1 OPCAB Made in Japan: Evidence on Off-Pump Coronary Artery Bypass Grafting from Japan

Hitoshi Yaku and Kiyoshi Doi

Abstract

Off-pump coronary artery bypass grafting (OPCAB) is a standard procedure for patients who require CABG in Japan, with OPCAB performed in >60 % of patients who undergo CABG. This widespread use of OPCAB in Japan is supported by a number of studies that have been performed in the Japanese population. This chapter introduces those studies that have had a significant impact on OPCAB-related practice and consists of four primary sections that summarize the technical aspects, patient management, intraoperative graft evaluation, and surgical outcomes related to OPCAB. Although the majority of these studies were conducted retrospectively in single institutions, they are well designed, relevant, and innovative. To establish evidence for guidelines to be used in Japanese clinical settings, larger multicenter, randomized prospective, and observational studies using nationwide databases should be conducted.

Keywords

Off-pump coronary artery bypass grafting • Internal thoracic artery • Bypass graft • Coronary artery disease • Drug-eluting stent

1.1 Introduction

Off-pump coronary artery bypass grafting (OPCAB) began in the mid-1980s [1] and has since become increasingly popular worldwide [2, 3]. In Japan, OPCAB was first performed in 1996 [4] and is now the standard strategy for surgical coronary revascularization. The ratio of the number of OPCAB procedures to the total number of coronary artery bypass grafting (CABG) procedures has progressively increased and has exceeded 65 % on an annual basis since 2000 [5]. Many studies worldwide have reported the effects and drawbacks of OPCAB and 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, a number of studies have been reported from Japan, although most are retrospective, single-institution studies. In this chapter, we describe relevant clinical studies conducted in Japan and published in the English language. All values are presented as mean ± SD except where otherwise noted.

1.2 Technical Aspects of OPCAB

1.2.1 Harvesting of the Conduits

To obtain high patency rates and good long-term outcomes, the quality of the grafts is crucial in both OPCAB and conventional CABG. Higami et al. [6] reported a unique method of harvesting the internal thoracic artery (ITA) using an ultrasonic scalpel. With their "quick touch method," the ITA can be skeletonized safely and efficiently by removing fat tissues surrounding the artery, and the branches of the ITA

H. Yaku (✉) • K. Doi
Department of Cardiovascular Surgery, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan
e-mail: yakuh@koto.kpu-m.ac.jp

T. Asai et al. (eds.), *Off-Pump Coronary Artery Bypass*, DOI 10.1007/978-4-431-54986-4_1

are divided by employing protein coagulation using the scalpel. A longer ITA could be obtained by skeletonization compared to a pedicle technique. This group also demonstrated excellent early (<30 days) patency of the grafts (99.7 % for the left ITA and 100 % for the right ITA) [7]. Dr. Higami was also involved in experimental research revealing that the improved blood flow achieved with this technique was associated with the release of nitric oxide [8].

Asai et al. [9] described a method for harvesting the right gastroepiploic artery (RGEA) also using an ultrasonic scalpel. The authors reported that the technique was safe, simple, and allowed them not only to harvest the artery faster but also to obtain large spasm-free arterial conduits. With respect to clinical outcomes, Suma et al. [10], who were the first in the world to use the RGEA as a graft in CABG, reported excellent long-term results in both conventional CABG and OPCAB.

1.2.2 Devices Facilitating OPCAB

A few useful devices have been developed to obtain a stable surgical view in OPCAB with no ischemic insult to the myocardium. Arai et al. [11] developed a new heart positioner called TENTACLES™, which comprises three 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 compromise in blood pressure.

Kamiya et al. [12] developed a synchronized, arterial flow-ensuring system to perform coronary anastomosis safely and without ischemia in OPCAB. Arterial blood from the femoral artery is perfused into the coronary artery in pulsatile mode regulated by a pump controller with synchronization during the diastolic period. Among 524 consecutive patients in whom this pump system was applied, they observed no intraoperative fatal arrhythmias, ventricular arrhythmias, short runs of ventricular tachycardia, or hemodynamic deterioration during anastomoses [13].

1.2.3 Proximal Anastomosis Devices

To avoid complications related to aortic manipulation, several devices have been developed to perform clampless anastomosis. However, only a few studies have reported the late patency of grafts constructed using these devices. Shimokawa et al. [14] investigated the early and 1-year patency rates of saphenous vein grafts (SVGs) constructed using an anastomosis device in patients who underwent OPCAB. They followed 232 patients who had undergone OPCAB using SVGs and received follow-up angiography. For proximal anastomosis, a clampless device was used in 73 patients (HEARTSTRING in 54; Enclose II in 19), and partial clamping was performed in 159 patients. The overall patency rates of SVGs at 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, the target vessel revascularization rates did not significantly differ during the follow-up examination (6.8 % vs. 10.1 %, $P=0.623$).

Fujii et al. [15] evaluated 39 grafts constructed using the PAS-Port proximal anastomosis system in 28 patients who underwent OPCAB. Early postoperative angiography indicated no bending or stenosis in any graft and a patency rate of 100 %. Kai et al. [16] investigated the mid-term patency rate of SVGs using the PAS-Port. Among 66 patients who had SVGs, 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 the 39 grafts were occluded, and the 1-year patency rate (FitzGibbon grade A) was 94.9 %. No obvious stenosis of SVGs was observed. Twenty-four patients underwent 2-year graft evaluation. The 2-year cumulative patency rate was 91.7 %.

1.2.4 Awake OPCAB

Watanabe et al. [17] reported awake subxiphoid CABG in three 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 comparing them with matched patients under general anesthesia [18]. Fifteen percent of the awake patients were able to leave the operating room in a wheelchair. The time until patients were able to drink water and walk and the duration of hospital stay were significantly shorter in the awake OPCAB group than in the general anesthesia group, with no operative or postoperative complications or deaths.

1.2.5 Revascularization Technique for Diffuse Coronary Lesions

Fukui et al. [19] developed a long-onlay patch method using the left ITA for diffusely diseased LAD. Endarterectomy is warranted depending on the severity of coronary atherosclerosis. In their study, preoperative angiography revealed the diffusely diseased LAD. The patent 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 between the graft and the native coronary artery was hardly visible. Event-free survival among patients who underwent this technique was excellent at 3 years [20].

