Current State-of-the-art of Coronary Artery Bypass Surgery

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I. Introduction

Even though percutaneous coronary intervention (PCI) has been developed, coronary artery bypass surgery (CABG) is still an important treatment for patients with coronary artery disease. Recent large scale randomized control studies revealed that outcomes of CABG are still better than those for PCI among patients with severe coronary artery disease.1–3 According to an annual report by the Japanese Association for Thoracic Surgery, more than approximately 15,000 CABG procedures have been performed over the past few years in Japan.4–14 More than 60% of CABG procedures were performed off-pump (i.e., without cardiopulmonary bypass on the beating heart). Another feature of CABG performed in Japan is the frequent use of arterial grafts (multiple arterial grafts) when compared with CABG performed elsewhere. Today, over 20% of CABG procedures were conducted with only arterial grafts (all arterial graft). These points highlight the difference between CABG performed in Japan versus elsewhere. Unfortunately, almost all previously reported results of CABG from around the world were on-pump CABG with several saphenous vein grafts. Several reports regarding the advantages of CABG performed in Japan have been published,15–26 but evidence for the benefits of off-pump coronary artery bypass (OPCAB) with multiple arterial grafts is not yet sufficient. The aim of this review was to discuss and assess contemporary CABG performed in Japan.

II. Current role of coronary artery bypass surgery

Fig. 1 shows the trends in CABG in Japan from 2001 to 2011, based on the annual reports of the Japanese Association for Thoracic Surgery.4–14 The number of CABG procedures performed annually in Japan had reached more than 20,000 by the start of the 2000s. The number of CABG has since gradually decreased to 15,000 annually over the past decade. The largest reason for the reduction in the use of CABG is the development of PCI. Notably, introduction of PCI using drug-eluting stents has broadened the inductions for PCI. The drug-eluting stent “sirolimus-eluting stent” was first used in Japan in 2004. While the use of drug-eluting stents was expected to improved outcome after PCI due to reduction of intra-stent restenosis, the initial outcomes associated with drug-eluting stent fell short of expectations among patients with severe coronary artery disease.1–3,22

Recent trials in which drug-eluting stents were used also demonstrated that CABG had better rates of survival and event-free survival than percutaneous intervention among patients with severe coronary artery disease. The Synergy between Percutaneous Coronary Intervention (PCI) with TAXUS and Cardiac Surgery (SYNTAX) trial included 1,800 patients who were randomly assigned to undergo either CABG or percutaneous intervention with drug-eluting stents.3 The results of the 5-year SYNTAX trial showed that major adverse cardiac and cerebral events were significantly lower in the patients who underwent CABG than in the patients who underwent percutaneous intervention with drug-eluting stents (27% vs 37%). In the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, 1,900 patients with diabetes were randomly assigned to undergo either CABG or PCI with drug-eluting stents.2 After 5 years of follow-up, the patients who underwent CABG had significantly lower mortality (11% vs 16%) and fewer myocardial infarctions (6.0% vs 14%) than the patients who underwent PCI. These studies concluded that, even in the era of drug-eluting stents, CABG should be used for patients with complex coronary disease and/or patients with diabetes.

While the use of PCI has gradually increased, the general condition of CABG patients has been worsening.26 Not only is the surgical procedure itself becoming increasingly difficult, but so is perioperative management, including that of complications, such as impaired left ventricular function and systemic disease. Fig. 2 shows the trend in perioperative mortality during CABG from 2001 to 2011. Despite these harsh conditions, surgeons in Japan are striving to maintain favorable outcomes via the use of OPCAB and the frequent use of arterial grafts.

III. Current state of coronary artery bypass surgery in Japan

Fig. 1 shows the trends in CABG use and outcomes over the 10 years up to 2011 from an annual report by the Japanese As-
The number of isolated CABG surgeries peaked at 21,626 cases in 2002, after which it declined over the years to 15,581 cases in 2011. The reason for this decline is thought to be a decrease in the revascularization rate due to a greater indication and improved outcomes for PCI. The OPCAB rate hovered in the 60–69% range from the early 2000s, dropping to 58% in 2011. While the reason for this is unclear, it may be due to the increased number of patients with...
impaired left ventricular systolic function or severe coronary disease. Intriguing results were also obtained concerning the types of grafts used (Fig. 3). Over 50% of CABG performed in 2003 used arterial grafts for all bypasses (all-arterial graft). Since then, the use of all-arterial grafts has decreased annually, dropping to as low as 20% in 2011. The change was likely due to a decrease in the experimental use of arterial grafts and the increasing number of older patients who were more likely to have CABG with saphenous vein grafts. Another possible reason is the discovery of the excellent effects of 3-hydroxy-3-methyl-glutaryl-coenzyme (HMG-CoA) reductase inhibitor post-grafting in preventing arteriosclerosis of the coronary artery and lesions in SVGs. 27–30)

