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Review

The Past, Present, and Future of Off-Pump Coronary Artery Bypass Grafting

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The evolution of treatment for ischemic heart disease has been driven by advancements in both diagnostic and therapeutic methods, including coronary angiography, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG). Initially, CABG relied on on-pump techniques using saphenous vein grafts; however, off-pump coronary artery bypass grafting (OPCAB) emerged as an alternative to reduce complications associated with cardiopulmonary bypass. Despite potential benefits—such as a reduced risk of stroke, shorter hospital stays, and fewer respiratory and renal complications—OPCAB has seen limited adoption, particularly in Western countries, owing to its technical demands and concerns regarding graft patency and complete revascularization. Large-scale randomized trials have reported mixed results, with outcomes strongly influenced by surgeon experience and patient selection. In contrast, smaller studies by experienced surgeons have demonstrated comparable graft patency and superior outcomes in high-risk patients. Recent meta-analyses underscore the need for total arterial revascularization and no-touch aortic techniques to further optimize OPCAB results, particularly in high-risk populations. Moving forward, OPCAB shows significant promise for patients with severe comorbidities, such as those with calcified aortas or poor ventricular function. Enhanced training programs and hybrid revascularization strategies that integrate minimally invasive CABG with PCI could further expand OPCAB adoption. By leveraging its unique strengths—including reduced postoperative complications and improved outcomes for high-risk patients—OPCAB could play a pivotal role in modern cardiac surgery. To remain competitive with PCI, surgeons must actively prepare for OPCAB by developing expertise in both techniques tailored to the patient's clinical condition.

Keywords: Coronary artery bypass, Off-pump coronary artery bypass, Stroke, Internal mammary-coronary artery anastomosis

Introduction

The diagnostic and therapeutic approaches for ischemic heart disease have progressively advanced thanks to the dedicated efforts of numerous surgeons and researchers [1]. Among these innovations, the development of coronary angiography, cardiac medications such as aspirin, and the implementation of percutaneous coronary intervention (PCI) have played pivotal roles [2]. These breakthroughs marked significant turning points in medical treatment and spurred rapid progress in the field. Similarly, the establishment of the cardiopulmonary bypass (CPB) technique, the introduction of coronary artery bypass grafting (CABG) using grafts, the adoption of arterial conduits such as the internal mammary artery (IMA), and the development of off-pump coronary artery bypass grafting (OPCAB) have been critical milestones in surgical treatment [3]. Nonetheless, advancements in surgical techniques have progressed more slowly compared to developments in PCI with medical therapy.

As society has evolved, the number of patients with coronary artery disease has increased, partly due to a higher prevalence of older individuals with metabolic syndromes such as hypertension and diabetes [1]. Additionally, the advent of noninvasive coronary computed tomography has significantly improved the diagnosis of coronary artery disease. Concurrently, treatment methods have advanced;

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both CABG and PCI, when combined with cardiac medications, now yield excellent therapeutic outcomes.

These 2 treatment modalities exist in a competitive yet complementary relationship. However, with the rapid expansion of indications for PCI over time, more patients are now treated with PCI than with CABG. Therefore, CABG is typically reserved for patients who are not suitable candidates for PCI. The target vessels in these patients are often smaller and more diffusely diseased due to increased atherosclerosis and calcification, frequently accompanied by deteriorating ventricular function compared to the past. These changes present significant challenges for surgeons and necessitate adjustments in grafting strategies and surgical techniques to achieve optimal outcomes. Therefore, when planning CABG, there is a growing need for advanced techniques and grafting strategies, particularly OPCAB combined with an arterial grafting approach. This represents a departure from the traditional concept of CABG, which involved bypassing an arrested heart using the left IMA (LIMA) and a saphenous vein (SV). Accordingly, we aimed to provide a detailed overview of the history and current status of OPCAB, as well as to consider its future role and direction.

