What Is the Most Preferable Treatment Strategy for Patients With Non-ST-Elevation Acute Coronary Syndrome With Multivessel Disease? — A Long-Term Perspective —

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Current guidelines recommend coronary artery bypass grafting (CABG) over percutaneous coronary intervention (PCI) for patients with left main or multivessel coronary artery disease (CAD). However, data are lacking regarding long-term clinical outcomes in patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) who undergo CABG, PCI, or medical therapy alone. The optimal management strategy for these patients in terms of the long-term (especially >5 years) clinical outcomes is still debatable because of the lack of randomized controlled trials regarding this issue. Therefore, long-term outcome data of this high-risk patient group should be collected in large-scale real-world registries.

In this issue of the Journal, Jia et al report the long-term clinical outcomes of patients with NSTE-ACS and 3-vessel disease who underwent PCI, CABG, or medical therapy alone in a large-scale single-center database. Their study showed that CABG was significantly associated with a lower risk of long-term cardiac death, revascularization, and major adverse cardiovascular events (MACCE) compared to PCI. Patients who received medical therapy alone had the highest risk of MACCE.

Table. Major Clinical Studies Regarding the Effect of Treatment Strategies on Long-Term Outcomes in Patients With NSTE-ACS and Left Main and/or Multivessel CAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Country / year</th>
<th>Study design</th>
<th>Study population</th>
<th>Follow-up period</th>
<th>Sample size</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jia et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>China / 2020</td>
<td>Single-center, prospective, observational cohort study</td>
<td>Patients with NSTE-ACS and 3-vessel CAD</td>
<td>Median: 7.5 years</td>
<td>PCI (n=1,589), CABG (n=1,230), medical therapy (n=1,109)</td>
<td>CABG was associated with a lower risk of cardiac death, revascularization, and MACCE than PCI. Patients who received medical therapy alone had the highest risk of MACCE.</td>
</tr>
<tr>
<td>Huckaby et al&lt;sup&gt;2&lt;/sup&gt;</td>
<td>USA / 2020</td>
<td>Single-institution, retrospective, observational cohort study</td>
<td>Patients with NSTEMI and multivessel CAD</td>
<td>Median: 3.6 years</td>
<td>PCI (n=521), CABG (n=1,480)</td>
<td>CABG was associated with a lower rate of death, MACCEs, and readmission than PCI, even in subgroup analysis of patients who underwent complete revascularization.</td>
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<tr>
<td>Freitas et al&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Portugal / 2019</td>
<td>Single-center, prospective, observational cohort study</td>
<td>Patients with NSTEMI and LM/multivessel CAD</td>
<td>Median: 4.8 years (58 months)</td>
<td>PCI (n=399), CABG (n=289), medical therapy (n=416)</td>
<td>Trend for lower 5-year mortality rate in the CABG group compared with the PCI group was found. Medical therapy alone was associated with worse prognosis than PCI or CABG.</td>
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<td>Chang et al&lt;sup&gt;4&lt;/sup&gt;</td>
<td>South Korea and others / 2017</td>
<td>Pooled data analysis from 3 randomized controlled trials</td>
<td>Patients with NSTE-ACS and LM/multivessel CAD</td>
<td>Median: 5.0 years (60 months)</td>
<td>PCI (n=612), CABG (n=634)</td>
<td>CABG was associated with a lower risk of 5-year mortality, myocardial infarction, or stroke than PCI.</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass grafting; CAD, coronary artery disease; LM, left main; MACCE, major adverse cardiac and cerebrovascular events; NSTE-ACS, non-ST-elevation acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention.

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and major adverse cardiac and cerebrovascular events (MACCE) compared with PCI. Additionally, patients who received medical therapy alone had the highest risk of long-term MACCE. The advantages of the current study include the large sample size of the database with a prospective design, sufficient data collection with long-term follow-up (median: 7.5 years, follow-up rate: 98.4%), and important statistical analyses, including multiple subgroup analyses and interaction tests.

Previous studies have shown that complete revascularization is significantly associated with better long-term clinical outcomes in patients with multivessel CAD undergoing PCI or CABG. Generally, the complete revascularization rate in patients with multivessel CAD who undergo CABG is significantly higher than that in those who undergo PCI. In the study by Jia et al, complete revascularization was achieved in only 5.2% of patients at the index procedure in the PCI cohort, and data regarding the prevalence of chronic total occlusion lesions were lacking. In a subgroup analysis of their study, myocardial infarction was observed more frequently in patients who underwent complete revascularization in the PCI cohort than in the CABG cohort during the follow-up period (12.0% vs. 2.7%, P<0.001). However, there were no significant differences in the risk of all-cause death, myocardial infarction, and MACCE after adjustment of confounding variables between the 2 groups. Therefore, a low complete revascularization rate is one of the potential explanations of the worse long-term clinical outcomes in the PCI group vs. the CABG group. However, another recent observational study showed that the overall survival rate and freedom from MACCE at 5 years after revascularization for NSTE-ACS with multivessel CAD remained higher in the CABG group than in the PCI group, even in patients who underwent complete revascularization. Clinical studies regarding long-term outcomes by treatment strategies in patients with NSTE-ACS and left main and/or multivessel CAD are summarized in the Table. These study results consistently suggest long-term clinical benefits of coronary revascularization over medical therapy alone, and CABG is superior to PCI from the long-term perspective in these patients. Among them, the study by Jia et al included the largest number of patients with NSTE-ACS and showed the longest follow-up data, which provides important clinical implications for management of such patients.

Generally, patients and physicians tend to make decisions on treatment strategy from a short-term perspective (e.g., PCI is less invasive than CABG). However, final decisions should be made from the perspective of long-term clinical outcomes. According to the study results by Jia et al, if a patient presenting with NSTE-ACS and 3-vessel CAD is eligible for CABG, this is the most preferable therapeutic option. In contrast, it is noteworthy that the average age of the patients was relatively young in Jia et al’s study (61.1 years in the PCI cohort, 61.7 years in the CABG cohort, and 64.3 years in the medical therapy cohort). However, the number of older patients with CAD undergoing PCI, including octogenarians and nonagenarians, has been increasing, particularly in advanced nations with seriously aging societies. Therefore, the decision-making process of the treatment strategy for older patients presenting with NSTE-ACS with multivessel CAD and multiple comorbidities who are ineligible for CABG may also be an important issue. Indeed, in a recent Japanese registry-based study, patients with left main or 3-vessel CAD with surgical eligibility who underwent PCI had significantly worse 5-year clinical outcomes (e.g., all-cause death and MACCE) compared with those without surgical eligibility. Because determining the optimal treatment strategy for these patients with high-risk profiles is sometimes difficult, the multidisciplinary heart team approach is the most important part of the decision-making process. Of note, the results of Jia et al’s study also suggest the importance of the multidisciplinary approach because the treatment strategy was determined by discussion of the heart team involving interventional cardiologists, cardiac surgeons, and other physicians. On the basis of these findings, discussion with the heart team should be routinely performed in each hospital for quality improvement of medical care.

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Disclosures
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