



The clinical impact of sex differences on ischemic postconditioning during primary percutaneous coronary intervention: a POST (the effects of postconditioning on myocardial reperfusion in patients with ST-segment elevation myocardial infarction) substudy

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Abstract

The POST (the effects of postconditioning on myocardial reperfusion in patients with ST-Segment elevation myocardial infarction) study showed that ischemic postconditioning did not improve myocardial reperfusion in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). However, it has not been determined whether postconditioning is effective in women. This study sought to evaluate the impact of sex differences on ischemic postconditioning during the primary PCI. We analyzed clinical outcomes at 1 year in the 537 men and 163 women with STEMI, who were randomized to the postconditioning or to the conventional PCI group. Women were older, had higher rates of hypertension, were less likely to be current smokers, and had longer symptom-to-reperfusion time. The rate of major adverse cardiac events (MACE: a composite of death, myocardial infarction, severe heart failure, stent thrombosis, or target vessel revascularization) 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, $p = 0.158$). 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, women were not an independent predictor in the postconditioning group.

Keywords Sex difference · Ischemic postconditioning · Myocardial infarction · Percutaneous coronary intervention

Introduction

Epidemiological studies suggest that gender differences exist in the susceptibility to cardiovascular diseases [1]. Ischemic postconditioning, which is performed by short periods of coronary occlusion at the onset of reperfusion, has been shown to protect the heart against the ischemia/reperfusion

injury [2]. Studies have suggested that the 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 min of ischemia [3]; however, another showed that ischemic postconditioning exerted cardioprotection in male rats only after 25 min of ischemia [4].

The POST (the effects of postconditioning on myocardial reperfusion in patients with ST-segment elevation myocardial infarction) study demonstrated that ischemic postconditioning did not improve myocardial reperfusion in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) [5]. In view of the conflicting data on

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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.

Methods

Study design and population

This study was a sex-specific analysis of the 1 year results of the POST study [5]. Details regarding the design, methods, and endpoints of this prospective, multicenter, randomized clinical trial have been reported. In brief, 700 patients with STEMI were randomly assigned to the postconditioning or 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 min with low-pressure (< 6 atm) inflations, each separated by 1 min of deflation. Patients were eligible for the trial if they had an acute STEMI within 12 h of symptom onset and primary PCI was planned. Exclusion criteria were (1) hemodynamic instability or cardiogenic shock (2) left bundle-branch block on ECG (3) left main lesion (4) rescue PCI after thrombolysis or facilitated PCI (5) noncardiac comorbid conditions with a life expectancy < 1 year or that may result in protocol noncompliance (per the site investigator's medical judgment), or (6) females of child-bearing potential, unless a recent pregnancy test was negative, who possibly planned to become pregnant any time after enrollment in this study.

All patients were recommended to receive optimal pharmacological therapy, including statins, β -blockers, or renin-angiotensin system blockade, following the current guidelines. Dual antiplatelet therapy (aspirin 100–200 mg/day plus clopidogrel 75 mg/day) was recommended for at least 12 months. The study complies with the Declaration of Helsinki and was approved by each institutional review committee. All patients provided written informed consent to the procedure and to the participation in this study.

Endpoint

All adverse clinical events were centrally adjudicated by an independent Clinical Events Committee blinded to treatment. The primary interest of this reanalysis was the occurrence of major adverse cardiac events (MACE), a composite of death, myocardial infarction (MI), severe heart failure, stent thrombosis, or the need for target vessel revascularization at 1 year after PCI in each sex. Details on these definitions have been described [5].

