Off-Pump Coronary Artery Bypass Grafting Revisited: Experience and Evidence from Japan

Hitoshi Yaku, MD, PhD, Kiyoshi Doi, MD, PhD, and Kazunari Okawa, MD, PhD

Off-pump coronary artery bypass grafting (OPCAB) is performed in about 65% of patients who require surgical coronary revascularization, and has become the standard procedure in coronary artery bypass grafting (CABG) in Japan. As a background of the high rate of OPCAB, many clinical and experimental studies have been performed and reported in Japan. In this review, several factors associated with OPCAB are discussed based on relevant and important clinical studies published in Japan in the English language.

Keywords: off-pump coronary artery bypass grafting, ischemic heart disease, perioperative complication, surgical results

Introduction

Off-pump coronary artery bypass surgery (OPCAB) emerged in the mid-1980s and has since become increasingly popular worldwide. In Japan, OPCAB was first performed in 1996 and has become the standard management strategy for surgical coronary revascularization. Since then, the ratio of OPCAB in coronary artery bypass grafting (CABG) has been increasing and especially since 2000, the annual rate is over 60%. Several studies have reported the effects and drawbacks of OPCAB and have compared OPCAB with conventional CABG. To evaluate the effects of OPCAB in the Japanese population and to devise a suitable surgical strategy, it would be ideal to refer to clinical studies specific to Japan. In fact, several studies have been reported in Japan, although most of them are retrospective and single-institution studies. In this review, several factors associated with OPCAB are discussed based on relevant and important clinical studies published in Japan in the English language.

All values are presented as mean ± SD except where otherwise noted.

Harvesting of the Conduits

To obtain high patency rates and good long-term outcomes, the quality of grafts is critical in both OPCAB and conventional CABG. Higami, et al. reported a unique method of harvesting the internal thoracic artery (ITA) by using a harmonic scalpel. With the harmonic scalpel, the ITA can be skeletonized safely and efficiently by the “quick touch method” to remove fat tissue surrounding the ITA and by protein coagulation to divide the branches from the ITA. A longer ITA could be obtained by skeletonization rather than by a pedicle technique. They also showed excellent early (<30 days) patency of grafts (99.7% for the left ITA and 100% for the right ITA).

Asai, et al. reported a method for harvesting the right...
gastroepiploic artery, also by using a harmonic scalpel. They reported that the technique was safe and simple, and that they could not only harvest the artery faster but also obtain large spasm-free arterial conduits.

**Devices Facilitating OPCAB**

A few useful devices have been developed to obtain a stable surgical view, without any ischemic insult of the myocardium in OPCAB. Arai, et al.\(^9\) developed a new heart positioner called TENTACLES™, which comprises 3 silicone tubes and a suction cup. The suction cup can be applied anywhere on the surface of the heart; subsequently, the heart can be rotated without a significant drop in blood pressure.

Kamiya, et al.\(^10\) developed a synchronized arterial-flow ensuring system to perform coronary anastomosis safely, without ischemia, in OPCAB. Arterial blood from the femoral artery is perfused into the coronary artery in the pulsatile mode regulated by the pump controller with synchronization during the diastolic period. They reported that, in 524 consecutive patients in whom this pump system was applied, there were no intraoperative fatal arrhythmias, ventricular arrhythmias or short runs of ventricular tachycardia, or hemodynamic deterioration during anastomoses.

**Proximal Anastomosis Devices**

For avoiding complications related to aortic manipulation, several devices were developed to perform a clampless anastomosis. However, only a few studies report the late patency of grafts constructed using these devices. Shimokawa, et al.\(^11\) investigated the early and 1-year patency rate of saphenous vein grafts constructed using an anastomosis device in patients undergoing OPCAB. They studied 232 patients who had undergone OPCAB using saphenous vein grafts and had received follow-up angiography. For proximal anastomosis, a clampless device was used in 73 patients (HEART-STRING in 54; Enclose II in 19), and a partial clamping was performed in 159 patients. The overall patency rates of saphenous vein grafts at the early and 1-year postoperative angiography were 95.7% and 83.0%, respectively. The patency rates were similar between the clampless and partial clamping groups (early: 97.3% vs. 98.1%, \(p = 0.729\); 1 year: 87.0% vs. 81.3%, \(p = 0.316\)). Moreover, no significant difference was found in the target vessel revascularization rate during the follow-up examination (6.8% vs. 10.1%, \(p = 0.623\)).

Fujii, et al.\(^12\) evaluated 39 grafts constructed using the PAS-Port in 28 patients who underwent OPCAB. Early postoperative angiography showed no bending or stenosis in any graft, and a patency rate of 100%. Kai, et al.\(^13\) reported mid-term patency rate of saphenous vein grafts using the PAS-Port. Among 66 patients who had saphenous vein grafts, 46 patients survived at least 1 year after surgery, and 38 patients consented to late follow-up graft evaluation by means of 3-dimensional computed tomography. Two of 39 devices were occluded, and the 1-year patency rate (FitzGibbon grade A) was 94.9%. No obvious stenosis of saphenous vein grafts was observed. Twenty-four patients underwent 2-year graft evaluation. The 2-year cumulative patency rate was 91.7%.