1.3 Patient Management During OPCAB

1.3.1 Intraoperative Management

Occasionally, because of hemodynamic instability or arrhythmia due to displacement of the heart without cardiopulmonary bypass, OPCAB must be converted to on-pump CABG. According to the annual report of the Japanese Association for Coronary Artery Surgery [21], operative mortality and the 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. [22] studied the financial implications of intraoperative conversion and its effect on quality of life using a decision-analysis model and the Monte Carlo simulation. They found that OPCAB is superior (less costly and more effective) if 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 that may cause deterioration of hemodynamics and lead to conversion to on-pump CABG. In an experimental study, Koga et al. [23] demonstrated that cardiac displacement alone did not cause MR if coronary perfusion was maintained and that 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. [24] investigated the relationship between left ventricular function and the severity of MR during OPCAB. They found that MR was most severe during anastomosis of the LCx, with 39 % of patients experiencing moderate to severe MR. Significant differences were observed in preoperative serum brain natriuretic peptide (BNP) levels, Tei index values, and 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. [25] reported the effects of landiolol, an ultra-short-acting selective β-1 blocker, on the motion of the LAD using 3D digital motion capture and reconstruction technology. Landiolol ($0.12\ \mu g \cdot kg^{-1} \cdot min^{-1}$) significantly decreased heart rate, the 3D distance moved, acceleration and deceleration, without inducing a significant change in systolic blood pressure, cardiac output, or pulmonary wedge pressure. This study demonstrated the possible application of landiolol as a chemical stabilizer during OPCAB.

1.3.2 Pathophysiology During OPCAB

Moriyama et al. [26] 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 two groups and received amino acid ($4\ kJ \cdot kg^{-1} \cdot hour^{-1}$) or saline treatment, which was infused over 2 h 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 partially contribute to the thermogenic response occurring during OPCAB.

Mitaka et al. [27] investigated nitric oxide (NO) production in OPCAB and on-pump CABG in 116 patients who had undergone elective CABG with ($n=66$) and without ($n=50$) cardiopulmonary bypass. Urinary nitrite/nitrate (NOx) excretion was measured as an index of endogenous NO production over 2 days after the operation. The mean urinary NOx/creatinine (Cr) excretion ratio did not significantly differ on the first day, and it 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 the OPCAB group than in the on-pump CABG group on the second day. The two groups demonstrated no significant differences in mean cardiac index or mean systemic vascular resistance index after the operation. The authors concluded that endogenous NO production in patients who underwent CABG is stimulated by a surgical inflammatory response and that cardiopulmonary bypass does not trigger NO production.

Miura et al. [28] tested the hypothesis that intraoperative hemodynamic compromise due to cardiac displacement during OPCAB is related to jugular bulb desaturation, which is related to 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 (S_VO_2) ≤70 %, arterial partial pressure of carbon dioxide ($PaCO_2$) ≤40 mmHg, and central venous pressure (CVP) ≥8 mmHg were likely predictors of the occurrence of jugular bulb desaturation, leading the authors to suggest that cerebral desaturation during OPCAB could be prevented by achieving normal values of S_VO2, PaCO2, and CVP.

1.4 Intraoperative Graft Evaluations

1.4.1 Imaging of Grafts

Suma et al. [29] demonstrated a thermal coronary artery imaging procedure, using a new-generation infrared camera for intraoperative graft evaluation, in 12 patients undergoing OPCAB. All grafts were clearly visualized, and the anastomosis and flow status could be observed by local epicardial cooling using a CO_2 blower on the normothermic heart. Among 17 grafts, one ITA graft showed anastomotic failure and was successfully revised. The results of postoperative coronary angiography confirmed the patency of all grafts.

Takahashi et al. [30] demonstrated 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 and successfully revised four anastomoses that had failed according to the SPY system.

1.4.2 Functional Evaluation of Grafts

Transit-time flow measurement for the intraoperative evaluation of grafts began being performed in the late 1990s and is now a standard method. Takami et al. [31] compared intraoperative parameters determined by a transit-time flowmetry with quantitative parameters determined by postoperative coronary angiograms. Patent and nonpatent grafts significantly differed in all intraoperative flow parameters. The cutoff value to distinguish patent from nonpatent grafts was a fast Fourier transformation ratio of 1.0. The degree of stenosis at the heel of the anastomosis correlated significantly with intraoperative mean flow values.

Tokuda et al. [32] showed that a mean flow of 15 ml/min, a pulsatility index of 5.1, and a backward flow of 4.1 % were the optimal cutoff criteria to predict early graft failure of the left coronary system. For the right coronary system, the cutoff values were 20 ml/min, 4.7, and 4.6 %, respectively. They also compared the intraoperative parameters determined by a transit-time flowmetry with mid-term graft patency from 1 to 4 years after surgery [33]. Of 104 grafts, 21 were found to have a new mid-term occlusion or worsening of stenosis. They concluded that grafts with lower intraoperative mean flow, and especially with a higher percentage of backward flow, should be carefully monitored, even if they were initially anatomically patent.

Harada et al. [34] conducted a prospective comparison of the diagnostic accuracy of both fast Fourier transformation analysis of transit-time flowmetry waveform and an intraoperative fluorescence imaging system to determine graft failure. Neither intraoperative fluorescence imaging nor the mean graft flow/pulsatility index could detect a SVG with 75 % stenosis diagnosed by postoperative angiography; however, harmonic distortion of the transit-time flowmetry from stenosed SVGs significantly differed from that of patent SVGs.

1.5 Surgical Outcomes of OPCAB

1.5.1 Surgical Results of OPCAB Compared to On-Pump CABG

The surgical results of OPCAB were first compared with those of conventional CABG by Ishida et al. [35]. This retrospective study demonstrated that the operating time, ICU stay, and ventilation time were statistically significantly shorter in the OPCAB group than in the conventional CABG group. Postoperative blood loss within 12 h and transfusion volume were statistically significantly lower in the OPCAB group, as were peak serum blood urea nitrogen and Cr concentrations. Notably, no perioperative strokes occurred in the OPCAB group, whereas 6.4 % of patients in the conventional group suffered from a stroke. Graft patency did not significantly differ between the two groups (95.6 % vs. 94.9 %).