Statistical analysis

Statistical comparisons based on sex were stratified by treatment method. Categorical variables are presented as numbers and relative frequencies (percentages), and continuous variables as means and standard deviations or medians with interquartile ranges (Q1–Q3) according to their distributions, which were checked by the Kolmogorov–Smirnov test. Between-group differences in categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate, and differences in continuous variables were assessed using Student *t* test. Analyses investigating the interaction between sex and treatment method were also performed using Breslow–Day test. Survival curves were constructed using the Kaplan–Meier method and compared with the log-rank test. Patients were censored at 1 year (365 days) or when events occurred. Two-tailed *p* values < 0.05 were considered statistically significant. All statistical analyses were performed using the commercially available software (SPSS version 17 for Windows, SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics and procedural results

A total of 700 patients were enrolled in the analysis, 537 (76.7%) were men, and 163 (23.3%) were women. Baseline clinical, angiographic, and procedural characteristics according to sex and treatment method are presented in Tables 1 and 2. Compared with men, women were significantly older (56.9 ± 11.4 years vs. 69.3 ± 9.2 years, $p < 0.001$), had lower body mass index (24.6 ± 3.1 vs. 23.2 ± 3.1 , $p < 0.001$), had higher rates of hypertension (41.2% vs. 61.7%, $p < 0.001$), and had lower rates of current smoking (65.0% vs. 11.8%, $p < 0.010$). Women had more multivessel disease compared to men. Although the time from symptom onset to reperfusion time was longer in women compared to men [230 (IQR, 140–388) min vs. 183 (120–337) min, $p = 0.003$], Thrombolysis in Myocardial Infarction (TIMI) flow state before PCI was not different. There was no gender difference in the door-to-reperfusion time. Drug-eluting stents were used more in women, while bare-metal stents were used more in men. Women had a longer total stent length (30.3 ± 12.0 mm vs. 27.9 ± 12.2 mm, $p = 0.034$) and smaller stent diameter compared to men (3.1 ± 0.4 mm vs. 3.3 ± 0.5 mm, $p < 0.001$). Myocardial blush grade after PCI was not different, but TIMI flow after PCI was lower in women. Syntax score and residual Syntax score after PCI were

Table 1 Baseline characteristics

	Total			Postconditioning			Conventional		
	Men (<i>n</i> =537)	Women (<i>n</i> =163)	<i>p</i> value	Men (<i>n</i> =276)	Women (<i>n</i> =74)	<i>p</i> value	Men (<i>n</i> =261)	Women (<i>n</i> =89)	<i>p</i> value
Age (years)	56.9±11.4	69.3±9.2	< 0.001	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)	24.6±3.1	23.2±3.1	< 0.001	24.5±3.2	22.9±3.1	< 0.001	24.7±3.0	23.4±3.1	< 0.001
Diabetes mellitus	134 (25.2)	37 (23.1)	0.596	65 (23.8)	19 (26.0)	0.695	69 (26.6)	18 (20.7)	0.268
Hypertension	220 (41.2)	100 (61.7)	< 0.001	116 (42.3)	45 (61.6)	0.003	104 (40.0)	55 (61.8)	< 0.001
Dyslipidemia	232 (43.4)	66 (41.2)	0.623	108 (39.6)	31 (43.1)	0.591	124 (47.5)	35 (39.8)	0.208
Current smoking	347 (65.0)	19 (11.8)	< 0.001	178 (64.7)	6 (8.3)	< 0.001	169 (65.3)	13 (14.6)	< 0.001
Previous myocardial infarction	18 (3.4)	1 (0.6)	0.093	10 (3.7)	0	0.225	8 (3.1)	1 (1.1)	0.457
Previous revascularization	28 (5.2)	8 (5.0)	0.890	17 (6.2)	3 (4.2)	0.776	11 (4.2)	5 (5.6)	0.566
Cerebrovascular disease	18 (3.4)	8 (5.0)	0.351	8 (2.9)	2 (2.8)	> 0.999	10 (3.9)	6 (6.7)	0.254
Chronic renal failure	5 (0.9)	1 (0.6)	> 0.999	3 (1.1)	1 (1.4)	> 0.999	2 (0.8)	0	> 0.999
Ejection fraction	50.4±11.0	49.0±11.8	0.177	50.4±10.5	48.6±12.0	0.241	50.4±11.6	49.4±11.7	0.490

Values are mean ± SD or *n* (%)

not different. The rate of complete ST-segment resolution (> 70% resolution of ST-segment compared to baseline electrocardiogram) was also similar in the two groups (Fig. 1).