**Awake OPCAB**

Watanabe, et al.\(^14\) reported awake subxiphoid CABG in 3 patients with severe pulmonary dysfunction. A catheter for high thoracic epidural anesthesia was inserted 1 day before surgery, and under the appropriate amount of epidural anesthesia, the right gastroepiploic artery was harvested through a small subxiphoid incision, and the artery was anastomosed to the left anterior descending artery (LAD). They further reported the results of awake OPCAB in 72 patients and compared them with matched patients under general anesthesia.\(^15\) Fifteen percent of the awake patients were able to leave the operating room in a wheelchair. The time taken to drink water and to walk and the duration of hospital stay were reported to be significantly shorter in the awake OPCAB group than in the general anesthesia group. There were no operative or postoperative complications or deaths.

**Revascularization Technique for Diffuse Coronary Lesions**

Fukui, et al.\(^16\) developed a long-onlay patch method using the left ITA for the diffusely diseased LAD. Endarterectomy is warranted depending on the severity of coronary atherosclerosis. In their study, preoperative angiography revealed the diffusely diseased LAD. The patient graft could be seen early postoperatively, but the reconstructed LAD was dilated and had an irregular wall. Interestingly, after 1 year, the LAD was reversely remodeled and the border of the graft and native coronary artery was hardly visible. Event-free survival for patients undergoing this technique was excellent at 3 years.\(^17\)
Intraoperative Management

Occasionally, because of hemodynamic instability or arrhythmia due to displacement of the heart without cardiopulmonary bypass, OPCAB has to be converted to on-pump CABG. According to the annual report of the Japanese Association for Coronary Surgery, operative mortality and incidence of stroke were significantly higher in patients converted intraoperatively from OPCAB to on-pump CABG than in patients in whom OPCAB or on-pump CABG treatment was planned and executed accordingly. Shiga, et al. studied the financial implications of intraoperative conversion and its effect on the quality of life. They used a decision-analysis model and Monte Carlo simulation and showed that OPCAB is dominant (less costly and more effective) when the conversion rate from OPCAB to on-pump CABG is below 8.5%, whereas, costs increase exponentially if the probability of conversion exceeds 15%.

Mitral regurgitation (MR) during OPCAB is a very important issue which may cause deterioration of hemodynamics and lead to conversion on-pump CABG. In an experimental study, Koga, et al. showed that cardiac displacement alone did not cause MR when coronary perfusion was maintained, and occlusion of the LAD rarely caused MR; however, occlusion of the left circumflex artery (LCx) caused MR from the posteromedial site. In a clinical study, Akazawa, et al. reported the relationship between left ventricular function and the severity of MR during OPCAB. MR was the most severe during anastomosis of the LCx, and 39% of the patients had moderate to severe MR during anastomosis of the LCx. Significant differences were found in preoperative serum brain natriuretic peptide (BNP) levels, the Tei index values, and the mitral inflow propagation velocity between patients who developed moderate to severe MR and patients who had no to mild MR during anastomosis of the LCx.

In an experimental study, Wakamatsu, et al. showed the effects of an ultra-short-acting selective β-1 blocker (landiolol) on the motion of the LAD using 3D digital motion capture and reconstruction technology. Landiolol (0.12 μg · kg⁻¹ · min⁻¹) significantly decreased heart rate, the 3D distance moved, acceleration, and deceleration, without inducing a significant change in the systolic blood pressure, cardiac output, or pulmonary wedge pressure. This study showed the possible application of landiolol as a chemical stabilizer during OPCAB.

Pathophysiology During OPCAB

Moriyama, et al. sought to verify the hypothesis that amino acid infusions stimulate the release of metabolic hormones during surgery and increase energy expenditure, resulting in thermogenesis. Twenty-four patients were randomly assigned to 2 groups and received amino acid (4 kJ · kg⁻¹ · hour⁻¹) or saline treatment, which was infused for 2 hours during OPCAB. Amino acid infusion significantly increased core body temperature and oxygen consumption during OPCAB. Given the release of insulin and leptin in response to amino acid infusion, these hormonal signaling pathways may have partly contributed to the thermogenic response occurring during OPCAB.

