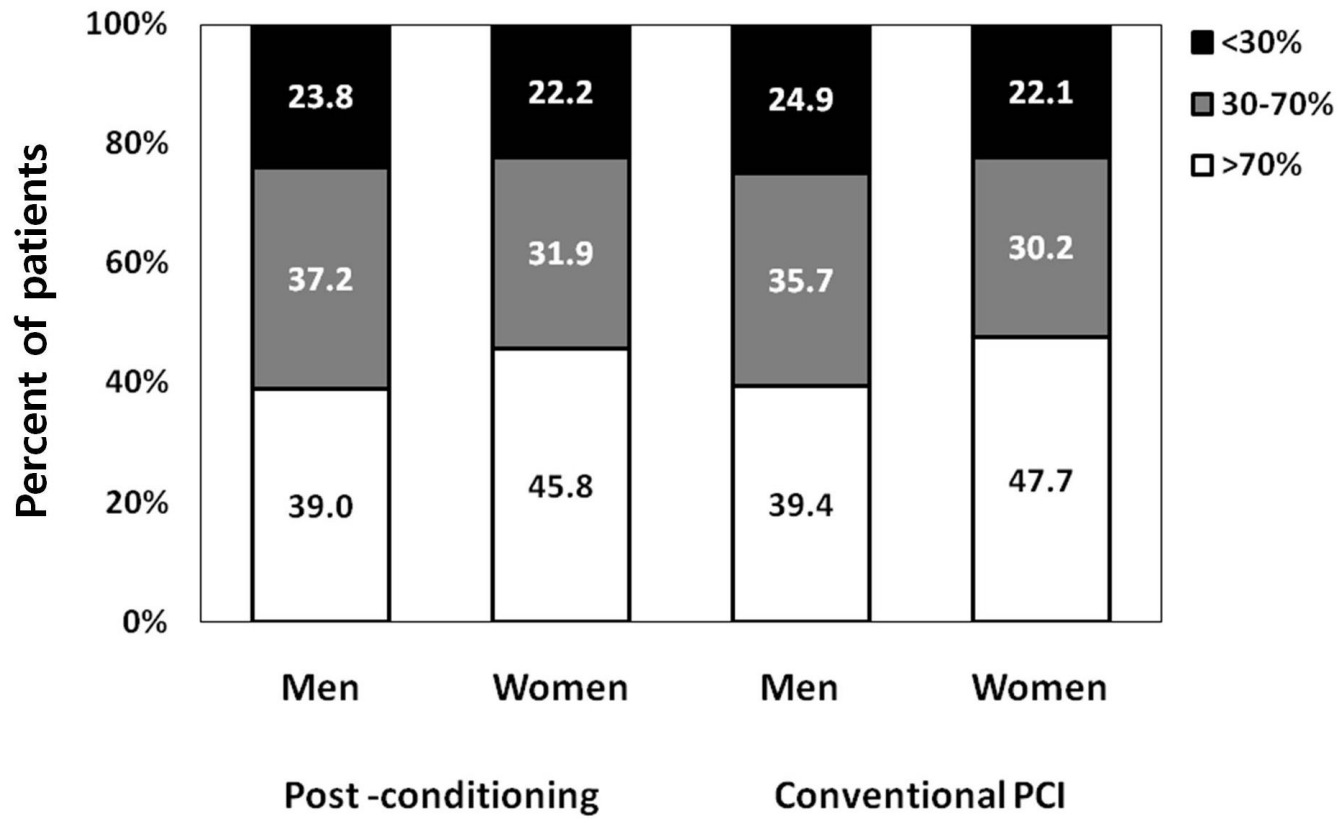
Kaplan-Meier curves of freedom from major adverse cardiac events

Results

- Women were older, more hypertension, less current smokers, and had longer symptom-to-reperfusion time.

- The rate of MACE (composite of death, MI, severe HF, stent thrombosis, or TVR) at 1 year was higher in women compared to men (9.8% vs. 5.4%, p = 0.044).

- MACE was significantly higher in women compared to men in the postconditioning group (12.2% vs. 5.4%, p = 0.042), but not in the conventional PCI group (7.9% vs. 5.4%, p = 0.391).

- However, women was not an independent predictor after adjusting baseline risk factors, angiographic and procedural parameters (HR 2.67, 95% CI 0.68-10.5, p = 0.158).

Conclusions

○ Despite women having more adverse clinical characteristics, their prognosis was similar to men in the conventional group.

○ Although women showed a higher rate of the MACE compared to men in the postconditioning group, women was not an independent predictor.

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