Sex differences in clinical outcomes at 1 year

The follow-up duration was 366 (353–382) days. The event rates were different between men and women according to method of treatment. Sex-specific clinical outcomes at 1-year follow-up are presented in Table 3. Women had a higher risk of death (8.0% vs. 3.5%, *p*=0.018), cardiac death (8.0% vs. 2.8%, *p*=0.003), and MACE (9.8% vs. 5.4%, *p*=0.044) compare to men (Fig. 2). When comparing women with postconditioning and conventional PCI, the outcome is not different. Postconditioning and conventional PCI outcomes in both men and women were similar (Table 4). While no gender differences were seen in MACE rates in the conventional PCI group (7.9% vs. 5.4%, *p*=0.391), women had a higher risk of MACE, especially of death and cardiac death in the postconditioning group (12.2% vs. 5.4%, *p*=0.042). The risk of each clinical event between men and women in postconditioning group are shown in Table 5. The risk of death and cardiac death in women was significantly higher than in men [hazard ratio (95% confidence interval) 3.00 (1.18–7.61), *p*=0.021 and 3.75 (1.41–9.99), *p*=0.008].

After adjustment for differences in baseline risk factors, angiographic and procedural parameters for postconditioning group, death and cardiac death were not significant, but showed similar trend of higher risk in women.

Discussion

The main findings of this study are: (1) compared to men, women were older, had a longer time between symptom onset and reperfusion and poorer antegrade flow post PCI; (2) women had a higher risk of death, cardiac death, and MACE; and (3), while the event rates were not different between women and men in the conventional PCI group, women had a higher risk of MACE, especially of death and cardiac death in the postconditioning group. However, women were not an independent predictor after adjusting baseline risk factors, angiographic, and procedural parameters.

Ischemic postconditioning has been reported to reduce infarct size in patients with STEMI undergoing primary PCI [6, 7]; however, most studies have had small sample sizes (mostly < 100 patients) and failed to demonstrate that this treatment effect had any meaningful clinical benefits. Recently, two big randomized clinical trials (POST and DANAMI-3-iPOST) demonstrated that routine ischemic

Table 2 Angiographic findings and procedural results

	Total		<i>p</i> value	Postconditioning		<i>p</i> value	Conventional		<i>p</i> value
	Men (<i>n</i> = 537)	Women (<i>n</i> = 163)		Men (<i>n</i> = 276)	Women (<i>n</i> = 74)		Men (<i>n</i> = 261)	Women (<i>n</i> = 89)	
Diseased vessels			0.045			0.503			0.078
1	282 (52.5)	72 (44.2)		153 (55.4)	36 (48.6)		129 (49.4)	36 (40.4)	
2	164 (30.5)	50 (30.7)		77 (27.9)	22 (29.7)		87 (33.3)	28 (31.5)	
3	91 (16.9)	41 (25.2)		46 (16.7)	16 (21.6)		45 (17.2)	25 (28.1)	
Infarct-related artery			0.337			0.783			0.126
Left anterior descending	242 (45.1)	78 (47.9)		126 (45.7)	37 (50.0)		116 (44.4)	41 (46.1)	
Left circumflex	65 (12.1)	13 (8.0)		30 (10.9)	8 (10.8)		35 (13.4)	5 (5.6)	
Right coronary artery	230 (42.8)	72 (44.2)		120 (43.5)	29 (39.2)		110 (42.1)	43 (48.3)	
TIMI flow before PCI			0.651			0.640			0.263
0/1	518 (96.5)	158 (96.9)		269 (97.5)	73 (98.6)		249 (95.4)	85 (95.5)	
2	13 (2.4)	5 (3.1)		7 (2.5)	1 (1.4)		6 (2.3)	4 (4.5)	
3	6 (1.1)	0		0	0		6 (2.3)	0	
Symptom-to-reperfusion time, median (IQR), min	183 (120–337)	230 (140–388)	0.003	185 (120–344)	229 (145–383)	0.044	181 (120–313)	232 (137–393)	0.025
Door-to-reperfusion time, median (IQR), min	53 (43–73)	56 (42–73)	0.413	51 (42–73)	58 (42–73)	0.324	56 (45–73)	55 (42–77)	0.936
Thrombus aspiration	250 (46.6)	86 (52.8)	0.165	121 (43.8)	37 (50.0)	0.344	129 (49.4)	49 (55.1)	0.359
Direct stenting	68 (12.7)	19 (11.7)	0.733	29 (10.5)	9 (12.2)	0.684	39 (14.9)	10 (11.2)	0.384
Obtaining method of reflow			0.864			> 0.999			0.765
Wire passage	65 (12.1)	16 (9.8)		29 (10.5)	7 (9.5)		36 (13.8)	9 (10.1)	
Thrombus aspiration	173 (32.2)	52 (31.9)		87 (31.5)	24 (32.4)		86 (33.0)	28 (31.5)	
Predilation ballooning	296 (55.1)	95 (58.3)		159 (57.6)	43 (58.1)		137 (52.5)	52 (58.4)	
Direct stenting	2 (0.4)	0		1 (0.4)	0		1 (0.4)	0	
Administration of glycoprotein IIb/IIIa inhibitor	128 (23.8)	33 (20.2)	0.340	70 (25.4)	11 (14.9)	0.057	58 (22.2)	22 (24.7)	0.628
Stent implantation	523 (97.4)	156 (95.7)	0.294	267 (96.7)	70 (94.6)	0.485	256 (98.1)	86 (96.6)	0.424
Type of stent									
Drug-eluting stent	440 (84.1)	144 (92.3)	0.010	225 (84.3)	65 (92.9)	0.065	215 (84.0)	79 (91.9)	0.069
Bare-metal stent	15 (2.9)	0	0.029	5 (1.9)	0	0.588	10 (3.9)	0	0.072
Total stent length	27.9 ± 12.2	30.3 ± 12.0	0.034	27.6 ± 11.6	30.6 ± 12.1	0.060	28.3 ± 12.8	30.1 ± 12.1	0.255