IV. Off-pump coronary artery bypass

OPCAB (i.e., CABG performed without cardiopulmonary bypass) was first used in the 1990s. OPCAB is less invasive than CABG and obviates the risk of adverse effects related to cardiopulmonary bypass, including physiological reactions and mechanical damage. The physiological effects of cardiopulmonary bypass include a systemic inflammatory response, hemorrhage, vascular hyperpermeability, and coagulation disorders. Mechanical damage related to cardiopulmonary bypass includes hemolysis due to artificial pump, hemodilution, organ ischemia, organ embolization, and aortic injury secondary to cannulation. Therefore, by avoiding cardiopulmonary bypass, OPCAB can reduce the complications of CABG.

Indeed, several studies reported that OPCAB was associated with decreased postoperative mortality and morbidity when compared with conventional CABG, 31–34) and another study indicated that the beneficial effect of off-pump CABG extended beyond patients who were at high risk for complications. 23, 35–37) A propensity analysis that enrolled 49,830 patients demonstrated that OPCAB was associated with lower in-hospital mortality and complications. 25) A meta-analysis assessed 35 studies with 123,127 patients and indicated that OPCAB was superior to on-pump CABG in terms of mortality and complications (including stroke, myocardial infarction, atrial fibrillation, renal failure, bleeding, and respiratory failure). 34) Several studies showed that OPCAB reduced the incidence of cerebroaphy, including cerebro infarction and neurocognitive disorders, when compared with conventional CABG. 38–42) Several studies demonstrated that OPCAB was associated with a decreased incidence of postoperative atrial fibrillation. 31, 43) A randomized control trial that compared OPCAB versus on-pump CABG enrolled 411 patients who were at high risk of operation (European System for Cardiac Operative Risk Evaluation score ≥6) demonstrated that OPCAB reduced early mortality and morbidity. 36) In addition to the off-pump strategy, the aorta no-touch technique, in which in situ arterial grafts are used for all grafts to avoid manipulation of the ascending aorta, has been shown to reduce the occurrence of stroke. 19, 44–47)

Meanwhile, several other studies suggested that OPCAB was not associated with reduction of postoperative complication. 46–53) For instance, the ongoing Coronary Artery Bypass Grafting Surgery Off- or On-pump Revascularization Study (CORONARY) trial enrolled 4752 patients and hypothesizes that OPCAB is better than CABG in terms of short-term and long-term outcomes. The first report from the CORONARY trial showed that 30-day composite endpoint did not significantly differ between OPCAB and on-pump CABG (9.8% vs 10%). 54) The second report from the CORONARY trial showed that 1-year composite endpoint
(all-cause death, stroke, myocardial infarction, re novo renal failure, repeat revascularization, and neurocognitive function) was also similar between the two groups (12% vs 13%). Therefore, OPCAB remains controversial on a global level, and the only consensus reached has been that OPCAB is beneficial for high-risk patients.

However, there are no data showing the inferiority of OPCAB when compared with on-pump CABG with regard to short-term outcomes. Hence, the primary purpose of OPCAB is to avoid perioperative complications by avoiding the use of cardiopulmonary bypass.

On-pump cardiac arrest CABG can achieve coronary anastomosis in the still heart and in bloodless fields. By contrast, OPCAB can be used to perform coronary anastomoses on the beating heart in bleeding fields. Thus, OPCAB requires more skill and should be performed only by expert surgeons.

Several recent studies compared OPCAB and conventional CABG and failed to demonstrate the advantages of OPCAB with regard to long-term outcomes. The Veterans Affairs Randomized On/Off Bypass Study (ROOBY) trial included 2203 patients who were randomly assigned to CABG or OPCAB. The 30-day complication after CABG was similar between the OPCAB and CABG groups (5.6% vs 7.0%). On the other hand, the rate of the 1-year composite endpoint (all-cause death, myocardial infarction, re-novo renal failure, repeat revascularization, and neurocognitive function) was also similar between the two groups (12% vs 13%). Therefore, OPCAB remains controversial on a global level, and the only consensus reached has been that OPCAB is beneficial for high-risk patients.