Kobayashi et al. [36] 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 per patient were similar. Completeness of revascularization was 98 % in both groups. The incidence of intraoperative and postoperative complications was comparable. The OPCAB group contained a larger number of patients without blood transfusion. Postoperative levels of S-100 protein and neuron-specific enolase were lower in the OPCAB group. The maximum CKMB level was also lower in the OPCAB group. The total patency rate was 98 % in both groups, and the stenosis-free patency rate was 93 % in the OPCAB group and 96 % in the on-pump group, with no significant difference. The authors concluded that OPCAB with multiple arterial grafts was as safe as conventional CABG, with similar completeness of revascularization and early graft patency.

1.5.2 Patients with Diabetes Mellitus (DM)

Tsuruta et al. [37] 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 three groups based on preoperative HbA1c levels (HbA1c $<$ 6.5 %, 6.5 % $\leq$ HbA1c $<$ 7.5 %, and HbA1c $\geq$ 7.5 %). No operative or in-hospital mortality occurred. All-cause mortality and cardiac mortality rates were 6.2 % (19 patients) and 1.3 % (four patients), respectively, during a mean follow-up period of 3.6 ± 1.7 years. Kaplan-Meier survival curves indicated no significant differences in all-cause or cardiac mortality (log-rank test, $P = 0.26$, and $P = 0.17$, respectively).

Kai et al. [38] retrospectively examined the effects of OPCAB with skeletonized bilateral ITAs in patients with insulin-dependent DM. Surgical outcomes were compared to those of on-pump CABG with 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 %; $P = 0.01$). Early angiographic results did not differ between the two groups. During the 3.4-year follow-up period (range 0.1–9.9 years), the two groups demonstrated no differences 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 mortality in the long-term period.

Fujii et al. [39] reported the usefulness of perioperative blood glucose control in patients undergoing OPCAB. Patients with DM were aggressively treated with intensive insulin therapy to achieve a preoperative fasting blood glucose level of 140 mg/dl and a postoperative level of 200 mg/dl. In comparing DM patients with non-DM patients, they 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 patients with a mean blood glucose level of <200 mg/dl in the ICU were compared to those with a mean blood glucose level of ≥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 those with a mean glucose level of ≥200 mg/dl.

1.5.3 Perioperative Stroke

Nishiyama et al. [40] investigated the temporal pattern of strokes after on-pump CABG and OPCAB. They analyzed 2,516 consecutive patients who underwent primary elective isolated CABG, and the primary end point in this study 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 awaking from surgery without a neurological deficit. In the study population, 63 % of strokes were delayed. Patients who underwent OPCAB had a significantly lower incidence of early stroke (0.1 % vs. 1.1 %, $P = 0.0009$), whereas the incidence of delayed strokes was not significantly different between the patients underwent OPCAB and on-pump CABG (0.9 % vs. 1.4 %, $P = 0.3484$). 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, $P = 0.1210$).

Another study revealed the importance of preoperative evaluation of intracranial and neck vessels for estimating patient prognosis in terms of stroke [41]. In that study, patients were divided into two groups, low risk and high risk, based on the findings of MRI and carotid Doppler imaging. No intraoperative stroke occurred in either group. The high-risk group had a higher incidence of delayed stroke and stroke even after 1 month. Univariate analysis revealed designation as high risk was 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. [42] investigated risk factors of stroke/transient ischemic attack (TIA) and delirium after OPCAB in a review of the medical records of 685 patients. The incidence of postoperative stroke/TIA and delirium after OPCAB was 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. Histories of atrial fibrillation ($P = 0.037$) or DM ($P = 0.041$) were risk factors of postoperative stroke/TIA. By 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. [43] reported that the effect of carotid artery stenosis on the incidence of perioperative stroke may be low 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. Neither stroke nor in-hospital mortality occurred in patients with carotid stenosis, although two strokes (0.49 %) and three in-hospital mortalities (0.73 %) were observed in patients without carotid stenosis.

Osawa et al. [44] studied the incidence of stroke in relation to surgical manipulation of the ascending aorta. Two of 451 patients (0.47 %) who underwent OPCAB using the aortic nonclamping technique developed delayed strokes, whereas one in nine patients who underwent OPCAB with aortic partial clamping for proximal anastomosis had an early stroke. The authors concluded that the aortic nonclamping technique might reduce the incidence of stroke. Kobayashi et al. [45] also reported no operative death or stroke by using an aorta no-touch technique with in situ graft and composite and sequential grafting methods.

1.5.4 Perioperative Neuropsychological Dysfunction

Baba et al. [46] conducted a prospective study in 218 patients who had undergone 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 of at least 20 % from baseline in more than two tests. 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.

1.5.5 Impact of Preoperative Renal Dysfunction

To study the association between renal dysfunction and OPCAB, Ogawa et al. divided patients into three groups depending on preoperative serum Cr levels: normal, moderately depressed, and severely depressed [47]. The severely depressed group included more patients with postoperative Cr levels >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. [48] divided patients undergoing OPCAB into three groups based on preoperative glomerular filtration rate (GFR), < 30 ml/min/1.73 m^2, 30–60 ml/min/1.73 m^2, and > 60 ml/min/1.73 m^2, and reported that long-term survival and freedom from cardiac death depended on preoperative renal function as indicated by GFR, but noncardiac death did not depend on preoperative renal function. Hayashida et al. [49] compared the postoperative renal function of 52 OPCAB patients to that of 53 matched patients undergoing conventional CABG. The increase in Cr levels was significantly smaller in the OPCAB group than in the conventional CABG group (0.16 ± 0.05 vs. 0.45 ± 0.06 mg/dl).

1.5.6 Patients on Hemodialysis

Oyamada et al. [50] 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 whom 29 had diabetic nephropathy (DN group) and the remaining 12 did not (NDN group). The two groups significantly differed in the duration of dialysis before surgery (4.2 ± 5.5 years in DN vs. 9.1 ± 7.5 years in NDN, $P=0.028$). Low cardiac output (LV ejection fraction <30 %) was observed only in the DN group (7/29, $P=0.048$). 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 predicted risk factors for OPCAB; however, diabetic nephropathy was not.

