Coronary Revascularization for Patients with Severe Coronary Artery Disease: An Overview of Current Evidence and Treatment Strategies

Hiroki Shiomi, Takeshi Kimura

The technical and device refinements in percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) has achieved the improvement of outcome in patients with coronary artery disease (CAD). Optimal revascularization methods (PCI or CABG) for severe CAD such as multivessel and/or left main CAD is still in debate in the current clinical practice. In this review, therefore, we discuss the current status of coronary revascularization and outcome in patients with severe CAD on the basis of the evidence of clinical trials in DES era.

KEY WORDS: coronary revascularization, PCI, CABG
cause death (14.6% versus 9.2%, P=0.006) as well as that of MI (22.0% versus 14.0%, P<0.001) was significantly higher in the PCI group than in the CABG group. On the other hand, the risk for stroke was not significantly different between PCI and CABG (3.0% versus 3.5%, P=0.66). The FREEDOM (the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) trial was a multi-center randomized clinical trial (RCT) in which 1900 MV-CAD patients with diabetes mellitus (DM) were randomly assigned to undergo PCI using DES or CABG, and reported that the primary endpoint of a composite of death/MI/stroke was significantly lower in the CABG group than in the PCI group (18.7% versus 26.6%, P=0.005).9

In Japan, the CREDO-Kyoto (Coronary Revascularization Demonstrating Outcome Study in Kyoto) registry cohort-2 reported long-term clinical outcomes after PCI and CABG in patients with 3-vessels CAD in DES era.10 Consistent with the results in RCTs and observational studies in foreign countries, the CREDO-Kyoto registry cohort-2 reported that the excess risks of PCI relative to CABG for death/MI/stroke (hazard ratio [HR]: 1.38 [95% confidence interval (CI): 1.13–1.68], P=0.002), all-cause death (HR: 1.38, 95%CI: 1.10–1.74, P=0.006), MI (HR: 2.81, 95%CI: 1.69–4.66, P<0.001), and any coronary revascularization (HR: 4.10, 95%CI: 3.32–5.06, P<0.001) were significant even after adjusting for confounders.8,10,11

In the second-generation (2-G) DES era, a large-scale observational study in New York State in the United States compared clinical outcomes of PCI using 2-G DES of everolimus-eluting stents (EES) with CABG.14 In this study using a propensity matched cohort, mortality risk was not significantly different between PCI with EES and CABG (3.1%/year versus 2.9%/year, HR: 1.04, 95%CI: 0.93–1.17, P=0.50), although PCI with EES as compared with CABG was significantly associated with higher risk for MI (HR: 1.51, 95%CI: 0.93–2.34, P=0.06) and repeat revascularization (HR: 3.0, 95%CI: 1.29–7.17, P<0.001). On the other hand, the BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease) trial, in which 880 patients with multivessel CAD randomly assigned to PCI using EES or CABG, reported that the risk of PCI with EES relative to CABG for the primary endpoint of death/MI/target-vessel revascularization was significantly higher (15.3% versus 10.6%, log-rank P=0.04).11

### IV. Treatment selection according to anatomical complexity

In the SYNTAX trial, SYNTAX score based on anatomical complexity of CAD was introduced and successfully stratified the different risk of PCI relative to CABG for clinical outcomes.15 Reflecting the results of the SYNTAX trial, the current clinical guidelines updated the recommendations of PCI for 3-vessels CAD according to SYNTAX score.15,16 Discordant with the SYNTAX trial, however, the CREDO-Kyoto registry cohort-2 and the FREEDOM trial could not demonstrate the utility of the SYNTAX score in selecting the mode of revascularization.
cumulative 5-year incidences of MACCE (36.9% versus 31.0%, P=0.12), all-cause death (12.8% versus 14.6%, P=0.53), and MI (8.2% versus 4.8%, P=0.10) in the PCI group was not significantly different with those in the CABG group.

The risk of PCI relative to CABG for stroke was significantly lower (1.5% versus 4.3%, P=0.03), while the risk for repeat revascularization was significantly higher in PCI than CABG (26.7% versus 15.5%, P<0.01). Favorable long-term mortality of LM-CAD patients after PCI was consistently observed in several clinical studies despite higher risk of PCI relative to CABG for repeat revascularization (Table 2).

In Japan, The CREDO-Kyoto registry cohort-2 reported long-term clinical outcomes after PCI and CABG in patients with LM CAD in DES era. 17) In the CREDO-Kyoto registry cohort-2, the cumulative 5-year incidences of a composite of death/MI/stroke (34.5% versus 24.1%, log-rank P<0.001) and all-cause death (25.3% versus 18.0%, log-rank P=0.001) were significantly higher in the PCI group than in the CABG group. After adjusting for confounders, the risk of PCI relative to CABG for all-cause death was not significantly different (HR: 1.32, 95%CI: 0.90–1.93, P=0.16), although that for death/MI/stroke was still signifi-

V. Future perspectives in the treatment of multivessel CAD

Most previous studies showed the benefit of CABG over PCI in long-term cardiovascular outcomes even in DES era. 8, 10, 12, 13, 17) However, newer adjunctive medical therapies such as novel P2Y12 receptor inhibitors and PCSK9 inhibitors, as well as newer device including newer generation DES and bioresorbable scaffolds might expect to improve clinical outcomes of multivessel CAD patients treated with PCI. 18–21) PCI guided by fractional flow reserve (FFR), furthermore, was reported to provide improved clinical outcomes as compared with conventional angiography-guided PCI in multivessel CAD. 22) The currently ongoing FAME 3 trial, in which 1,500 patients with multivessel CAD randomly assign to PCI guided by FFR or CABG, would provide further guidance for treatment for multivessel CAD.