Table 2 (continued)

	Total		<i>p</i> value	Postconditioning		<i>p</i> value	Conventional		<i>p</i> value
	Men (<i>n</i> = 537)	Women (<i>n</i> = 163)		Men (<i>n</i> = 276)	Women (<i>n</i> = 74)		Men (<i>n</i> = 261)	Women (<i>n</i> = 89)	
Stent diameter	3.3 ± 0.5	3.1 ± 0.4	< 0.001	3.3 ± 0.5	3.1 ± 0.4	< 0.001	3.3 ± 0.5	3.1 ± 0.5	0.024
Myocardial blush grade after PCI			0.841			0.872			0.843
0/1	102 (19.1)	36 (22.1)		45 (16.4)	15 (20.3)		57 (22.0)	21 (23.6)	
2	167 (31.3)	47 (28.8)		85 (30.9)	23 (31.1)		82 (31.7)	24 (30.0)	
3	265 (49.6)	80 (49.1)		145 (52.7)	36 (48.6)		120 (46.3)	44 (49.4)	
TIMI flow after PCI			0.039			0.874			0.514
0/1	21 (3.9)	6 (3.7)		7 (2.6)	1 (1.3)		14 (5.4)	5 (5.6)	
2	26 (4.9)	17 (10.4)		13 (4.7)	7 (9.5)		13 (5.0)	10 (11.2)	
3	487 (91.2)	140 (85.9)		255 (92.7)	66 (89.2)		232 (89.6)	74 (83.2)	
Syntax score	15.1 ± 8.6	15.8 ± 9.5	0.334	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 ± 6.1	4.3 ± 6.6	0.164	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 ± 192.2	219.8 ± 175.7	0.410	233.7 ± 168.9	224.1 ± 182.5	0.670	233.7 ± 214.5	216.2 ± 170.8	0.487
ST-segment resolution, > 70%	203 (39.1)	74 (46.8)	0.096	105 (39.0)	33 (45.8)	0.344	98 (39.4)	41 (47.7)	0.205

Values are mean ± SD, median (IQR) or *n* (%)

PCI percutaneous coronary intervention, TIMI thrombolysis in myocardial infarction

