

Staged versus One-Time Percutaneous Coronary Intervention Strategy for Multivessel Non-ST Segment Elevation Acute Coronary Syndrome

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Patients with non-ST segment elevation acute coronary syndrome (NSTEMI-ACS) often have multiple non-culprit lesions in addition to culprit lesion.^{1,2} Previous studies suggest that performing "one-time" interventions to non-culprit lesions of multivessel NSTEMI-ACS patients improve clinical outcomes as compared to culprit-only intervention.^{3,4} Shishebor et al.³ reported that multivessel percutaneous coronary intervention (PCI) strategy reduces composite endpoint of all-cause death, myocardial infarction (MI), and revascularization (hazard ratio [HR] 0.67, 95% confidence interval [CI] 0.51-0.88, $p=0.004$) compared to culprit only PCI strategy. Most of the benefits were driven by reduction in revascularization (HR 0.59, 95% CI 0.41-0.84, $p=0.003$) and there was no statistically significant difference in the rate of death or composite of death and MI. In the study reported by Kim et al.,⁴ multivessel PCI strategy reduced major adverse cardiovascular events (a composite of all-causes deaths, myocardial infarction, repeated revascularization, and coronary artery bypass grafting) (HR 0.658, 95% CI 0.45-0.96, $p=0.031$), death or myocardial infarction (HR 0.58, 95% CI 0.35-0.97, $p=0.037$), and non-target vessel revascularization (HR 0.44, 95% CI 0.24-0.81, $p=0.008$)

compared to culprit only, staged PCI strategy.

There are 2 strategies to perform PCI in NSTEMI-ACS patients with multivessel disease: staged PCI and "one-time" PCI. Although multivessel PCI is considered to be a reasonable approach in NSTEMI-ACS patients with significant multivessel lesions,^{3,4} whether to undergo staged PCI or to perform one-time PCI in such patients is an area of active debate. The study performed by Yu et al.⁵ attempts to provide an answer to this important issue in the field of interventional cardiology.

Principal findings of the study

This study performed by Yu et al.⁵ raises the hypothesis that staged PCI for intermediate to very high risk multivessel NSTEMI-ACS patients offers a better clinical results as compared to one-time PCI strategy in terms of cardiac death and MI. More than 1500 consecutive intermediate to very high risk multivessel NSTEMI-ACS patients were analyzed. Staged PCI was performed in 672 patients and one-time PCI in 859 patients. The primary endpoint was a composite of 3-year cardiac death, MI, and target vessel revascularization (TVR). Because of the inherent nature of non-randomized study, the baseline clinical and angiographic characteristics of the 2 groups were significantly different with unfavorable clinical and angiographic characteristics in the staged PCI group. The staged PCI group had a higher rate of previous MI, current-smoker, and 3 vessel disease. Stent numbers and total stent length per patient were significantly higher, and complete revascularization rate was significantly lower in the staged PCI group. Therefore, a propensity score matching was performed for further analysis. In the raw comparison, there was no significant difference in the primary outcome endpoint, a composite of 3-year cardiac death, MI, and TVR, between the staged PCI group and the one-time PCI group. A propensity matched analysis also showed similar results with respect to the primary outcome endpoint between the 2 groups (18.9% vs. 21.8%, $p=0.249$). However, cardiac death and MI was significantly lower in the staged PCI group in the propensity matched analysis (7.0% vs. 11.1%, $p=0.033$). Ninety

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day landmark propensity matched analysis showed a favorable result for the staged PCI strategy in terms of the primary outcome endpoint (1.2% vs. 3.3%, $p=0.037$) and cardiac death/MI (0.7% vs. 2.6%, $p=0.031$).