VI. Left main coronary artery disease

In the LM-CAD stratum (N=705) of the SYNTAX trial, the cumulative 5-year incidences of MACCE (36.9% versus 31.0%, P=0.12), all-cause death (12.8% versus 14.6%, P=0.53), and MI (8.2% versus 4.8%, P=0.10) in the PCI group was not significantly different with those in the CABG group. 23) The risk of PCI relative to CABG for stroke was significantly lower (1.5% versus 4.3%, P=0.03), while the risk for repeat revascularization was significantly higher in PCI than CABG (26.7% versus 15.5%, P<0.01). Favorable long-term mortality of LM-CAD patients after PCI was consistently observed in several clinical studies despite higher risk of PCI relative to CABG for repeat revascularization (Table 2). 17, 23–25)

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<td>LM-CAD</td>
<td>5</td>
<td>CABG (N=690) PCI with DES (N=784)</td>
<td>Death/MI/stroke</td>
<td>16.3% 12.7%</td>
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<td>Milan-LMT registry(2010)</td>
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<td>LM-CAD</td>
<td>5</td>
<td>CABG (N=142) PCI with DES (N=142)</td>
<td>MACCE</td>
<td>38.3% 32.4%</td>
<td>0.26</td>
<td>18.3% 15.9%</td>
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<td>PRECOMBAT (2011)</td>
<td>RCT</td>
<td>LM-CAD</td>
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<td>CABG (N=300) PCI with SES (N=300)</td>
<td>MACCE</td>
<td>8.1% 12.2%</td>
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<td>LE MANS (2011)</td>
<td>RCT</td>
<td>LM-CAD</td>
<td>1</td>
<td>CABG (N=101) PCI with SES (N=100)</td>
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<td>13.9% 19.0%</td>
<td>0.19 (P for noninferiority)</td>
<td>5.0% 2.0%</td>
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<td>SYNTAX-LM (2014)</td>
<td>RCT</td>
<td>LM-CAD</td>
<td>5</td>
<td>CABG (N=348) PCI with DES (N=357)</td>
<td>MACCE</td>
<td>31.0% 36.9%</td>
<td>0.12</td>
<td>14.6% 12.8%</td>
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<td>CREDO-Kyoto Cohort-2 (2015)</td>
<td>Observational study</td>
<td>LM-CAD</td>
<td>5</td>
<td>CABG (N=640) PCI (N=364, DES: 78%)</td>
<td>Death/MI/stroke</td>
<td>24.1% 34.5%</td>
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<tr>
<td>PRECOMBAT-2 (2012)</td>
<td>Historical comparison</td>
<td>LM-CAD</td>
<td>1.5</td>
<td>CABG (N=272) PCI with DES (N=334)</td>
<td>MACCE</td>
<td>6.7% 8.9%</td>
<td>0.26</td>
<td>3.3% 2.2%</td>
</tr>
<tr>
<td>Yonsei University Registry (2013)</td>
<td>Observational study</td>
<td>LM-CAD</td>
<td>3</td>
<td>OPCAB (N=251) PCI with 2G-DES (N=236)</td>
<td>MACCEs</td>
<td>3.6% 15.4%</td>
<td>0.001</td>
<td>2.1% 6.7%</td>
</tr>
</tbody>
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cantly higher (HR: 1.48, 95%CI: 1.07–2.05, P=0.02).

VII. Treatment selection according to anatomical complexity

Consistent with the SYNTAX trial, the CREDO-Kyoto registry cohort-2 showed the utility of SYNTAX score for risk stratification and selection of mode of revascularization procedure in LM-CAD. In the CREDO-Kyoto registry cohort-2, the adjusted risk for death/MI/stroke was not significantly different between PCI and CABG in low (HR: 1.76, 95%CI: 0.99–3.10, P=0.0504), or intermediate (HR: 1.53, 95%CI: 0.88–2.66, P=0.14) SYNTAX scores, whereas it was significantly higher in PCI than CABG for patients with high SYNTAX score (HR: 2.09, 95%CI: 1.26–3.46, P=0.004). The current clinical guidelines updated the recommendations of PCI for LM CAD according to SYNTAX score.

VIII. Future perspectives in the treatment of LM CAD

The previous studies reporting favorable long-term clinical outcomes after PCI using DES suggest that further shifting to PCI could be possible without impairing long-term outcome in selected patients with LM CAD. The currently ongoing EXCEL trial, in which 2,600 LM CAD patients with SYNTAX score<33 randomly assign to PCI with EES or CABG, would provide further guidance for treatment for LM CAD.

IX. Conclusion

After the introduction of DES in daily clinical practice, the selection of mode of coronary revascularization has dramatically changed over time in Japan. The currently available evidence based on the results of clinical studies comparing PCI with CABG in DES era suggest that CABG is still standard treatment for advanced multivessel CAD, while PCI can be a reasonable alternative to CABG in selected patients with LM CAD. More appropriate indication for coronary revascularization and selection of revascularization procedure as well as stringent adherence to evidence-based medicines might lead further improvement of outcome in patients with severe CAD.

All authors declare no conflict of interest.

References


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