Mitaka, et al. studied nitric oxide (NO) production in OPCAB and on-pump CABG. In their study 116 patients undergoing elective CABG with (n = 66) and without cardiopulmonary bypass (n = 50) were enrolled. Urinary nitrate/nitrite (NOx) excretion was measured as an index of endogenous NO production during the 2 days after an operation. There was no significant difference in urinary NOx/creatinine (Cr) excretion on the first day. The mean urinary NOx/Cr excretion ratio significantly decreased (p < 0.01) from the first day to the second day in the on-pump CABG group, but not in the OPCAB group. The mean urinary NOx/Cr excretion ratio was significantly higher (p < 0.01) in the OPCAB group than in the on-pump CABG group (0.51 ± 0.26 vs. 0.38 ± 0.20, p < 0.01). The mean serum C-reactive protein (CRP) concentration was also significantly higher (p < 0.01) in OPCAB group than in the on-pump CABG group on the second day. No significant difference was observed in the mean cardiac index or the mean systemic vascular resistance index between the 2 groups after an operation. They concluded that endogenous NO production is stimulated by a surgical inflammatory response and that cardiopulmonary-bypass does not trigger NO production in patients undergoing CABG.

Miura, et al. tested the hypothesis that intraoperative hemodynamic compromise during OPCAB due to cardiac displacement is associated with jugular bulb desaturation which is associated with specific hemodynamic and physiological changes. Jugular bulb desaturation (≤50%) frequently occurred during surgical displacement of the heart. Multivariate logistic regression analysis demonstrated that mixed venous oxygen saturation (Svo2) ≤70%, arterial partial pressure of carbon dioxide (Paco2) ≤40 mmHg, and central venous pressure (CVP) ≥8 mmHg were likely predictors of the occurrence.
of jugular bulb desaturation. They suggested that cerebral desaturation during OPCAB could be prevented by achieving normal values of \( S_{\text{VO2}} \), \( P_{\text{aCO2}} \), and CVP.

**Intraoperative Graft Evaluation**

Suma, et al.\(^{26}\) demonstrated a thermal coronary artery imaging procedure, using a new-generation infrared camera for evaluation of grafts intraoperatively, in 12 patients undergoing OPCAB. All grafts were clearly visualized, and the anastomosis and flow status could be observed using by local epicardial cooling using a CO\(_2\) blower on the normothermic heart. Among 17 grafts, 1 ITA graft showed anastomotic failure and was successfully revised. The results of postoperative coronary angiography confirmed patency of all the grafts.

Takahashi, et al.\(^{27}\) showed the importance of graft evaluation during the operation using the SPY system, which is an imaging system based on the fluorescence of indocyanine green dye. They obtained high-quality images of all 290 grafts in 72 OPCAB patients. They successfully revised 4 anastomosis which had failed according to the SPY system.

**Surgical Results of OPCAB Compared to On-Pump CABG**

The surgical results of OPCAB were compared with those of conventional CABG and published for the first time by Ishida, et al.\(^{28}\) This retrospective study showed that the operating time, ICU stay, and ventilation time were statistically significantly shorter in the OPCAB group than those in the conventional CABG group. The postoperative blood loss within 12 h and the transfusion volume were statistically significantly smaller in the OPCAB group. Peak serum blood urea nitrogen and creatinine concentrations were lower in the OPCAB group. Notably, there were no perioperative strokes in the OPCAB group, whereas 6.4% of the patients in the conventional group suffered a stroke. There was no significant difference in graft patency between the two groups (95.6% vs. 94.9%).

Kobayashi, et al.\(^{29}\) reported the surgical results of a prospective randomized controlled trial comparing OPCAB to on-pump CABG. In this study, 167 consecutive patients were randomly assigned to multiple arterial OPCAB and on-pump CABG groups. The number of grafts per patient and the number of arterial grafts performed per patient were similar. Completeness of revascularization was 98% in both groups. The incidence of intraoperative and postoperative complications was comparable. The OPCAB group comprised a larger number of patients without blood transfusion. The postoperative levels of S-100 protein and neuron-specific enolase were lower in the OPCAB group. The maximum CKMB level was less in the OPCAB group. As for graft patency rates, the total patency rate was 98% in both groups, and the stenosis-free patency rate was 93% in the OPCAB and 96% in the on-pump group, which was not significantly different. They concluded that OPCAB with multiple arterial grafts was as safe as conventional CABG, with similar completeness of revascularization and early graft patency.

**Diabetes Mellitus (DM)**

Tsuruta, et al.\(^{30}\) reported the impact of preoperative HbA1c levels in diabetic patients on long-term outcomes after OPCAB. They divided 893 patients who underwent primary isolated OPCAB into 3 groups based on the preoperative HbA1c levels (HbA1c <6.5%, 6.5% ≤HbA1c <7.5%, HbA1c ≥7.5%). No operative or in-hospital mortality occurred. All-cause mortality and cardiac mortality rates were 6.2% (19 patients) and 1.3% (4 patients), respectively during the mean follow-up period of 3.6 ± 1.7 years. Kaplan–Meier’s survival curve showed no significant differences in all-cause or cardiac mortality (log-rank test, \( p = 0.26 \), \( p = 0.17 \), respectively).

