Ischemic Postconditioning After STEMI

Written by ***Tony Rizzo***

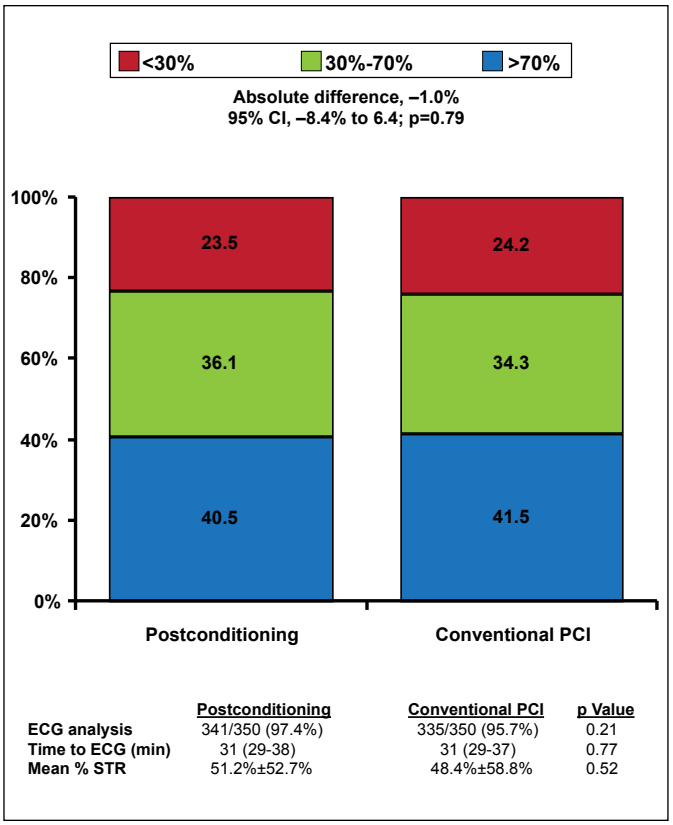
While it has been reported that ischemic postconditioning reduces infarct size in patients with ST-segment myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) [Staat P et al. *Circulation* 2005], other trials have reported inconsistent results [Lonborg J et al. *Circ Cardiovasc Interv* 2010; Sorensson P et al. *Heart* 2010; Freixa X et al. *Eur Heart J* 2012; Tarantini G et al. *Int J Cardiol* 2012] and there have been no large-scale trials to date. The objective of the Effects of Postconditioning on Myocardial Reperfusion [POST; NCT00942500] study presented by Joo-Yong Hahn, MD, Samsung Medical Center, Seoul, Korea, was to evaluate the safety and efficacy of postconditioning in patients with STEMI undergoing primary PCI.

A total of 700 patients with STEMI undergoing primary PCI from 17 South Korean hospitals were randomized after diagnostic coronary angiography to primary PCI with postconditioning (n=350) or conventional primary PCI (n=350). Postconditioning consisted of 4 episodes of 1-minute balloon occlusion and 1-minute deflation immediately after restoration of coronary flow. Patients were treated with aspirin (300 mg) and clopidogrel (600 mg). The primary endpoint was complete ST-segment resolution (STR >70%) at 30 minutes after the procedure. The secondary endpoints were TIMI flow grade after PCI, myocardial blush grade (MBG), major adverse cardiac events (MACE; composite of death, reinfarction, severe heart failure, or stent thrombosis), MACE components, and target vessel revascularization at 30 days.

Patients' mean age was 60 and ~75% were male. Baseline clinical characteristics and angiographic findings were well balanced between the 2 treatment groups. ECG was performed in 97.4% of postconditioning patients and 95.7% of conventional PCI patients (p=0.21). Time to ECG was 31 minutes in both groups (p=0.77). There was no significant difference in the primary endpoint (complete STR) for those patients who had postconditioning versus conventional PCI (40.5% vs 41.5%; 95% CI, −8.4% to 6.4%; p=0.79; Figure 1). The primary endpoint results were consistent across prespecified subgroups.

There was no significant difference in TIMI flow grade (p=0.08) or MBG (p=0.20) after PCI with postconditioning versus conventional PCI. Clinical outcomes at 1-month after PCI were not significantly different between the 2 groups (Table 1). STR <30, MBG of 0/1, and postprocedural TIMI flow grade of 0/1 were significantly associated with higher rates of mortality and MACE.

Figure 1. Primary Endpoint: Complete ST-Segment Resolution.



	Postconditioning	Conventional PCI	p Value
ECG analysis	341/350 (97.4%)	335/350 (95.7%)	0.21
Time to ECG (min)	31 (29-38)	31 (29-37)	0.77
Mean % STR	51.2%±52.7%	48.4%±58.8%	0.52

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Table 1. Clinical Outcomes at 1 Month.

	Post-conditioning (n=350)	Conventional PCI (n=350)	RR (95% CI)*	p Value
Death	13 (3.7%)	10 (2.9%)	1.30 (0.58-2.92)	0.53
Cardiac death	10 (2.9%)	9 (2.6%)	1.11 (0.46-2.70)	0.82
Reinfarction	2 (0.6%)	1 (0.3%)	2.00 (0.18-21.74)	0.99†
Severe HF	2 (0.6%)	5 (1.4%)	0.40 (0.08-2.05)	0.29†
Stent thrombosis	7 (2.0%)	6 (1.7%)	1.17 (0.40-3.44)	0.78
TVR	3 (0.9%)	3 (0.9%)	1.00 (0.20-4.92)	0.99
MACE‡	15 (4.3%)	13 (3.7%)	1.15 (0.56-2.39)	0.70

HF=heart failure; MACE=major adverse cardiac event; TVR=target-vessel revascularization. *Relative risk is for the postconditioning group as compared with the conventional PCI group; †The p value was calculated with the use of Fisher's exact test; ‡MACE was a composite of death, reinfarction, severe HF, or stent thrombosis; Reproduced with permission from JY Hahn, MD.