Sunagawa et al. [51] compared the mid-term clinical results of CABG and PCI with drug-eluting stents (DES) in patients with chronic renal failure on hemodialysis. Thirty-day mortality was 3.3 % for CABG including OPCAB (83 % of the total cases) and 4.0 % for PCI. The 2-year survival rate was 84.0 % for CABG and 67.6 % for PCI ($P=0.0271$). The cardiac death-free curve at 2 years was 100 % for CABG and 84.1 % for PCI ($P=0.0122$). The major adverse cardiac event-free rate at 2 years was 75.8 % for CABG and 31.5 % for PCI ($P<0.0001$). During the follow-up period, six late deaths occurred in the CABG group and 27 late deaths, including six sudden deaths, occurred in the PCI group.

1.5.7 Patients with 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. [52] reviewed 268 patients with significant LMD among 665 patients who underwent OPCAB and compared them with 237 propensity score-matched patients without LMD. The operative mortality rate was 0.8 % in the LMD group and 1.7 % in the non-LMD group. The rate of 6-year freedom from all-cause death was 87.3 % in the LMD group and 60.7 % in the non-LMD group ($P=0.17$), and the rate of 6-year freedom from cardiac events was 80.4 % in the LMD group and 70.4 % in the non-LMD group ($P=0.98$). The authors concluded that LMD did not significantly affect OPCAB outcomes in either the short or long term.

Fukui et al. [53] retrospectively reviewed 768 patients who underwent OPCAB with 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 two groups. In the patients without LMD, the left and right ITAs were used for the LAD in 87.4 % and 12.2 % of the 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 the patients without LMD, the 1-year patency rate of left and right ITAs was 97.6 % and 91.6 %, respectively, whereas in the patients with LMD, it was 97.0 % and 93.2 %, respectively. The patency rates of the left and right ITAs did not significantly differ in patients with or without LMD ($P=0.9803$ and $P=0.7205$ for left and right ITAs, respectively).

1.5.8 Patients with Previous Percutaneous Coronary Intervention (PCI)

Previous PCI was reported to have an adverse impact on the surgical outcomes of CABG [54], and several Japanese studies have investigated this impact. Fukui et al. [55] retrospectively reviewed 545 patients who underwent first-time isolated OPCAB. Among them, 154 had previous PCIs, including 99 patients with stents. The number of anastomoses per patient was lower in the PCI patients than in the non-PCI patients (3.8 vs. 4.2; $P=0.0066$). Neither operative mortality (0 % vs. 1.8 %; $P=0.1995$) nor major morbidity rates differed between these groups. Similar results were obtained for the comparison between patients with stents and those without stents. No significant difference was observed in graft patency rates between the PCI patients and non-PCI patients (97.1 % vs. 97.9 %; $P=0.4976$).

Kinoshita et al. [56] compared patients with previous PCI to those without PCI after OPCAB. The patients with previous PCI had a significantly higher prevalence of history of myocardial infarction, renal dysfunction, and hemodialysis. The rate of surgical mortality was higher in the 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 (odd 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 remain significant (matching odd ratio, 6.5; 95 % confidence interval, 0.8–55.0; $P=0.088$; regression adjustment odd ratio, 6.3; 95 % confidence interval, 1.2–33.6; $P=0.031$).

1.5.9 Postoperative Atrial Fibrillation (AF)

AF is the most common complication 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. [57] retrospectively reviewed 296 consecutive patients who underwent OPCAB, in whom 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-year increase; confidence interval 1.06–1.95), intraoperative core body temperature (odd ratio 1.64; 95 % confidence interval 1.05–2.56), average cardiac index in the ICU (odd ratio 0.37; 95 % confidence interval 0.19–0.71), and intraoperative fluid balance (odd 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. [58] 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 case series of 39 patients, 11 of whom (28 %) developed AF postoperatively. Patients with postoperative AF had higher levels of interleukin-6 at 3 and 6 h after anastomoses, which was a significant predictor of postoperative AF along with age, whereas tumor necrosis factor-α levels did not change during the study period. Interleukin-8 and CRP levels significantly increased after surgery; however, no significant difference was detected between the two groups.

Akazawa et al. [59] investigated the relationship between preoperative BNP levels and postoperative AF after OPCAB. They analyzed the data of 150 patients without a history of AF who underwent elective OPCAB, 26 of whom (17.3 %) developed postoperative AF. Univariate analysis demonstrated that age (odd ratio 1.060; 95 % confidence interval 1.008–1.114; $P=0.023$), previous myocardial infarction (odd ratio 2.628; 95 % confidence interval 1.031–6.697; $P=0.043$), and BNP level (odd 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 (odd ratio 1.059; 95 % confidence interval 1.002–1.120; $P=0.043$) and BNP level (odd 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. Fujii et al. [60] 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 ($5\ \mu g \cdot kg^{-1} \cdot min^{-1}$) in the ICU immediately after surgery until carvedilol was administered orally. All patients received oral carvedilol (2.5–5 mg/day) after extubation and this treatment was continued even after discharge. Postoperative AF occurred in four (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 the development of AF was significantly inhibited by landiolol treatment ($P=0.042$).

Kinoshita et al. [61] assessed the preventive effect of preoperative statin treatment on the 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. The authors identified 195 propensity score-matched pairs. AF occurred in 14.4 % of the patients in the statin group and in 24.6 % of the patients in the no statin group ($P=0.01$). Multivariate logistic regression, including potential univariate predictors, identified statin treatment (odd ratio 0.49; 95 % confidence interval 0.22–0.81; $P=0.01$), age (odd ratio 1.33 per 10-year increase; 95 % confidence interval 1.04–1.69; $P=0.02$), and transfusion (odd ratio 2.21; 95 % confidence interval 1.38–3.55; $P=0.01$) as independent predictors of postoperative AF.

Ito et al. [62] assessed the efficacy of treatment with the antiarrhythmic drug propafenone hydrochloride, which was administered in the early postoperative period to prevent development of AF. Seventy-eight patients undergoing isolated OPCAB were divided into two groups: propafenone hydrochloride (P group) and control (C group). 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 indicated that propafenone hydrochloride was the sole factor that prevented the development of AF after OPCAB (odd ratio 0.207; 95 % confidence interval 0.053–0.804; $P=0.0229$).

Kinoshita et al. [63] investigated the association between preoperative heart rate variability and the 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 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 patients with AF, with a median SDNN of 91 ms vs. 121 ms and median RMSSD of 19 ms vs. 25 ms. Reduced heart rate variability was significantly associated with a lower risk of postoperative AF (SDNN ≤ 99 ms, odd 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; $P<0.01$).