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These findings suggest that OPCAB is not aimed at every surgeon, but aimed only at selected surgeons who can perform OPCAB in the same outcome as on-pump CABG in most cases. If surgeons who cannot perform OPCAB and on-pump CABG observed the same results, surgeons should perform CABG with cardiopulmonary bypass. In Japan, where 60% of CABG surgeries are OPCAB, it appears that the same quality is being achieved with OPCAB as with on-pump CABG. In other countries, OPCAB is considered a palliative coronary revascularization procedure based on the results of clinical trials, and is only performed for high-risk patients for whom the efficacy of OPCAB has been proven. If the same quality can be achieved with OPCAB and on-pump CABG, as is the case in Japan, OPCAB, which is the optimal treatment for high-risk patients, may also be expected to be a better treatment option for low-risk patients. In Japan, OPCAB has become well-established as the radical coronary revascularization treatment, because surgeons have passed through the learning curve for attaining a high proficiency and have improved the quality of OPCAB surgeries by performing high-quality coronary revascularization by OPCAB, even in low-risk patients. Unfortunately, it is difficult to perform prospective studies comparing OPCAB and on-pump CABG in Japan today, and as a result, OPCAB outcomes in Japan cannot be examined adequately.

V. Multiple arterial grafts

Long-term graft patency determines long-term outcomes of CABG. In the 1960s (at the start of CABG use), most grafts were SVGs. Later, in the 1970s, ITA grafts became recognized as the gold standard for revascularization of the left anterior descending artery, and the CABG practice of using a single ITA in combination with the SVG became well-established. This remains the main style in other countries. The reason why multiple arterial grafts have not become a popular choice is that arterial graft harvesting prolongs the operation time. In contrast, saphenous vein graft (SVG) can be harvested in a short period of time, is used instead. However, SVGs have a low long-term patency rate and are inferior to arterial grafts. Indeed, several studies showed all arterial grafts is associated with better long-term survival compared with a single ITA with SVGs. Hence, multiple arterial grafts should be encouraged in patients with a good life expectancy.

In the half-century history of CABG procedures, various other graft materials have been used, with some making it to clinical practice and some having disappeared. The types of graft materials in use today are the ITA, the right gastroepiploic artery (GEA), the radial artery, and the SVG. Grafting methods include in situ grafting that directly uses anatomical inflow, free grafts with an inflow site created through anastomosis between the coronary artery and the ascending aorta, and composite grafts receiving a blood supply via anastomosis with other grafts. The design of graft used is based on the anatomy of the coronary artery, the condition of the ascending aorta and the availability of...
each graft. Our routine method of arterial graft harvesting is full skeletonization by the use of an ultrasonic scalpel. With any method, carefully inspecting the condition of the graft material to determine feasibility is the key to long-term patency.

1. Internal thoracic artery

Left internal thoracic artery (LITA) grafts are high-quality grafts with an extremely low arteriosclerosis rate of less than 1%. The ITA has several excellent properties as a coronary artery graft. First, it can be used as an in situ graft to the left coronary system. Second, its histological and vasophysiological properties, including a thin smooth muscle layer, abounding elastic fibers, and nitric oxide production, are relatively protective against progression of atherosclerosis and thereby result in excellent graft patency. Kitamura hypothesized that preservation of endothelium from the ITAs to the native coronary arteries results in restoration of otherwise compromised coronary endothelial function, especially in patients with diabetes, advanced age, or multivessel disease.

Right internal thoracic artery (RITA) grafts are used in combination with LITA grafts, as bilateral internal thoracic artery (BITA) grafts, and BITA grafts have been shown to result in a better prognosis than single internal thoracic artery (SITA) grafts. Most of those studies were retrospective, and there is a bias in that BITA grafts tend to be performed on younger and low-risk patients. A randomized clinical trial comparing the long-term follow-up results of SITA and BITA grafts is currently in progress (the Arterial Revascularisation Trial) and the results are eagerly awaited. There was a tendency to avoid using BITA grafts in diabetic patients, as they are associated with a higher risk of developing a deep sternal infection in such patients. However, we have shown in a meta-analysis that no such risk exists when skeletonized harvests are performed and that BITA grafts result in lower long-term postoperative all-cause and cardiac mortality rates in diabetic patients when compared with SITA grafts.

Despite these advantages of BITA, BITA is used infrequently in countries other than Japan. In fact, the usage rate of BITA in the United States is only about 4%. The superiority of BITA grafts for diabetic patients with severe coronary disease suggests that they may gain favor around the world as the leading graft design.

LITA is principally performed by isolated anastomosis to the left anterior descending (LAD) artery but may also be performed by sequential anastomosis if there is advanced stenosis or occlusion between the LAD and the diagonal branch. RITA grafts are usually performed by in situ grafting through the transverse pericardial sinus or in the left circumflex branch region as a Y-composite graft with LITA grafts. BITA grafts are generally used when there are multiple sites requiring anastomosis on the left coronary artery.