The past of off- and on-pump coronary artery bypass grafting

In the early days of treating ischemic heart disease, the CPB technique was not yet established, and no method existed to accurately delineate coronary anatomy prior to surgery; thus, it was challenging to establish an effective treatment method. Nonetheless, the fundamental concept of delivering oxygen to the heart muscle was already recognized. Although extensive research had been conducted to achieve this goal, a definitive method remained elusive. Early treatments involved blind operations without accurate information about coronary lesions or the use of CPB, which resulted in suboptimal outcomes for ischemic heart disease. However, the development of coronary cine-arteriography by Sones and Shirey [4] in 1962, coupled with the establishment of the CPB technique around the same time, led to rapid advances in the treatment of ischemic heart disease.

Beginning of off-pump coronary artery bypass grafting

Early studies on ischemic heart disease were conducted by Beck [5]. Vineberg and Miller [6] performed direct implantation of the LIMA into the myocardium through a tunnel, and Murray et al. [7] reported animal experiments in which the LIMA was directly bypassed into a coronary artery. Later, Longmire et al. [8] performed coronary endarterectomy in humans without CPB. In 1961, Senning [9] performed patch enlargement in the stenotic area of the coronary artery under CPB, and in 1965, Effler et al. [10] simultaneously attempted endarterectomy with patch graft reconstruction. This period was challenging because CPB was still under research and not yet fully established. Consequently, animal experiments and surgeries were performed on beating hearts or under unstable CPB conditions. Despite these difficulties, surgeons continued to innovate, establishing effective treatment concepts for ischemic heart disease and laying the groundwork for modern bypass grafting techniques in humans.

In 1964, Kolessov [11], who was conducting animal experiments in the Soviet Union—isolated from Western knowledge—successfully performed bypass surgery using the LIMA to the left circumflex artery without the aid of CPB or coronary angiography. This represented the first successful case of bypass surgery using an autologous graft for treating ischemic heart disease in humans, as well as the first recorded instance of OPCAB. However, due to limited communication between the Soviet Union and the West at the time, this achievement remained unknown to Western surgeons until 1967, when a case series involving 6 patients was presented at a European meeting [11]. Despite this, the technique by Kolessov [11] for beating-heart anastomoses using the LIMA did not attract much attention from the Western community. In the United States, Favaloro [12] and Johnson et al. [13] were developing bypass graft surgery in an arrested, bloodless field using the SV with CPB and coronary angiography, a method that rapidly became common, particularly in the United States.

At that time, it was believed that arterial conduits, including the LIMA, could develop diseases similar to those affecting the coronary arteries. Consequently, it was recommended that arteries, including the LIMA, should not be used as CABG conduits. Furthermore, it was advocated that the operation be performed on an arrested heart in a bloodless field for greater precision, rather than on a beating heart. Given the longer harvesting time and limited length of the LIMA, it was thought unsuitable for anastomosing multiple target vessels, particularly since composite grafting techniques had not yet been developed. Therefore, most surgeons refrained from using the LIMA as a CABG conduit.

In contrast, the SV was relatively easy to harvest and handle, and its ample length allowed for anastomosis to multiple target vessels, making it the preferred graft material for most surgeons. Moreover, rapid advances in the CPB technique enabled bypass surgery to be performed in a motionless and bloodless field. Consequently, the combination of CPB and SV made bypass surgery relatively straightforward, and CABG using only the SV as a graft became widespread worldwide.

Conversely, research on the LIMA, now recognized as the best CABG conduit, diminished significantly. Nonetheless, a few surgeons, including Green et al. [14]—who reported the first CABG using the LIMA in the Western world in 1968—continued to investigate its potential. However, due to the numerous advantages of the SV, this approach did not gain widespread adoption, and only a small group of surgeons continued to utilize the LIMA. Over time, the benefits of the LIMA's long-term patency and improved survival have been documented, and its use in CABG has gradually become more common. These efforts eventually led to the introduction of surgery using bilateral IMA (BIMA) in 1972. Despite this, BIMA is still performed in fewer than 5% of all CABG patients in the West, particularly in the United States [15]. This may be attributed to the fact that sequential grafting using the SV, first reported by Flemma et al. [16] in 1971, proved easier to perform than BIMA. This strategy paved the way for LIMA grafting to the left anterior descending artery (LAD) and sequential SV grafting to other target vessels, and it has become the most common grafting strategy in Western countries.