1.5.10 Quality of Grafting

Nakjima et al. [64] examined the detailed characteristics of the arterial composite and sequential grafts and delineated the risk factors of graft occlusion. Intermediate patency of a graft with competitive or reverse flow was much lower when it was grafted to a 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 for intermediate graft occlusion in OPCAB.

Manabe et al. [65] evaluated the angiographic outcomes of composite grafting in patients undergoing OPCAB. They retrospectively reviewed 830 distal anastomoses in 256 patients who underwent OPCAB and 1-year follow-up coronary angiograms, comparing 410 anastomoses that used a composite grafting technique with 420 anastomoses that used 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 %, $P=0.09$). By 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. [66] 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, no deaths occurred, the incidence of graft failure was 22.6 %, and the incidence of angina recurrence was 13.2 %. A significantly higher rate of graft failure was evident when one end of the composite graft was anastomosed to a coronary artery with 75 % stenosis and the other end to a coronary artery with more than 90 % stenosis.

Matsuura et al. [67] evaluated graft patency and quality of anastomoses to small coronary arteries in OPCAB by early postoperative angiography. 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 in group L (97.5 % and 97.1 %, respectively).

1.5.11 The Impact of the Use of Bilateral ITA vs. Single ITA

The bilateral use of ITAs has been reported to be associated with higher survival benefit than the use of a single ITA. However, whether bilateral ITAs remain beneficial in the elderly population is less clear. Kinoshita et al. [68] compared outcomes in propensity score-matched patients, 70 years of age or older, undergoing isolated OPCAB using bilateral ITAs or a single ITA. A total of 217 pairs were matched using propensity scores calculated from nine preoperative factors. The rate of postoperative complications was similar between the two groups. The rate of 5-year freedom from overall death was 86.4 ± 3.2 % in the bilateral group and 73.5 ± 3.9 % in the single group ($P=0.01$), and the rate of 5-year freedom from cardiac events was 93.2 ± 2.7 % in the bilateral group and 87.5 ± 3.0 % in the single group ($P=0.01$). In multivariate Cox models, the bilateral use of ITAs was significantly associated with a lower risk of overall death (odd ratio 0.56; 95 % confidence interval 0.31–0.99; $P=0.04$) and cardiac events (odd ratio 0.36; 95 % confidence interval 0.15–0.88; $P=0.03$) even in elderly patients.

Saito et al. [69] evaluated early outcomes of bilateral ITA compared with single ITA in patients who had undergone isolated CABG from the Japan Adult Cardiovascular Surgery Database. Among 8,136 single ITA and 4,093 bilateral ITA patients, they performed a one-to-one matched analysis on the basis of estimated propensity scores for patients in each group balanced for baseline characteristics. The rate of off-pump CABG was similar (75 %) in both groups, and the mean number of anastomoses was 3.1 in the single ITA and 3.4 in the bilateral ITA group ($P<0.0001$). Thirty-day operative mortality was 1.2 % in both groups, and the overall incidence of postoperative complications was also similar, although deep sternal infection was more frequent with bilateral ITA (1.3 % of single ITA and 2.3 % of bilateral ITA patients; $P=0.0001$).

1.5.12 Outcomes of 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. [70] analyzed the largest registry of CABG and PCI involving bare metal stents in Japan, called the KREDO-Kyoto registry. From this registry, 6,327 patients with multivessel disease and/or LMD were enrolled in the study. Among them, 3,877 patients were treated with PCI, 1,388 received with on-pump CABG, and 1,069 received with 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 (odd 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 (odd ratio 0.75; 95 % confidence interval 0.59–0.96; $P=0.02$). Propensity score-adjusted all-cause mortality after PCI was higher than that after OPCAB (odd 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 (odd 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 (odd 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 (odd 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 superior to 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. [71] 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 that in the OPCAB group (21 % vs. 6.9 %, $P=0.003$). By contrast, the incidence of cerebrovascular events was higher in the OPCAB group than that in the SES group. The cumulative risk of major adverse cardiac and cerebrovascular events (defined as all-cause death, nonfatal myocardial infarction, cerebrovascular events, and repeat revascularization) was similar between the two groups (27 % vs. 23 %, $P=0.492$).

Dohi et al. [72] 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.

Shimizu et al. [73] compared intermediate outcomes between CABG including OPCAB (92 % in the total number of CABG) and PCI with DES in patients with unprotected LMD. The overall survival rate did not differ (CABG 93.4 %, DES 91.9 % at 2 years; ns). Major cardiac and cerebrovascular event-free survival was superior in the CABG group (CABG 82.2 %, DES 62.6 % at 2 years; $P=0.033$), and the total hospitalization costs were lower in the CABG group (CABG, median 3.225 million yen; DES, median 4.192 million yen; $P=0.013$).

1.5.13 Redo OPCAB

Dohi et al. [74] performed a propensity analysis based on the Japan Cardiovascular Surgical Database (JCVSD) comparing the early surgical results between off- and on-pump CABG in patients who had undergone previous CABG. Operative mortality tended to be lower, and the composite endpoint of mortality or major complications was statistically significantly less frequent for off-pump redo CABG compared to on-pump redo CABG.

1.6 Summary

A number of excellent and interesting studies have been performed in Japan on factors associated with OPCAB. The high rate of OPCAB among CABG procedures (more than 60 %) has been supported by these clinical results. However, most were observational studies performed in single institutions. To establish evidence applicable to instituting guidelines for Japanese clinical settings, larger multicenter, randomized prospective, and observational studies using nationwide databases should be conducted.