Kai, et al.\(^{31}\) retrospectively studied the effects of OPCAB by skeletonized bilateral ITAs in patients with insulin-dependent DM. Surgical outcomes were compared to those of on-pump CABG by pedicled bilateral ITAs. No 30-day mortality occurred in either group. The incidence of deep sternal infection was significantly lower in the OPCAB group than in the on-pump CABG group (0.6% vs. 13.0%; \( p = 0.01 \)). The early angiographic results did not differ between the 2 groups. During the follow-up period of 3.4 years (0.1 years–9.9 years), there were no differences between the 2 groups in survival, freedom from cardiac mortality, and freedom from cardiac-related events. Dialysis, peripheral vascular disease, ejection fraction less than 0.40, and age were independent risk factors of late death.

Fuji, et al.\(^{32}\) reported the usefulness of perioperative blood glucose control in patients undergoing OPCAB. For achieving a preoperative fasting blood glucose level of 140 mg/dl and a postoperative level of 200 mg/dl, DM patients were aggressively treated with intensive insulin
therapy. They compared DM patients with non-DM patients, and found that the amount of insulin used during surgery was greater, the duration of intensive care unit (ICU) stay was longer, and the incidence of all complications was higher in patients with DM. When they compared patients with mean blood glucose level <200 mg/dl in the ICU with those with mean blood glucose level ≥200 mg/dl, the proportion of patients with DM was higher, duration of ICU stay was longer, and the incidence of all complications was higher in patients with mean glucose level ≥200 mg/dl.

**Perioperative Stroke**

Nishiyama, et al.\(^{33}\) investigated the temporal pattern of strokes after on-pump CABG and OPCAB. They analyzed 2,516 consecutive patients who underwent primary elective isolated CABG. The primary end point was stroke. The temporal onset of the deficits was classified as "early stroke" or "delayed stroke". An early stroke was defined as a stroke presenting just after emergence from anesthesia, and a delayed stroke as a stroke presenting after awakening from surgery without a neurologic deficit. In the study population, 63% of strokes were delayed strokes. Patients undergoing OPCAB had a significantly lower risk of early stroke (0.1% vs. 1.1%, \(p = 0.0009\)), whereas the incidence of delayed strokes was not significantly different (0.9% vs. 1.4%, \(p = 0.3484\)) between patients undergoing OPCAB and on-pump CABG. Multivariate analyses revealed that undergoing OPCAB was an independent protective factor for all strokes (relative risk 0.29, 95% confidence interval: 0.14–0.56, \(p = 0.0005\)) and early strokes (relative risk 0.05, 95% confidence interval: 0.003–0.24, \(p < 0.0001\)); however, it was not an independent protective factor for delayed strokes (relative risk 0.54, 95% confidence interval: 0.24–1.17, \(p = 0.1210\)).

Doi and Yaku showed the importance of preoperative evaluation of intracranial and neck vessels for estimating patient prognosis in terms of stroke.\(^{34}\) In that study, the patients were divided into 2 groups: low-risk group and high-risk group, based on the findings of MRI and carotid Doppler imaging. There was no intraoperative stroke in both groups. The high-risk group had a higher incidence of delayed stroke and stroke even after 1 month. Univariate analysis revealed that the high-risk group is the only predictor of delayed stroke. Moreover, the high-risk group had a significantly lower freedom from stroke in the long-term.

Miyazaki, et al.\(^{35}\) studied risk factors of stroke/transient ischemic attack (TIA) and delirium after OPCAB. The medical records of patients (\(n = 685\)) who underwent OPCAB were reviewed. The incidences of postoperative stroke/TIA and delirium after OPCAB were 2.6% (\(n = 18\)) and 16.4% (\(n = 112\)), respectively. Carotid artery stenosis >50% was a significant risk factor of stroke or TIA (\(p = 0.02\)) as well as delirium (\(p = 0.04\)) after OPCAB. A history of atrial fibrillation (\(p = 0.037\)) and DM (\(p = 0.041\)) were risk factors of postoperative stroke/TIA. In contrast, age >75 years (\(p = 0.006\)), serum Cr >1.3 mg/dl (\(p = 0.011\)), history of hypertension (\(p = 0.001\)), history of atrial fibrillation (\(p = 0.024\)), and smoking (\(p = 0.048\)) were significant risk factors of postoperative delirium.

Contrary to these studies, Manabe, et al.\(^{36}\) reported that the impact of carotid artery stenosis on the incidence of perioperative stroke may be little in OPCAB. They conducted a retrospective study of 461 patients who underwent elective OPCAB after screening for carotid artery stenosis. The screening detected significant carotid artery stenosis in 49 patients. There was neither stroke nor in-hospital mortality in patients with carotid stenosis, although there were 2 strokes (0.49%) and 3 in-hospital mortalities (0.73%) in patients without carotid stenosis.

