Coronary artery bypass grafting has long been considered the standard revascularization treatment for unprotected left main trunk disease (ULMTD). Percutaneous coronary intervention (PCI) with bare metal stent (BMS) was performed on patients for whom coronary artery bypass grafting was a high risk or those selected by lesion anatomy such as large simple ostial or body lesion. However, its clinical indication is limited by the high rate of target lesion revascularization (TLR). PCI with drug-eluting stent (DES) is increasingly being performed because of its lower TLR rate. Randomized and meta-analysis studies demonstrate that PCI with DES for ULMTD, compared with BMS, could be more strongly associated with a significant reduction in the need for TLR without any additional adverse outcomes, although it has some limitations on indications. (Circ J 2011; 75: 1250–1254)

Key Words: Bare metal stents; Drug-eluting stent; Restenosis; Thrombosis

Among patients with coronary artery disease those with unprotected left main trunk disease (ULMTD) are at higher risk. Some evidence suggests that ULMTD patients have better prognosis after coronary artery bypass grafting (CABG) than those treated with medical therapy. Therefore, CABG has long been considered the standard revascularization treatment for ULMTD. In the bare metal stent (BMS) era, percutaneous coronary intervention (PCI) with BMS was performed on either patients for whom CABG was a high risk or those selected by lesion anatomy such as large simple ostial or body lesion. PCI with drug-eluting stent (DES) is being increasingly performed because of its lower TLR rate. Randomized and meta-analysis studies demonstrate that PCI with DES for ULMTD, compared with BMS, could be more strongly associated with a significant reduction in the need for TLR without any additional adverse outcomes, although it has some limitations on indications. (Circ J 2011; 75: 1250–1254)

Key Words: Bare metal stents; Drug-eluting stent; Restenosis; Thrombosis

Benefit of DES:

TLR or Target Vessel Revascularization (TVR)

Many large-scale randomized observational studies have shown lower rates of TLR/TVR after DES implantation than BMS in the non-ULMTD cohort. One small-scale randomized study compared PCI for ULMTD patients between paclitaxel-eluting stent implantation and BMS, in which the TLR rate after paclitaxel-eluting stent implantation was significantly lower than BMS (Table 1). A meta-analysis that compared DES with BMS in PCI for ULMTD patients also showed the

<table>
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<th>Table 1. Comparison of PES vs. BMS 6-Month Cumulative Outcomes</th>
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<td>Total death, n (%)</td>
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<td>TLR-PCI, n (%)</td>
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<td>TLR-CABG, n (%)</td>
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<td>MACE, n (%)</td>
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PES, paclitaxel-eluting stent; BMS, bare metal stent; MI, myocardial infarction; TLR, target lesion revascularization; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; MACE, major adverse cardiac events.

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

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superiority of DES to BMS in terms of TLR/TVR at 3-year follow-up (Table 2). However, a large-caliber subset of left main arteries could attenuate the benefit of restenosis reduction by DES. A recent randomized study that compared DES with BMS implanted in large coronary arteries demonstrated a significant reduction in TVR in the DES group without any significant difference in the rates of stent thrombosis, myocardial infarction (MI), and death. Although that study included a small number of ULMTD patients, the results suggested that PCI with DES might be superior to
BMS for large-vessel ULMTD patients.

Risk of DES: Stent Thrombosis, MI, and Death After BMS or DES Implantation

Stent thrombosis, especially VLST, has emerged as a major safety concern about stenting in current clinical practice. A meta-analysis that compared DES with BMS showed no difference in the rates of early and late stent thrombosis after DES or BMS implantation; however, it also showed a high incidence of VLST after DES implantation than BMS (Figure). Furthermore, the incidence of stent thrombosis kept increasing 0.2–0.6% per year. It could depend on indications and occur more frequently with off-label use than with on-label use. Although PCI for ULMTD patients is an off-label use of DES, the reported rate of stent thrombosis in a greater than 2-year follow-up after DES implantation was not so high (Table 3). Although the exact mechanism of a low incidence of stent thrombosis remains unclear, a larger coronary artery in ULMTD might contribute. Stent thrombosis is associated with MI and cardiac death after DES implantation, but no randomized or registry study has shown higher rates of MI and mortality in any subset including DES for ULMTD compared with BMS. At present, there is no evidence showing higher rates of MI and cardiac death after DES implantation for ULMTD compared with BMS.

Effect of Lesion Site

ULMTD lesions, except those with distal bifurcation, are associated with a high rate of procedural success, and favorable long-term outcomes with regard to death and repeated revascularization. In contrast, PCI for ULMTD bifurcation lesions is more technically challenging and has a higher risk of TVR. The impact on long-term outcomes, especially TLR, could be affected by stent type: DES or BMS. To analyze PCI for ULMTD, Kim et al evaluated the effect of stent type on 3-year outcomes after LMT stenting. Among all patients, the 3-year adjusted risk of TLR was significantly lower with the use of DES than BMS (5.4% vs. 12.1%; hazard ratio, 0.40; 95% confidence interval (CI) 0.22–0.73; P=0.003). When patients were classified by lesion location, DES was still associated with a lower risk of TLR in patients with bifurcation (6.9% vs. 16.3%; hazard ratio, 0.38; 95%CI 0.18–0.78; P=0.009) or non-bifurcation (3.4% vs. 10.3%; hazard ratio, 0.39; 95%CI 0.17–0.88; P=0.024). In their study, the adjusted risks of death and MI were not different in the overall and subgroup populations. In contrast, Tamburino et al reported different results. The adjusted 3-year rates of TLR were not significantly lower in the DES group than in the BMS group (11.4% vs. 10.7%; hazard ratio, 0.79; 95%CI 0.33–1.90; P=0.60). The adjusted hazard ratio for the risk of mortality after DES implantation was 0.37 (95%CI 0.15–0.96; P=0.04). The reason for this discrepancy in the TLR rates remains unclear; however, DES might be superior to BMS in both bifurcated and non-bifurcated lesions for major adverse cardiac events.