2. Radial artery

The radial artery and gastroepiploic artery are the most commonly used arterial grafts after the ITA. Even though they are all muscular arteries, the ITA is more similar in properties to an elastic artery and is resistant to arteriosclerosis and spasms. However, radial artery and gastroepiploic artery grafts are likely to cause arteriosclerosis and spasms, which are complications characteristic to muscular arteries. Histologically, the radial artery also differs from the ITA in that it has a thicker media comprised of smooth muscle. While the radial artery has an arteriosclerosis rate of about 6%, which is higher than that of the ITA, it also has excellent properties as CABG graft material. The radial artery offers a wide selection of graft lengths and inflow sites, enabling extensive revascularization. Nevertheless, the radial artery has considerable individual variability as a graft material and is not a viable option for patients with a history of degeneration from arteriosclerosis or punctures, early postoperative spasms, or renal dysfunction.

A number of studies have investigated the patency rate of radial artery grafts, and the results vary. A meta-analysis of five studies showed no remarkable superiority of radial artery grafts over SVGs, due to string phenomenon that occurs with the former. In contrast, the recent randomized controlled Radial Artery Versus Saphenous Vein Patency (RSVP) trial found a higher patency rate with radial arteries when compared to SVGs over 5 years of follow-up. Such variability of the results is of course thought to be dependent on the level of expertise of the surgeon harvesting the graft. Empirically speaking, a high-quality radial artery graft harvested using skilled techniques may be expected to have the same patency rate as an ITA graft.

3. Gastroepiploic artery

As with radial artery grafts, gastroepiploic artery (GEA) grafts are also arterial grafts with a media comprised of smooth muscle that is thicker than that of ITA grafts. While offering superior long-term outcomes to SVGs, there is considerable individual variability in characteristics, and arteriosclerosis is sometimes a problem. Although denervation by performing a skeletonized harvest has been experimentally shown to suppress spasms, tonus is also increased when compared with ITA grafts.

When using the GEA for in situ grafts, the anatomic target is the right coronary artery or the distal the circumflex branch. If there is excessive native flow in the coronary artery, the string phenomenon may occur due to flow competition. The SVG, which has a large graft diameter, should therefore be used if stenosis of the native coronary is mild.

4. Saphenous vein

The great saphenous vein is the oldest type of graft material but has a poor patency rate when compared with arterial
grafts. Unlike arterial grafts, this vein has a thin intima comprised of sparse endothelial cells and has a media and adventitia comprised of thin elastic fibers and smooth muscle. Grafts of the great saphenous vein are both histologically and vaso-physiologically inferior to arterial grafts. That said, there are also many benefits of these grafts, such as a large blood vessel diameter and the fact that harvest can be commenced at the start of surgery, and they are thus used frequently. From the view of graft length, coronary arteries in almost any area can be a target, but unfavorable results have often been reported for composite grafts with arterial grafts, and so they are mostly used as a material for aorta-coronary bypasses.

VI. Execution of OPCAB

With the development of suction stabilizers and other devices, the OPCAB has become a standard procedure that can be performed more safely. The following is a description of the OPCAB method that we use at Juntendo. The arterial grafts are covered with warm papaverine hydrochloride gauze, and spasms are released with olprinone injections. The left side pericardium retracted sutures and two deep pericardial sutures are placed to position the apex towards the ceiling. These procedures and a suction stabilizer enable us to approach any region. For anastomosis of the circumflex branch or right coronary artery, the operative field is widened, and hemodynamics are stabilized with a head down, right rotation. A suction stabilizer is used to fix the coronary artery site for anastomosis in place, and the coronary artery is exposed. An incision is made in the coronary artery, and the proximal side is snared with an elastic string to create a bloodless operative field. Internal shunt tubes are used if there is excessive coronary blood flow and if hemorrhage or myocardial ischemia is a concern. Carbon dioxide (which is water-soluble and not prone to causing embolisms) is blown on with a CO2 blower to locally disperse blood and to achieve a bloodless operative field. Internal shunt tubes are used if there is excessive coronary blood flow and if hemorrhage or myocardial ischemia is a concern. Carbon dioxide (which is water-soluble and not prone to causing embolisms) is blown on with a CO2 blower to locally disperse blood and to achieve a bloodless operative field. Internal shunt tubes are used if there is excessive coronary blood flow and if hemorrhage or myocardial ischemia is a concern. Carbon dioxide (which is water-soluble and not prone to causing embolisms) is blown on with a CO2 blower to locally disperse blood and to achieve a bloodless operative field. 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VII. Conclusions

We discussed the latest findings on CABG and the current state of CABG in Japan. Although CABG is becoming less popular due to broader indications for PCI, it remains an important treatment for coronary artery disease. Especially in Japan, OPCAB can reduce the invasiveness and complications associated with CABG surgeries, and favorable long-term outcomes can be achieved with multiple arterial grafts. Although there is unfortunately a lack of studies demonstrating the excellent outcomes of CABG in Japan at present, it is our role and responsibility to maintain the excellent results of CABG in Japan and share those results with the world.

VIII. Acknowledgments

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References

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