Osawa, et al.\(^{37}\) studied the incidence of stroke in relation to surgical manipulation of the ascending aorta adopted by them. Two patients of 451 patients (0.47%) who underwent OPCAB using the aortic nonclamping technique developed delayed strokes, whereas 1 in 9 patients who underwent OPCAB with aortic partial clamping for proximal anastomosis had an early stroke. They concluded that the aortic nonclamping technique might reduce the incidence of stroke. Kobayashi, et al.\(^{38}\) also reported that there was no operative death or stroke by using an aorta no-touch technique with in-situ graft and composite and sequential grafting methods.

**Perioperative Neuropsychological Dysfunction**

Baba, et al.\(^{39}\) conducted a prospective study in 218 patients who underwent elective OPCAB (\(n = 89\)) or on-pump CABG (\(n = 129\)). Four cognitive tests were performed preoperatively and at 1 week postoperatively. Neuropsychological dysfunction was defined as a decrease in an individual’s performance in more than 2 tests of at least 20% from baseline. The incidence of
neuropsychological dysfunction was 11.2% in the OPCAB group and 22.5% in the on-pump group (p = 0.02). Multivariate analysis revealed that neuropsychological dysfunction was associated with cardiopulmonary bypass and multiple cerebral infarctions.

**Perioperative Renal Dysfunction**

Ogawa, et al.\(^4\) studied the association between renal dysfunction and OPCAB. Patients undergoing OPCAB were divided into 3 groups depending on the preoperative serum Cr levels: normal, moderately depressed, and severely depressed.\(^4\) The severely depressed group had more patients with postoperative Cr levels more >1.6 times the preoperative levels. The predictors of postoperative renal impairment were preoperative Cr >2.5 mg/dl, ejection fraction <40%, amount of blood transfusion, and >4 grafts.

Kinoshita, et al.\(^4\) divided patients undergoing OPCAB into 3 groups based on preoperative glomerular filtration rate (GFR): <30 ml/min/1.73 m\(^2\), 30–60 ml/min/1.73 m\(^2\), >60 ml/min/1.73m\(^2\), and reported that long-term survival and freedom from cardiac death depended on preoperative renal function as indicated by GFR, but non-cardiac death did not depend on preoperative renal function.

Hayashida, et al.\(^4\) compared postoperative renal function of 52 OPCAB patients to that of 53 matched patients undergoing conventional CABG. The OPCAB group showed a significantly smaller increase in Cr levels than did the conventional CABG group (0.16 ± 0.05 vs. 0.45 ± 0.06 mg/dl).

**Hemodialysis**

Oyamada, et al.\(^4\) investigated the preoperative risk factors of performing OPCAB in patients on chronic dialysis. Forty-one patients on chronic dialysis who underwent OPCAB were retrospectively reviewed. Of these, 29 had diabetic nephropathy (DN group) and the remaining 12 did not (NDN group). There was a significant difference between the 2 groups in the duration of dialysis before surgery (4.2 years ± 5.5 years in DN vs. 9.1 years ± 7.5 years in NDN, p = 0.028). Low cardiac output (LVEF <30%) was found only in the DN group (7/29, p = 0.048). The early mortality was 6.9% (2/29) in the DN group and 16.7% (2/12) in the NDN group (p = 0.349). The actuarial survival rates in the DN group were 85% at 1 year, 45% at 3 years, and 30% at 5 years, whereas in the NDN group, they were 71%, 49%, and 49%, respectively (p = 0.789). For patients on chronic dialysis, arteriosclerosis and age (>65 years) were the predicted risk factors for OPCAB; however, diabetic nephropathy was not.

**Left Main Disease (LMD)**

Stenosis in the left main trunk has historically been recognized as a risk factor for patients undergoing CABG. To analyze the effects of OPCAB in patients with significant stenosis in the left main trunk.

Suzuki, et al.\(^4\) reviewed 268 patients with significant LMD among 665 patients who underwent OPCAB, and compared them with 237 propensity score-matched patients without LMD. Operative mortality rates were 0.8% in the LMD group and 1.7% in the non-LMD group. The 6-year freedoms from all-cause death were 87.3% in the LMD group and 60.7% in the non-LMD group (p = 0.17), and the 6-year freedoms from cardiac events were 80.4% in the LMD group and 70.4% in the non-LMD group (p = 0.98). They concluded that LMD did not significantly affect OPCAB outcomes in either the short- or long-term.

Fukui, et al.\(^4\) retrospectively reviewed 768 patients who underwent OPCAB using bilateral ITAs. Among them, 268 patients had LMD and 500 patients did not. Operative mortality and the incidence of complications were not significantly different between the 2 groups. In patients without LMD, the left and right ITAs were used for the LAD in 87.4% and 12.2% of patients, respectively, whereas in patients with LMD, the left and right ITAs were used for the LAD in 70.5% and 29.1%, respectively. In patients without LMD, the 1-year patency rate of the left and right ITAs were 97.6% and 91.6%, respectively, whereas in patients with LMD, they were 97.0% and 93.2%, respectively. The patency rates of the left and right ITAs did not differ significantly in patients with or without LMD (p = 0.9803 and p = 0.7205 in the left and right ITAs, respectively).