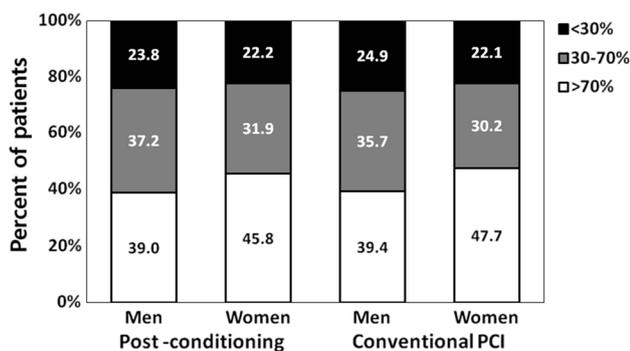


Fig. 1 ECG data according to treatment group. The percentages of patients are shown with regard to ST-segment resolution. PCI percutaneous coronary intervention

postconditioning during primary PCI did not reduce MACE in patients with STEMI [5, 8]. However, whether there are any gender differences in these clinical results has not been previously evaluated. In this study, we demonstrated a significantly higher rate of MACE in women. Of note, these differences were seen only in the postconditioning group and not in the conventional PCI group.

Females have been shown to have endogenous cardioprotection. In many studies, females have smaller infarcts than males [9–11], while the addition of estrogen has been shown to reduce infarct size [12]. This endogenous protection may account for the smaller cardioprotective role of postconditioning in females as a result of an overlap between cardioprotective and postconditioning signaling. Hence, the loss of cardioprotection may be due to activation of endogenous protection (as in females), such that the observed benefit of postconditioning is reduced because of an increase in baseline protection, making it harder to detect any significant treatment benefits from the treatment [13].

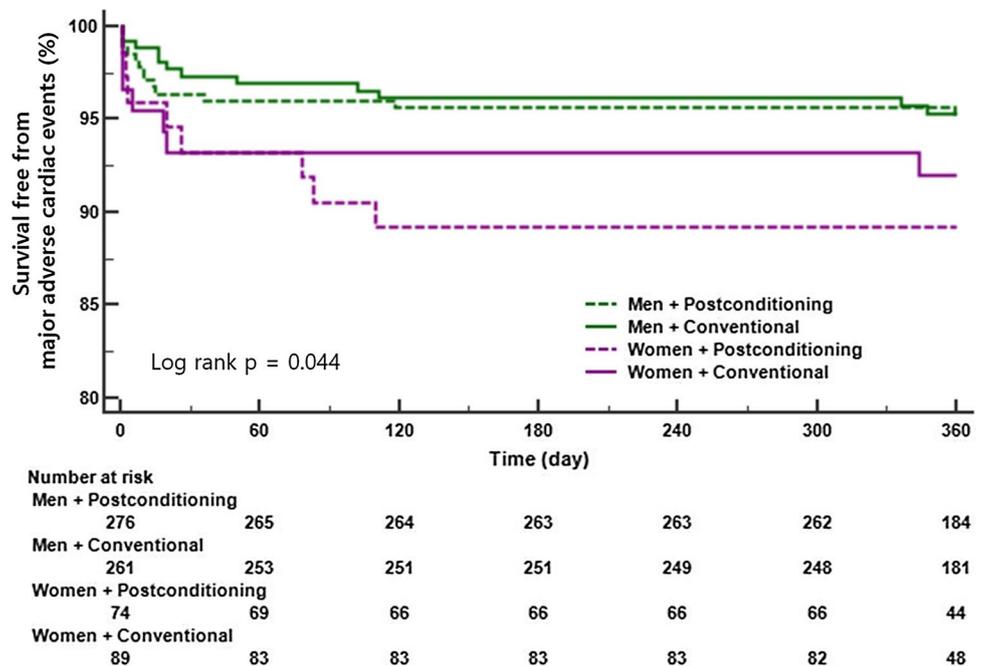
Nitric oxide has been shown to elicit cardioprotection [14], with elevated levels of endothelial nitrous oxide synthase at baseline thought to contribute to endogenous protection in females [11]. Postconditioning is also thought to protect via the same pathways; hence, there will be less protection (as a percentage of baseline protection) with postconditioning. As protection in females is lost in ovariectomized animals, one would expect that postconditioning would be more protective in ovariectomized compared to non-ovariectomized females. However, cardiovascular disease typically occurs in postmenopausal females, and therefore, the