In distal LMT bifurcation, especially true bifurcation, a 2-stent strategy is sometimes necessary, even when single stenting is planned. The 2-stent technique does not have a long-term advantage in terms of the incidence of any MACE compared with single stent technique. Toyofuku et al reported that patients with stenting in both main and side branches had significantly higher rates of cardiac death (12.2% vs. 5.5%; P=0.02) and TLR (30.9% vs. 11.1%, P<0.0001) than those with main branch stenting alone in the j-Cypher registry. Their result suggested a limitation of treatment of bifurcation by 2-stent technique with sirolimus-eluting stents (SES), but there is a possibility that a specific 2-stent technique with other DES could obtain better long-term prognosis. Recently, the second-generation DES has shown its superiority to the first generation in the rates of TLR and stent thrombosis. Using second-generation DES may improve long-term outcomes after PCI for ULMTD bifurcation lesions. The EXCEL (Evaluation of XIENCE PRIMETM versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial is also being carried out to compare PCI with CABG among approximately 2,500 patients with ULMTD.

Duration of Dual Antiplatelet Therapy (DAPT)

DAPT after DES implantation is recommended for at least 1 year by the AHA/ACC guidelines. Recently, Park et al demonstrated in a randomized study that there was no benefit of DAPT after 1 year. Their data and a lower incidence of stent thrombosis after PCI with DES for ULMTD suggest that the optimal DAPT duration might be determined as at least 1 year. However, stent thrombosis in the LMT can have devastating consequences, so any measure to reduce its occurrence is important. Therefore, DAPT for longer than 1 year might be recommended as long as the patients has no bleeding complications. In contrast, DAPT after PCI with BMS implantation is recommended for at least 1 month. These different recommended periods of DAPT could have an effect on bleeding complications. In patients at high risk for bleeding or DAPT discontinuation, PCI with BMS or CABG could be recommended.
Other Concerns About DES

Pathological and clinical follow-up data have revealed some concerns about DES other than VLST. Late catch-up phenomenon and stent fracture have emerged as DES-specific events and they occur more commonly in DES than BMS. The incidence of each of these phenomena is relatively low and their clinical impact on PCI remains unclear, including for LMTD. Late catch-up phenomenon was initially an issue in brachytherapy, but now it is well known as a phenomenon after DES implantation. Nakagawa et al report that the incidence of late catch-up phenomenon is more common with off-label lesion treatment than in on-label lesions. There are some predictors of late catch-up phenomenon after SES implantation and use of 2 stents for bifurcation is 1; however, LMTD itself is not included. Therefore, careful long-term follow-up is important, especially for 2-stent PCI with SES for LMT bifurcation lesion. Stent fracture is reportedly related to restenosis and stent thrombosis in case reports or observational studies.

The common site of stent fracture is the right coronary artery, especially the ostium, saphenous vein graft, and severely tortuous lesions. Because the LMT lesion is not a common site of stent fracture, the effect of stent fracture on long-term outcomes of PCI for LMTD may be trivial.

Conclusions

Although having some limitations in indications, revascularization with DES for ULMTD, compared with BMS, is more strongly associated with a significant reduction in the need for re-revascularization without any additional adverse outcomes, such as stent thrombosis, MI, and cardiac death. In addition, the long-term prognosis could be acceptable.

References

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Author’s Comments on the BMS-Side Authors

Dr Kaneko et al raise concerns about the safety and efficacy of DES implantation by pointing out several findings such as late catch-up phenomenon, coronary artery aneurysm formation, and peri-stent contrast staining. The true incidences of these findings, especially after LMT stenting with DES, remain unclear. If they are very low, the efficacy of DES to reduce restenosis could outweigh concerns. The true incidence of these findings, especially after LMT stenting with DES, remain unclear. If they are very low, the efficacy of DES to reduce restenosis could outweigh concerns. Large-scale and long-term angiographic follow-up data may be necessary to investigate this issue further.

Dr Kaneko et al describe the limitation of bifurcation stenting with DES, especially when using the 2-stent strategy. Indeed, concerns remain about the safety and efficacy of the 2-stent strategy for true LMT bifurcation lesions. However, there are no data to confirm the superiority of LMT bifurcation stenting with BMS, especially of that using a 2-stent strategy, because it was rarely performed in the BMS era. Thus, when evaluating the initial and long-term results in patients with LMT bifurcation lesions, it is preferable to compare between DES implantation and CAGB rather than between DES and BMS. As we mentioned, the effect of specific stenting strategies such as modified T or culotte stenting and that of newer DES should be investigated.