References

1. Benetti FJ (1985) Direct coronary surgery with saphenous vein bypass without cardiopulmonary bypass or cardiac arrest. J Cardiovasc Surg 26:217–222
2. Calafiore AM, Di Giammarco GD, Teodori G, Bosco G, D'Annunzio E, Barsotti A, Maddestra N, Paloscia L, Vitolla G, Sciarra A, Fino C, Contini M (1996) Left anterior descending coronary artery grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann Thorac Surg 61:1658–1663
3. Buffalo E, Summo H, Aguiar LF, Teles CA, Branco JNR (1997) Myocardial revascularization in patients 70 years of age and older without the use of extracorporeal circulation. Am J Geriatr Cardiol 6:6–9
4. Sezai Y, Tsukamoto S (1998) Coronary artery surgery results 1996. Ann Thorac Cardiovasc Surg 4:103–106
5. Sakata R, Fujii Y, Kuwano H, Committee for Scientific Affairs (2011) Thoracic and cardiovascular surgery in Japan during 2009. Annual report by the Japanese Association for Thoracic Surgery. Gen Thorac Cardiovasc Surg 59:636–667
6. Higami T, Kozawa S, Asada T, Shida T, Ogawa K (2000) Skeletonization and harvest of the internal thoracic artery with an ultrasonic scalpel. Ann Thorac Surg 70:307–308
7. Higami T, Yamashita T, Nohara H, Iwahashi K, Shida T, Ogawa K (2001) Early results of coronary grafting using ultrasonically skeletonized internal thoracic arteries. Ann Thorac Surg 71:1224–1228
8. Maruo A, Hamner CE, Rodrigues AJ, Higami T, Greenleaf JF, Schaff HV (2004) Nitric oxide and prostacyclin in ultrasonic vasodilatation of the canine internal mammary artery. Ann Thorac Surg 77:126–132
9. Asai T, Tabata S (2002) Skeletonization of the right gastroepiploic artery using an ultrasonic scalpel. Ann Thorac Surg 74:1715–1717
10. Suma H, Tanabe H, Takahashi A, Horii T, Isomura T, Hirose H, Amano A (2007) Twenty years experience with the gastroepiploic artery graft for CABG. Circulation 116(11 Suppl):I188–I191
11. Arai H, Mizuno T, Yoshizaki T, Itoh F, Oi K, Someya T, Tanaka H, Sunamori M (2006) A new multisuction cardiac positioner for multivessel off-pump coronary artery bypass grafting. Innovations 1:126–130
12. Kamiya H, Watanabe G, Doi T, Saito T, Takahashi M, Tomita S, Tsukioka T, Kanamori T (2002) Coronary active perfusion system can maintain myocardial blood flow and tissue oxygenation. Eur J Cardiothorac Surg 22:410–414
13. Watanabe G, Kamiya H, Nagamine H, Tomita S, Koshida Y, Nishida S, Ohtake H, Arai S, Yasuda T (2005) Off-pump CABG with synchronized arterial flow ensuring system. Ann Thorac Surg 80:1893–1897
14. Shimokawa T, Manabe S, Sawada T, Matsuyama S, Fukui T, Takanashi S (2009) Intermediate-term patency of saphenous vein graft with a clampless hand-sewn proximal anastomosis device after off-pump coronary bypass grafting. Ann Thorac Surg 87:1416–1420
15. Fujii T, Watanabe Y, Shiono N, Ozawa T, Hamada S, Masuhara H, Teramoto C, Hara M, Koyama N (2009) Study of coronary artery bypass using the PAS-Port device: assessment by multidetector computed tomography. Gen Thorac Cardiovasc Surg 57:79–86
16. Kai M, Hanyu M, Soga Y, Nomoto T, Nakano J, Matsuo T, Kawato M, Okabayashi H (2009) Mid-term patency rate after saphenous vein grafting with a PAS-Port device. J Thorac Cardiovasc Surg 137:503–504
17. Watanabe G, Yamaguchi S, Tomiya S, Ohtake H (2008) Awake subxiphoid minimally invasive direct coronary artery bypass grafting yielded minimum invasive cardiac surgery for high risk patients. Interact Cardiovasc Thorac Surg 7:910–912
18. Watanabe G, Tomita S, Yamaguchi S, Yashiki N (2011) Awake coronary artery bypass grafting under thoracic epidural anesthesia: great impact on off-pump coronary revascularization and fast-track recovery. Eur J Cardiothorac Surg 40:788–793
19. Fukui T, Tabata M, Taguri M, Manabe S, Morita S, Takanashi S (2011) Extensive reconstruction of the left anterior descending coronary artery with an internal thoracic artery graft. Ann Thorac Surg 91:445–451
20. Shimokawa T, Manabe S, Fukui T, Takanashi S (2009) Remodeling of reconstructed left anterior descending coronary arteries with internal thoracic artery graft. Ann Thorac Surg 88:54–57
21. Sezai Y, Orime Y, Tsukamoto S (2007) Coronary artery surgery results in Japan 2005. Ann Thorac Cardiovasc Surg 13:220–223
22. Shiga T, Apfel CC, Wajima Z, Ohe Y (2007) Influence of intraoperative conversion from off-pump to on-pump coronary artery bypass grafting on costs and quality of life: a cost-effectiveness analysis. J Cardiothorac Vasc Anesth 21:793–799
23. Koga S, Okazaki Y, Kataoka H, Ikeda K, Furukawa K, Ohtsubo S, Itoh T (2007) Configurations of the mitral valve during off-pump coronary artery bypass grafting: endoscopic and three-dimensional analysis. J Heart Valve Dis 16:602–607
24. Akazawa T, Iizuka H, Aizawa M, Warabi K, Ohshima M, Amano A, Inada E (2008) The degree of newly emerging mitral regurgitation during off-pump coronary artery bypass is predicted by preoperative left ventricular function. J Anesth 22:13–20
25. Wakamatsu H, Watanabe T, Sato Y, Takase S, Omata S, Yokoyama H (2012) Landiolol reduces coronary artery motion in an open-chest porcine model: implications for off-pump coronary artery bypass surgery. Surg Today 42:205–208
26. Moriyama T, Tsuneyoshi I, Omae T, Takeyama M, Kanmura Y (2008) The effect of amino-acid infusion during off-pump coronary arterial bypass surgery on thermogenic and hormonal regulation. J Anesth 22:354–360
27. Mitaka C, Yokoyama K, Imai T (2007) Nitric oxide production is more prominent in off-pump than in on-pump coronary artery bypass surgery. Anaesth Intensive Care 35:505–509
28. Miura N, Yoshitani K, Kawaguchi M, Shinzawa M, Irie T, Uchida O, Ohnishi Y, Mackensen GB (2009) Jugular bulb desaturation during off-pump coronary artery bypass surgery. J Anesth 23:477–482
29. Suma H, Isomura T, Horii T, Sato T (2000) Intraoperative coronary artery imaging with infrared camera in off-pump CABG. Ann Thorac Surg 70:1741–1742
30. Takahashi M, Ishikawa T, Higashidani K, Katoh H (2004) SPY™: an innovative intra-operative imaging system to evaluate graft patency during off-pump coronary artery bypass grafting. Interact Cardiovasc Thorac Surg 3:479–483
31. Takami Y, Ina H (2001) Relation of intraoperative flow measurement with postoperative quantitative angiographic assessment of coronary artery bypass grafting. Ann Thorac Surg 72:1270–1274
32. Tokuda Y, Song M-H, Ueda Y, Usui A, Akita T (2007) Predicting early coronary artery bypass graft failure by intraoperative transit time flow measurement. Ann Thorac Surg 84:1928–1934
33. Tokuda Y, Song M-H, Oshima H, Usui A, Ueda Y (2008) Predicting mid-term coronary artery bypass graft failure by intraoperative transit time flow measurement. Ann Thorac Surg 86:532
34. Hatada A, Okamura Y, Kaneko M, Hisaoka T, Yamamoto S, Hiramatsu T, Nishimura Y (2011) Comparison of the waveforms of transit-time flowmetry and intraoperative fluorescence imaging for assessing coronary artery bypass patency. Gen Thorac Cardiovasc Surg 59:14–18
35. Ishida M, Kobayashi J, Tagusari O, Bando K, Niwaya K, Nakajima H, Kitamura S (2002) Perioperative advantages of off-pump coronary artery bypass grafting. Circ J 66:795–799
36. Kobayashi J, Tashiro T, Ochi M, Yaku H, Watanabe G, Satoh T, Tagusari O, Nakajima H, Kitamura S, Japanese Off-Pump Coronary Revascularization Investigation (JOCRI) Study Group (2005) Early outcome of a randomized comparison of off-pump and on-pump multiple arterial coronary revascularization. Circulation 112(9 Suppl):I338–I343