Clinical impact of the study

Previous studies indicate that ST segment elevation myocardial infarction (STEMI) patients with multivessel disease is better treated with culprit lesion only PCI followed by staged PCI for other diseased vessels.⁶⁻⁸ In the post-hoc analysis of the HORIZONS-AMI trial,⁶ one-time PCI strategy was associated with higher 1-year mortality (HR 4.1, 95% CI: 1.93–8.86, $p<0.0001$), cardiac mortality (HR 3.14, 95% CI 1.35–7.27, $p=0.005$), definite/probable stent thrombosis (HR 2.49, 95% CI 1.09–5.70, $p=0.02$), and a trend toward greater major adverse cardiovascular events (HR 1.42, 95% CI 0.96–2.1, $p=0.08$) compared to staged PCI strategy. In a meta-analysis performed by Vlaar et al.⁷ the pooled odds ratios of short term mortality (within 30 days) (HR 5.31, 95% CI 2.31–12.21, $p<0.0001$) and long term mortality (HR 2.28, 95% CI 1.39–3.72, $p=0.001$) were all in favor of staged PCI strategy compared to one-time PCI strategy in patients with STEMI. Additionally, staged PCI strategy was also superior to culprit only PCI strategy (HR 3.03, $p=0.005$ for short term mortality; HR 1.74, $p=0.03$ for long term mortality).⁷ The best treatment strategy for multivessel NSTEMI-ACS patients, however, is still not elucidated. According to this study performed by Yu et al.,⁵ it seems that staged PCI strategy might be a better option for intermediate to very high risk NSTEMI-ACS patients with multivessel disease. The staged PCI group showed a similar 3-year cumulative incidence of primary outcome endpoint despite clearly unfavorable baseline clinical and angiographic characteristics. The propensity matched analysis revealed that staged PCI strategy was associated with favorable results with respect to (1) 90-day incidence of the primary outcome endpoint, (2) 90-day incidence of cardiac death or MI, and (3) 3-year cumulative incidence of cardiac death or MI.

The results of the present study⁵ are in contrast to the previous study performed by Hannan et al.⁹ which reported that patients with NSTEMI-ACS do not benefit from staged PCI strategy compared to complete revascularization at the index admission. In the propensity matched analysis, there was no significant difference in the all-cause mortality rate at 3-year between patients who underwent complete revascularization at the index hospitalization and patients staged for complete revascularization within 60 days of discharge (6.59% and 5.92%, $p=0.41$).⁹ However, there were several major differences between the 2 studies in terms of inclusion criteria and outcome measurements. Hannan et al.⁹ compared the efficacy of complete revascularization at the index admission vs. staged complete revascularization in the

subsequent admission. Patients who underwent staged PCI in the index admission were classified as one-time strategy in the study performed by Hannan et al.,⁹ whereas they were included in the staged PCI group in the study performed by Yu et al.⁵ Additionally, Yu et al.⁵ excluded low risk NSTEMI-ACS patients in their analysis. Hannan et al.⁹ only evaluated all cause death whereas Yu et al.⁵ evaluated cardiac death, MI, and TVR simultaneously. Since Yu et al.⁵ only included intermediate to very high risk NSTEMI-ACS patients and evaluated clinical outcomes more specific to coronary artery disease, this might be the reason for the discordance between the 2 studies.

The results of the present study are valuable not only to cardiologists but also to those associated with insurance industry. National or private insurance committees in various countries tend to discourage staged procedures, especially if it is associated with readmission and, in real world clinical practice, numerous cardiologists have experienced rejection of reimbursements for the staged procedures in intermediate to very high risk patients with NSTEMI-ACS. It is obvious that staged procedures are associated with increased medical costs and previous studies reported that the medical cost of staged PCI is twice as expensive as that of one-time PCI.^{9,10} Therefore, in order to justify the extra medical cost of staged PCI for NSTEMI-ACS patients with multivessel disease, we need clear and robust evidences that staged PCI is better than one-time PCI in terms of clinical outcomes. Although the present study is a retrospective study and has several intrinsic limitations, it strongly suggests that the staged PCI strategy is better than one-time PCI strategy, especially in terms of reducing cardiac death and MI, and motivates us to design and conduct a prospective randomized clinical trial that compares the 2 treatment strategy in NSTEMI-ACS patients.

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