The study had several limitations. Providers were not blinded to treatment allocation, the study was underpowered for clinical outcomes, postconditioning was not performed per protocol in ~8% of patients, and ECGs before and 30 minutes post-procedure were not available in 3.5% of patients. Patients with hemodynamic instability, cardiogenic shock, or a left main lesion who might have had lethal reperfusion injury and received potential benefit from postconditioning were excluded.

The investigators concluded that ischemic postconditioning with primary PCI did not improve myocardial reperfusion compared with conventional primary PCI. Clinical outcomes at 1 month were not significantly different between 2 groups. A cardioprotective effect of ischemic postconditioning was not observed in any of the prespecified subgroups.

Benefit of PFO Closure in Cryptogenic Stroke Remains Elusive

Written by ***Rita Buckley*** *and* ***Toni Rizzo***

Approximately 30% to 40% of ischemic strokes are classified as cryptogenic because a recognized cause is not identified [Sacco RL et al. *Ann Neurol* 1989]. Paradoxical embolism due to patent foramen ovale (PFO) is a possible cause of ischemic stroke, particularly in young cryptogenic stroke patients. However, it is often difficult to establish a firm etiological association [Horner S et al. *J Neurol* 2012] and optimal treatment for secondary prevention in patients with cryptogenic stroke and PFO is still undefined [O'Gara PT et al. *J Am Coll Cardiol* 2012]. Several presentations at TCT 2012 added important data to the growing literature about PFO closure and highlighted how elusive secondary stroke prevention with device therapy remains.

The PC-Trial: Patent Foramen Ovale Closure Versus Medical Therapy

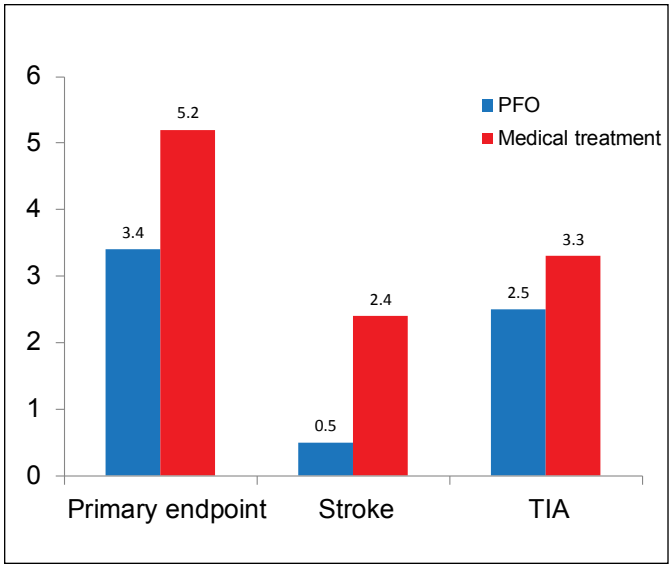
The Patent Foramen Ovale and Cryptogenic Embolism trial [PC-Trial; NCT00166257] presented by Stephan Windecker, MD, Swiss Cardiovascular Center, Bern, Switzerland, tested whether percutaneous closure of PFO using the Amplatzer PFO Occluder would be superior to medical treatment for secondary prevention of thromboembolism in patients with cryptogenic stroke and peripheral embolism.

The trial randomized 414 patients to PFO closure (n=204) with the Amplatzer device along with acetylsalicylic acid and ticlopidine or clopidogrel for 6 months or to optimal medical treatment (n=210) with oral anticoagulation or antiplatelet therapy. Patients had to be <60 years of age and have clinically and neuroradiologically verified ischemic stroke or transient ischemic attack (TIA) with a documented corresponding intracranial ischemic lesion or extracranial peripheral thromboembolism. Patients with any other cause for a thromboembolic event were excluded.

The primary endpoint was the composite of death from any cause, nonfatal stroke, TIA, and peripheral embolism. The secondary endpoints were myocardial infarction (MI), new atrial fibrillation, rehospitalization for PFO, and device-related problems.

PFO closure was successful in 96.9% of patients; 95.9% had effective closure at 6 months. Residual shunt was absent in 91.7%, minimal in 6.2%, moderate in 0.7%, and severe in 1.4% of PFO closure patients. At a mean follow-up of 4 years, the primary endpoint occurred in 3.4% of patients (142) in the PFO closure arm versus 5.2% (131) in the medical treatment arm, a nonsignificant 37% relative risk reduction (RRR) with PFO closure (HR, 0.63; 95% CI, 0.24 to 1.62; p=0.34; Figure 1).

Figure 1. Results.



RRR=relative risk reduction; TIA=transient ischemic attack.

Stroke occurred less frequently in the PFO closure group than in the medical treatment group, but the difference was not statistically significant (0.5% vs 2.4%; HR, 0.20; 95% CI, 0.02 to 1.72; p=0.14). Similar findings were noted for TIA (HR, 0.71; 95% CI, 0.23 to 2.24; p=0.56). There were no significant differences between PFO closure and medical treatment in MI (1.0% vs 0.5%; HR, 2.04; 95% CI, 0.19 to 22.5; p=0.56) and PFO-related hospitalizations (6.4% vs 6.2%; HR, 1.02; 95% CI, 0.48 to 2.21; p=0.95).

There were no significant differences between PFO