37. Tsuruta R, Miyauchi K, Yamamoto T, Dohi S, Tambara K, Dohi T, Inaba H, Kuwaki K, Daida H, Amano A (2011) Effect of preoperative hemoglobin A1c levels on long-term outcomes for diabetic patients after off-pump coronary artery bypass grafting. J Cardiol 57:181–186
38. Kai M, Hanyu M, Soga Y, Nomoto T, Nakano J, Matsuo T, Umehara E, Kawato M, Okabayashi H (2007) Off-pump coronary artery bypass grafting with skeletonized bilateral internal thoracic arteries in insulin-dependent diabetes. Ann Thorac Surg 84:32–36
39. Fujii T, Watanabe Y, Shiono N, Kawasaki M, Yokomuro H, Ozawa T, Hamada S, Masuhara H, Koyama N (2007) Usefulness of perioperative blood glucose control in patients undergoing off-pump coronary artery bypass grafting. Gen Thorac Cardiovasc Surg 55:409–415
40. Nishiyama K, Horiguchi M, Shizuta S, Doi T, Ehara N, Tanuguchi R, Haruna Y, Nakagawa Y, Furukawa Y, Fukushima M, Kita T, Kimura T (2009) Temporal pattern of strokes after on-pump and off-pump coronary artery bypass graft surgery. Ann Thorac Surg 87:1839–1844
41. Doi K, Yaku H (2010) Importance of cerebral artery risk evaluation before off-pump coronary artery bypass grafting to avoid perioperative stroke. Eur J Cardiothorac Surg 38:568–572
42. Miyazaki S, Yoshitani K, Miura N, Irie T, Inatomi Y, Ohnishi Y, Kobayashi J (2011) Risk factors of stroke and delirium after off-pump coronary artery bypass surgery. Interact Cardiovasc Thorac Surg 12:379–383
43. Manabe S, Shimokawa T, Fukui T, Fumimoto KU, Ozawa N, Seki H, Ikenaga S, Takanashi S (2008) Influence of carotid artery stenosis on stroke in patients undergoing off-pump coronary artery bypass grafting. Eur J Cardiothorac Surg 34:1005–1008
44. Osawa H, Inaba H, Kinoshita O, Akashi O, Minegishi S (2011) Off-pump coronary artery bypass grafting with an aortic nonclamping technique may reduce the incidence of cerebral complications. Gen Thorac Cardiovasc Surg 59:681–685
45. Kobayashi J, Sasako Y, Bando K, Niwaya K, Tagusari O, Nakajima H, Nakamura Y, Ishida M, Kitamura S (2002) Multiple off-pump coronary revascularization with "aorta no-touch" technique using composite and sequential methods. Heart Surg Forum 5:114–118
46. Baba T, Goto T, Maekawa K, Ito A, Yoshitake A, Koshiji T (2007) Early neuropsychological dysfunction in elderly high-risk patients after on-pump and off-pump coronary bypass surgery. J Anesth 21:452–458
47. Ogawa M, Doi K, Yamada Y, Okawa K, Kan'bara T, Koushi K, Yaku H (2007) Renal outcome in off-pump coronary artery bypass grafting: predictors for renal impairment with multivariate analysis. Innovations 2:192–197
48. Kinoshita T, Asai T, Murakami Y, Suzuki T, Kambara A, Matsubayashi K (2010) Preoperative renal dysfunction and mortality after off-pump coronary bypass grafting in Japanese. Circ J 74:1866–1872
49. Hayashida N, Teshima H, Chihara S, Tomoeda H, Takaseya T, Hiratsuka R, Shoujima T, Takagi K, Kawara T, Aoyagi S (2002) Does off-pump coronary artery bypass grafting really preserve renal function? Circ J 66:921–925
50. Oyamada S, Kobayashi J, Tagusari O, Nakajima H, Nakamura S, Yagihara T, Kitamura S (2009) Is diabetic nephropathy a predicted risk factor? – Kaplan-Meier and multivariate analysis of confounding risk factors in off-pump coronary artery bypass grafting for chronic dialysis patients. Circ J 73:2056–2060
51. Sunagawa G, Komiya T, Tamura N, Sakaguchi G, Kobayashi T, Murashita T (2010) Coronary artery bypass surgery is superior to percutaneous coronary intervention with drug-eluting stents for patients with chronic renal failure on hemodialysis. Ann Thorac Surg 89:1896–1900
52. Suzuki T, Asai T, Matsubayashi K, Kambara A, Hiramatsu N, Kinoshita T, Nishimura O (2010) Left main coronary artery disease does not affect the outcome of off-pump coronary artery bypass grafting. Ann Thorac Surg 90:1501–1506
53. Fukui T, Tabata M, Manabe S, Shimokawa T, Shimizu J, Morita S, Takanashi S (2010) Off-pump bilateral internal thoracic artery grafting in patients with left main disease. J Thorac Cardiovasc Surg 140:1040–1045
54. Thielmann M, Leyh R, Massoudy P, Neuhäuser M, Aleksic I, Kamler M, Herold U, Piotrowski J, Jakob H (2006) Prognostic significance of multiple previous percutaneous coronary interventions in patients undergoing elective coronary artery bypass surgery. Circulation 114(1 Suppl):1441–1447
55. Fukui T, Manabe S, Shimokawa T, Takanashi S (2010) The influence of previous percutaneous coronary intervention in patients undergoing off-pump coronary artery bypass grafting. Ann Thorac Cardiovasc Surg 16:99–104
56. Kinoshita T, Asai T, Murakami Y, Takashima N, Hosoba S, Nishimura O, Ikegami H, Hiramatsu N, Suzuki T, Kambara A, Matsubayashi K (2009) Impact of previous PCI on hospital mortality after off-pump coronary artery bypass grafting in diabetic patients with multivessel disease. Innovations 4:334–339
57. Hosokawa K, Nakajima Y, Umenai T, Ueno H, Taniguchi S, Matsukawa T, Mizobe T (2007) Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery. Br J Anaesth 98:575–580
58. Ishida K, Kimura F, Imamaki M, Ishida A, Shimura H, Kohno H, Sakurai M, Miyazaki M (2006) Relation of inflammatory cytokines to atrial fibrillation after off-pump coronary artery bypass grafting. Eur J Cardiothorac Surg 29:501–505
59. Akazawa T, Nishihara H, Iwata H, Warabi K, Ohshima M, Inada E (2008) Preoperative plasma brain natriuretic peptide level is an independent predictor of postoperative atrial fibrillation following off-pump coronary artery bypass surgery. J Anesth 22:347–353
60. Fujii M, Bessho R, Ochi M, Shimizu K, Terajima K, Takeda S (2012) Effect of postoperative landiolol administration for atrial fibrillation after off pump coronary artery bypass surgery. J Cardiovasc Surg (Trino) 53:369–374
61. Kinoshita T, Asai T, Nishimura O, Hiramatsu N, Suzuki T, Kambara A, Matsubayashi K (2010) Statin for prevention of atrial fibrillation after off-pump coronary artery bypass grafting in Japanese patients. Circ J 74:1846–1851
62. Ito N, Tashiro T, Morishige N, Nishimi M, Hayashida Y, Takeuchi K, Minematsu N, Kuwahara G, Sukehiro Y (2010) Efficacy of propafenone hydrochloride in preventing postoperative atrial fibrillation after coronary artery bypass grafting. Heart Surg Forum 13:E223–E227
63. Kinoshita T, Asai T, Ishigaki T, Suzuki T, Kambara A, Matsubayashi K (2011) Preoperative heart rate variability predicts atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 91:1176–1181
64. Nakajima H, Kobayashi J, Funatsu T, Shimahara Y, Kawamura M, Kawamura A, Yagihara T, Kitamura S (2007) Predictive factors for the intermediate-term patency of arterial grafts in aorta no-touch off-pump coronary revascularization. Eur J Cardiothorac Surg 32:711–717
65. Manabe S, Fukui T, Shimokawa T, Tabata M, Katayama Y, Morita S, Takanashi S (2010) Increased graft occlusion or string sign in composite arterial grafting for mildly stenosed target vessels. Ann Thorac Surg 89:683–687
66. Sugimura Y, Toyama M, Katoh M, Kotani M, Kato Y, Hisamoto K (2011) Outcome of composite arterial Y-grafts in off-pump coronary artery bypass. Asian Cardiovasc Thorac Ann 19:119–122
67. Matsuura K, Kobayashi J, Tagusari O, Bando K, Niwaya K, Nakajima H, Yagihara T, Kitamura S (2004) Rationale for off-pump coronary revascularization to small branches: angiographic study of 1,283 anastomoses in 408 patients. Ann Thorac Surg 77: 1530–1534

