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INTERVENTIONAL CARDIOLOGY

Does preventive PCI reduce the risk of adverse events in patients with acute STEMI?

In addition to percutaneous coronary intervention (PCI) in the infarct artery, PCI in noninfarct, but >50% stenosed, arteries in patients presenting with an acute ST-segment elevation myocardial infarction (STEMI) might reduce the risk of adverse cardiovascular events. These findings from the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial were presented at the 2013 ESC Congress in Amsterdam, Netherlands.

Current guidelines for the management of patients with STEMI recommend PCI only in the infarct artery. Notably, however, patients who present with an acute STEMI are at substantial risk of experiencing recurrent events. "When a patient is admitted with an acute myocardial infarction (MI), it is known that PCI to the blocked culprit artery is life-saving, but there is uncertainty as to whether doctors should undertake preventive PCI in vessels that are partially blocked but did not cause the MI," explains David Wald, who presented the trial findings at the ESC Congress. This uncertainty prompted the PRAMI investigators to undertake their single-blind, randomized trial.

Patients attending one of five centres in the UK were enrolled in PRAMI over a 5-year period (2008–2013). Eligible patients were individuals who presented with a STEMI and multivessel coronary disease at the time of emergency PCI, and had >50% stenosis in ≥1 noninfarct coronary artery that was thought to be treatable by PCI. Eligibility was decided in the catheterization laboratory after successful PCI on the infarct artery, and all patients deemed eligible were randomly assigned to no further PCI procedures at that time or to immediate 'preventive PCI'. A cardiologist and a cardiac surgeon who were unaware of patients' study-group assignments assessed the specified outcomes.

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The PRAMI investigators planned to enrol 600 patients into the trial; however, in January 2013, the data and safety monitoring committee recommended that patient recruitment be halted, owing to a highly statistically significant between-group difference in the primary outcome. In total, 465 patients were enrolled in the trial. Medical therapy was similar in the two treatment groups. Although procedure duration, contrast volume, and fluoroscopy dose were increased in the group that underwent preventive PCI, rates of procedure-related complications were similar for the two groups. Mean follow-up was 23 months.

The composite primary outcome—death from cardiac causes, nonfatal MI, or refractory angina—occurred in 9% of the preventive-PCI group and 23% of those who did not undergo preventive PCI (HR 0.35, 95% CI 0.21–0.58, $P<0.001$). The reduction in risk of the composite primary outcome in patients who underwent preventive PCI was apparent within 6 months after the intervention. The PRAMI investigators acknowledge that "refractory angina is a more subjective outcome than MI or cardiac death," but say that they included it in the primary outcome "because it is a serious symptomatic condition that warrants prevention".

When each component of the primary end point was assessed individually, the difference in deaths from cardiac causes did not reach statistical significance (2% with preventive PCI vs 4% in controls; HR 0.34, 95% CI 0.11–1.08, $P=0.07$), but differences in nonfatal MI (3% vs 9%; HR 0.32, 95% CI 0.13–0.75, $P=0.009$) and refractory angina (5% vs 13%; HR 0.35, 95% CI 0.18–0.69, $P=0.002$) were highly statistically significant. The secondary outcome of repeat revascularization was also found to be reduced with preventive PCI (7% vs 20% in controls; HR 0.30, 95% CI 0.17–0.56, $P<0.001$). The rate of death from noncardiac causes did not differ between the two groups (3% in both groups; $P=0.86$).

"The PRAMI study did not examine whether preventive PCI is best performed during the emergency procedure," highlights Laura Mauri in an editorial that accompanied the PRAMI trial report in the *New England Journal of Medicine*. "Although the risks of recurrent myocardial infarction were highest in the first few days, it is unknown whether the risk–benefit ratio could be preserved if preventive PCI were performed soon after, rather than during, the initial procedure." The PRAMI investigators acknowledge that this aspect needs to be addressed in a separate trial.

The PRAMI findings were described by multiple cardiologists at the ESC Congress as hypothesis-generating and deserving of further investigation, owing to the unblinded study design and premature trial cessation, lack of fractional flow reserve measurement, and the small number of patients and events. Dr Wald responds by saying that "in fact, the trial was hypothesis-testing and single-blind. We could not blind to the operators because they did the procedures, and the clear result meant no further recruitment was justified. The role of fractional flow reserve in this setting is unknown."

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Original article Wald, D. S. *et al.* Randomized trial of preventive angioplasty in myocardial infarction. *N. Engl. J. Med.* doi:10.1056/NEJMoa1305520