**Previous Percutaneous Coronary Intervention (PCI)**

Previous PCI was reported to have an adverse impact on the surgical outcomes of CABG, and this impact has been investigated in a few studies.\(^4\)

Fukui, et al.\(^4\) retrospectively reviewed 545 patients who underwent first-time isolated OPCAB. Among them, 154 had previous PCIs, including 99 patients with stents.
The number of anastomosis per patient was lower in PCI patients than in non-PCI patients (3.8 vs. 4.2; p = 0.0066). Operative mortality did not differ between these groups (0% vs. 1.8%; p = 0.1995), neither did the major morbidity rates. Similar results were obtained for the comparison between patients with stents and those without stents. No significant difference was observed in the graft patency rates between PCI patients and non-PCI patients (97.1% vs. 97.9%; p = 0.4976).

Kinoshita, et al.48 compared patients with previous PCI with those without PCI after OPCAB. Patients with previous PCI had a significantly higher prevalence of history of myocardial infarction, renal dysfunction, and hemodialysis. Rates of surgical mortality were higher in patients with previous PCI (7.6% vs. 1.0%, p = 0.008). A multivariate logistic regression analysis revealed that previous PCI remained a strong predictor of surgical mortality (odds ratio, 6.9; 95% confidence interval, 1.2–4.2; p = 0.035). After matching and regression adjustment by propensity score, the impact of previous PCI on surgical mortality was found to be similar (matching odds ratio, 6.5; 95% confidence interval, 0.8–55.0; p = 0.088; regression adjustment odds ratio, 6.3; 95% confidence interval, 1.2–33.6; p = 0.031).

**Postoperative Atrial Fibrillation (AF)**

AF is the most common complications after CABG and is associated with an increased risk of stroke and longer hospital stay. As described below, several studies have examined the predictors of AF after OPCAB.

Hosokawa, et al.49 retrospectively reviewed 296 consecutive patients who underwent OPCAB. The incidence of AF was 32%. AF prolonged the hospital stay by 3 days (p <0.01). Stepwise multivariate analysis identified increasing age (odd ratio 1.44 per 10-yr increase; confidence interval 1.06–1.95), intraoperative core body temperature (odds ratio 1.64; 95% confidence interval 1.05–2.56), average cardiac index in the ICU (odds ratio 0.37; 95% confidence interval 0.19–0.71), and intraoperative fluid balance (odds ratio 0.96 per 100-ml increase; 95% confidence interval 0.93–0.99) as independent predictors for the development of AF.

Ishida, et al.50 examined the relationship between proinflammatory cytokines, which play an important role in the upstream regulation of inflammatory cascades, and the development of AF after OPCAB in a 39 patients’ case series. Eleven patients (28%) developed AF postoperatively. Patients with postoperative AF had a higher value of interleukin-6 at 3 and 6 hours after anastomoses, and it was a significant predictor of postoperative AF along with age, whereas TNF-α levels did not change during the study period. Interleukin-8 and CRP levels significantly increased after surgery; however, there was no significant difference between the 2 groups.

Akazawa, et al.51 investigated the relationship between the preoperative BNP levels and postoperative AF after OPCAB. They analyzed the data of 150 patients without a history of AF who underwent elective OPCAB. Twenty-six patients (17.3%) developed postoperative AF. Univariate analysis demonstrated that age (odds ratio 1.060; 95% confidence interval 1.008–1.114; p = 0.023), previous myocardial infarction (odds ratio 2.628; 95% confidence interval 1.031–6.697; p = 0.043), and BNP level (odds ratio 7.336; 95% confidence interval 2.401–22.409/log BNP level; p <0.001) were accurate predictors of postoperative AF. Stepwise multivariate regression analysis indicated that age (odds ratio 1.059; 95% confidence interval 1.002–1.120; p = 0.043) and BNP level (odds ratio 6.272; 95% confidence interval 1.980–19.861/log BNP level; p = 0.002) were the only independent predictors of postoperative AF.

Several studies have focused on the prevention of AF after CABG. Fuji, et al.52 conducted a randomized prospective trial to determine the efficacy of intravenous landiolol administration in the early period after OPCAB followed by treatment with carvedilol for prevention of AF. Seventy consecutive patients were enrolled in the study. Patients in the treatment group received landiolol intravenously (5 μg·kg⁻¹·min⁻¹) in the ICU immediately after surgery until carvedilol was administered orally. All patients received oral carvedilol (2.5 mg–5 mg/day) after extubation, and this treatment was continued even after discharge. Postoperative AF occurred in 4 (11.1%) of the 36 patients in the landiolol group, and in 11 (32.3%) of the 34 patients in the control group, indicating that development of AF was significantly inhibited by landiolol treatment (p = 0.042).