68. Kinoshita T, Asai T, Nishimura O, Suzuki T, Kambara A, Matsubayashi K (2010) Off-pump bilateral versus single skeletonized internal thoracic artery grafting in patients with diabetes. Ann Thorac Surg 90:1173–1179
69. Saito A, Miyata H, Motomura N, Ono M, Takamoto S, Japan Cardiovascular Surgery Database Organization (2013) Propensity-matched analysis of bilateral internal mammary artery vs single internal mammary artery in 7702 cases of isolated coronary artery bypass grafting. Eur J Cardiothorac Surg 44:711–717
70. Marui A, Kimura T, Tanaka S, Furukawa Y, Kita T, Sakata R, CREDO-Kyoto Investigators (2012) Significance of off-pump coronary artery bypass grafting compared with percutaneous intervention: a propensity score analysis. Eur J Cardiothorac Surg 41:94–101
71. Yamagata K, Kataoka Y, Kokubu N, Kasahara Y, Abe M, Nakajima H, Kobayashi J, Otsuka Y (2010) A 3-year clinical outcome after percutaneous coronary intervention using sirolimus-eluting stent and off-pump coronary artery bypass grafting for the treatment of diabetic patients with multivessel disease. Circ J 74:671–678
72. Dohi S, Kajimoto K, Miyauchi K, Yamamoto T, Tambara K, Inaba H, Kuwaki K, Tamura H, Kojima T, Yokoyama K, Kurata T, Daida H, Amano A (2012) Comparing outcomes after off-pump coronary artery bypass versus drug-eluting stent in diabetic patients. J Cardiol 59:195–201
73. Shimizu T, Ohno T, Ando J, Fujita H, Nagai R, Motomura N, Ono M, Kyo S, Takamoto S (2010) Mid-term results and costs of coronary artery bypass vs drug-eluting stents for unprotected left main coronary artery disease. Circ J 74:449–455
74. Dohi M, Miyata H, Doi K, Okawa K, Motomura N, Takamoto S, Yaku H (2015) The off-pump technique in redo coronary artery bypass grafting reduces mortality and major morbidities: propensity score analysis of data from the Japan Cardiovascular Surgery Database. Eur J Cardiothorac Surg 47(2):299–307