Table 3 Clinical outcomes at 1-year between men and women for each group

	Total			Postconditioning			Conventional		
	Men (<i>n</i> = 537)	Women (<i>n</i> = 163)	<i>p</i> value	Men (<i>n</i> = 276)	Women (<i>n</i> = 74)	<i>p</i> value	Men (<i>n</i> = 261)	Women (<i>n</i> = 89)	<i>p</i> 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 ^a	29 (5.4)	16 (9.8)	0.044	15 (5.4)	9 (12.2)	0.042	14 (5.4)	7 (7.9)	0.391

Values are *n* (%)

^aMajor adverse cardiac event was a composite of death, myocardial infarction, severe heart failure, and stent thrombosis, target vessel revascularization

Fig. 2 Kaplan–Meier curves of freedom from major adverse cardiac events

cardioprotective effects of estrogen observed in premenopausal women are lost.

In this study, women had many more adverse clinical features than men; however, their prognosis in the conventional PCI group was still comparable suggesting the presence of endogenous cardioprotection in women. In contrast, women's prognosis was poorer in the postconditioning group. These differences indicate that postconditioning might

actually do harm in women rather than having no effect, as previously suggested by randomized studies. Freixa et al. reported that primary PCI patients with STEMI and TIMI grade flow 0–1 who received postconditioning had higher peak cardiac troponin I (299 ± 72 vs. 148 ± 23.8 ng/ml, $p = 0.05$) and less myocardial salvage effect (myocardial salvage index: 18.9 ± 27.4 vs. $30.9 \pm 20.5\%$ area at risk, $p = 0.038$) compared with conventional PCI patients,

Table 4 Comparison of treatment group in men and women

	Men			Women		
	Postconditioning (<i>n</i> = 276)	Conventional (<i>n</i> = 261)	<i>p</i> value	Postconditioning (<i>n</i> = 74)	Conventional (<i>n</i> = 89)	<i>p</i> 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	15 (5.4)	14 (5.4)	0.971	9 (12.2)	7 (7.9)	0.359

Values are *n* (%)

Table 5 Adjusted comparison in postconditioning group only

	Postconditioning		Unadjusted		Adjusted ^a	
	Men (<i>n</i> = 276)	Women (<i>n</i> = 74)	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> 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

Values are *n* (%)

CI confidence interval, HR hazard ratio

^aThe included covariates were age, body mass index, hypertension, smoking, ejection fraction, symptom to reperfusion time and stent diameter

suggesting that the treatment may actually be harmful [15]. Giuseppe Tarantini et al. concluded that postconditioning did not have the expected cardioprotective effect and on the contrary might harm STEMI patients treated by primary PCI. The 30-day and at 6-month MACE (the combination of death, re-infarction, re-hospitalization for heart failure, or repeat revascularization) were not significantly different with a trend toward a worse outcome in postconditioning patients [16]. Although women showed a higher rate of the MACE compared to men, women were not an independent predictor in the postconditioning group. Until now, it is not known whether postconditioning has a negative effect on prognosis for women compared to men. We need a prospective RCT to prove this, but it is difficult to achieve ethically. Therefore, although this study could be said to be difficult to make statistical conclusions, it might be concluded from this result that women do not have the effect of postconditioning.

Limitations

The main limitations of this study include that it was a post hoc subanalysis of patients in the POST study, and therefore, the findings should only be hypothesis generating.

Because a relatively small number of women were included, the subanalysis is underpowered to determine whether postconditioning is harmful to conventional PCI in women with STEMI. Although caution is required in generalizing our findings to all patients with STEMI, this study was the first, to our knowledge, to evaluate the effect of sex differences on ischemic postconditioning for the patients of STEMI during the primary PCI.

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, women were not an independent predictor in the postconditioning group.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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