Kinoshita, et al.53 assessed the preventive effect of preoperative statin treatment on development of AF after elective isolated OPCAB. Among 584 patients, 364 patients received statin at least 5 days before surgery and 220 patients received no statin. They identified 195 propensity score-matched pairs. AF occurred in 14.4% of patients in the statin group and in 24.6% of patients in the no statin group (p = 0.01). Multivariate logistic regression, including potential univariate predictors, identified statin treatment (odds ratio 0.49; 95% confidence interval
0.22–0.81; p = 0.01), age (odds ratio 1.33 per 10-yr increase; 95% confidence interval 1.04–1.69; p = 0.02), and transfusion (odds ratio 2.21; 95% confidence interval 1.38–3.55; p = 0.01) as independent predictors of postoperative AF.

To prevent the development of AF, Ito, et al.\textsuperscript{54} assessed the efficacy of treatment with the anti-arrhythmic drug propafenone hydrochloride, which was administered in the early postoperative period. Seventy-eight patients undergoing isolated OPCAB were divided into 2 groups; propafenone hydrochloride group (P group) and control group (C group). The patients in the P group were given propafenone hydrochloride (150–450 mg/day orally) for 10 days from the day of surgery. The incidence of AF was 35% in the C group and 12% in the P group (p = 0.0337). Multiple logistic regression analysis showed that propafenone hydrochloride was the sole factor that prevented the development of AF after OPCAB (odds ratio 0.207; 95% confidence interval, 0.053–0.804; p = 0.0229).

Kinoshita, et al.\textsuperscript{55} investigated the association between preoperative heart rate variability and incidence of AF after OPCAB. The following time-domain factors of heart rate variability were calculated: standard deviation of all normal-to-normal QRS (SDNN) and square root of mean of the sum of squares of differences between adjacent normal-to-normal QRS (RMSSD). AF occurred in 98 (25%) of 390 patients undergoing elective OPCAB. Patients without AF had significantly lower heart rate variability than did patients with AF, with a median value of 91 ms vs. 121 ms for SDNN and 19 ms vs. 25 ms for RMSSD. Reduced heart rate variability was significantly associated with a lower risk of postoperative AF (SDNN ≤99 ms; odds ratio 0.29; confidence interval 0.17–0.49; p <0.01, RMSSD ≤20 ms; odd ratio 0.47; 95% confidence interval 0.30–0.74; p <0.01).

Quality of Grafting

Nakjima, et al.\textsuperscript{56} examined the detailed characteristics of the arterial composite and sequential grafts and delineated the risk factors of graft occlusion. Intermediate graft patency of the graft with competitive or reverse flow was much lower when it was grafted to the coronary artery with mild disease or the main trunk of the LAD. Side-to-side anastomosis had higher graft patency than end-to-side anastomosis, and the fashion of composite graft (Y-, I, or K-graft) did not affect graft patency. Multivariate and univariate analyses showed that mild stenosis of the coronary artery, and competitive or reverse flow of the graft were important risk factors of intermediate graft occlusion in OPCAB.

Manabe, et al.\textsuperscript{57} evaluated the angiographic outcomes of composite grafting in patients undergoing OPCAB. They retrospectively reviewed 830 distal anastomoses in 256 patients who underwent OPCAB and the 1-year follow-up coronary angiograms. They compared 410 anastomoses using a composite grafting technique with 420 anastomoses using individual grafting. In target vessels with mild stenosis, the incidence of graft occlusion or string sign was significantly higher in composite ITAs than in individual ITAs (composite 20.3% vs. individual 7.3%; p = 0.018), and a higher tendency was shown in composite radial artery than in individual radial artery grafts (59.3% vs. 36.4%; p = 0.09). In contrast, in target vessels with severe stenosis, the incidence of graft occlusion was similar between composite and individual ITAs (5.7% vs. 3.3%, p = 0.278) and composite and individual radial artery grafts (11.5% vs. 9.6%, p = 0.297).

Sugimura, et al.\textsuperscript{58} assessed graft patency and long-term clinical outcomes in 53 patients who underwent primary isolated elective OPCAB with composite arterial Y-grafts. During the follow-up period of 18–97 months, there was no mortality, the incidence of graft failure was 22.6%, and the incidence of recurrence of angina was 13.2%. A significantly higher rate of graft failure was evident when 1 end of the composite graft was anastomosed to the coronary artery with 75% stenosis and the other end to the coronary artery with more than 90% stenosis.

Matsura, et al.\textsuperscript{59} evaluated graft patency and quality of anastomoses to small coronary arteries by early postoperative angiography in OPCAB. The coronary artery branches were categorized as large (>1.5 mm, group L) or small (<1.5 mm, group S) by intraoperative measurement. The overall patency and stenosis free (FitzGibbon Type A) rates were 97.2% and 96.2%. Graft patency (96.7%) and stenosis free rates (93.3%) in group S were comparable to those (97.5% and 97.1%, respectively) in group L.

Use of Bilateral ITA vs. Single ITA

It has been reported that the bilateral use of ITAs is associated with higher survival benefit than that of the single use of ITA. However, whether bilateral ITAs remain beneficial in the elderly population was not clear. Kinoshita, et al.\textsuperscript{60} compared outcomes in propensity...
score-matched patients, aged 70 years or more, undergoing isolated OPCAB using bilateral ITAs or a single ITA. A total of 217 pairs were matched using propensity scores calculated from 9 preoperative factors. The rate of postoperative complications was similar between the 2 groups. The 5-year freedoms from overall deaths were 86.4±3.2% in the bilateral group and 73.5±3.9% in the single group (p = 0.01), and the 5-year freedoms from cardiac events were 93.2±2.7% in the bilateral group and 87.5±3.0% in the single group (p = 0.01). In multivariCox models, the bilateral use of ITAs was significantly associated with a lower risk of overall death (odds ratio 0.56; 95% confidence interval 0.31–0.99; p = 0.04) and cardiac events (odds ratio 0.36; 95% confidence interval 0.15–0.88; p = 0.03) even in elderly patients.

**OPCAB vs. PCI**

A number of studies compared the efficacy of PCI and CABG. However, the impact of OPCAB has not been well elucidated. Marui, et al.\(^6\) analyzed the largest registry of CABG and PCI using bare metal stents in Japan, called the KREDO-Kyoto registry. From this registry, 6327 patients with multivessel and/or LMD were enrolled in the study. Among them, 3877 patients received PCI, 1388 received on-pump CABG, and 1069 received OPCAB. The median follow-up period was 3.5 years. The propensity score-adjusted all-cause mortality after PCI was higher than that after on-pump CABG or OPCAB (odds ratio 1.37; 95% confidence interval 1.15–1.63; p <0.01). The incidence of stroke was lower after PCI than that after on-pump CABG or OPCAB (odds ratio 0.75; 95% confidence interval 0.59–0.96; p = 0.02). Comparing OPCAB with PCI or on-pump CABG, propensity score-adjusted all-cause mortality after PCI was higher than that after OPCAB (odds ratio 1.50; 95% confidence interval 1.20–1.86; p <0.01). The adjusted mortality rate was similar between the OPCAB and on-pump CABG groups (odds ratio 1.18; 95% confidence interval 0.93–1.51; p = 0.33). The incidence of stroke after OPCAB was similar to that after PCI (odds ratio 0.98; 95% confidence interval 0.71–1.34; p >0.99); however, the incidence of stroke after on-pump CABG was higher than that after OPCAB (odds ratio 1.59; 95% confidence interval 1.16–2.18; p <0.01). In contrast to many randomized studies showing comparable survival between PCI and CABG, in this real-world registry in Japan, the survival advantage of CABG including OPCAB was clearly better than that of PCI with bare metal stents in patients with multivessel disease and/or LMD.

A few studies have compared PCI with drug-eluting stents and OPCAB. Yamagata, et al.\(^5\) examined 208 patients with multivessel disease and DM, including 92 patients treated with sirolimus-eluting stents (SES) and 116 patients with OPCAB. During the mean follow-up period of 42±8 months, the rate of repeat revascularization was significantly higher in the SES group than in the OPCAB group (21% vs. 6.9%, p = 0.003). On the other hand, the incidence of cerebrovascular events was higher in the OPCAB group than in the SES group. The cumulative MACCE (defined as all-cause death, non-fatal myocardial infarction, cerebrovascular events, and repeat revascularization) was similar between the 2 groups (27% vs. 23%, p = 0.492).

Dohi, et al.\(^5\) compared the long-term outcomes after OPCAB or PCI with SES in DM patients with multivessel disease and/or LMD. They enrolled 350 patients who underwent OPCAB and 143 patients who were treated with SES implantation. During the mean follow-up period of 2.6±1.6 years, no difference was observed between OPCAB and SES implantation in all-cause mortality or cardiac death. However, acute coronary syndrome, target vessel revascularization, and major adverse cardiac and cerebrovascular events were markedly lower in patients undergoing OPCAB than in those receiving SES.

In summary, several excellent and interesting studies have been performed in Japan on factors associated with OPCAB. The high rate of OPCAB in CABG (more than 60%) has been supported by those clinical studies. However, most of them were observational studies performed in a single center. To establish evidence for use as guidelines in Japanese clinical settings, larger multicenter randomized prospective and observational studies using nation-wide data bases should be conducted.

**References**

4) Sezai Y, Tsukamoto S. Coronary artery surgery results
Yaku H, et al.