Early results of off-pump coronary artery bypass grafting

Although OPCAB in humans was first introduced by Kolessov [11] in 1967, it was not widely adopted by surgeons. However, Ankeney [17] presented the results of 143 OPCAB cases at the Society of Thoracic Surgeons meeting in 1972; although the target sites were limited to the LAD or right coronary artery (RCA), this report brought OPCAB to the attention of Western surgeons. Even though relatively few surgeons practiced this technique at the time, it sparked interest among some. Nevertheless, on-pump CABG remained the dominant technique in the United States and other Western countries.

OPCAB began to develop rapidly in the late 1970s at several centers in South America, where economic constraints made the high expense of CPB and the limited availability of necessary instruments a significant challenge. Consequently, OPCAB proved to be more cost-effective in that region. Benetti et al. [18] reported 700 OPCAB cases in 1991, which encouraged more surgeons worldwide to adopt the technique. However, the instruments used in contemporary OPCAB, such as the stabilizer, had not yet been developed, meaning that the procedure demanded greater technical skill than it does today. To overcome the initial learning curve, Benetti et al. [18] performed fewer than 50 cases per year for the first 10 years; the average number of bypass grafts was 2.2, and only 18% of patients received a circumflex artery bypass, highlighting the limitations of early OPCAB. Nonetheless, the surgical mortality rate was 1%, which was superior to that of on-pump CABG. The data by Benetti et al. [18] demonstrated excellent early postoperative outcomes—similar to those seen with current OPCAB techniques—including faster patient recovery, reduced mechanical ventilation time, lower requirements for blood transfusion and inotropic support, and cost savings.

Subsequently, Buffolo et al. [19], Tasdemir et al. [20], Trehan et al. [21], and others published favorable results for OPCAB, spurring further adoption in the West and around the globe. Since then, excellent surgical outcomes for OPCAB have been reported in the United States and Europe, with improvements in graft patency attributed to the development of stabilizing devices and advanced exposure techniques [22-25]. Based on these results, many surgeons have recognized OPCAB as a viable alternative to on-pump CABG. However, due to the inherent technical challenges of performing bypass on a beating heart, OPCAB has not been widely adopted. In contrast, the use of on-pump CABG has increased over time, driven by advancements in equipment and techniques that have reduced CPB-associated complications, as well as a growing preference among surgeons to avoid technically demanding procedures. Consequently, OPCAB has experienced a slight decline in popularity.

Present studies of off-pump coronary artery bypass grafting

Initially, OPCAB posed challenges not only for surgeons but also for anesthesiologists, due to the lack of essential instruments such as stabilizers, CO_2 blowers, and intracoronary shunts, as well as insufficient experience with anesthesia protocols and appropriate cardiac medications for OPCAB. Consequently, the technique was not widely considered by the Western world, including the United States, and did not emerge as a viable alternative to on-pump

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CABG until it began to attract the attention of surgeons in the 1980s.

Current status of off-pump coronary artery bypass grafting

In the 1990s, many excellent OPCAB outcomes were reported by surgeons in the United States and Europe. However, OPCAB did not receive widespread attention at that time because few large-scale randomized studies existed; most data were based on retrospective analyses from individual institutions. Although on-pump CABG outcomes have steadily improved, surgeons have been unable to overcome a 2% perioperative mortality rate and a 2%–5% incidence of perioperative myocardial infarction (MI), renal failure, and stroke associated with CPB. Moreover, continuous improvements in PCI—particularly in stent functionality—have further challenged CABG. As a result, to overcome the limitations of on-pump CABG and to achieve outcomes superior to PCI, further improvements in bypass surgery are necessary. In this context, many surgeons advocate for OPCAB as an alternative technique, and ongoing efforts aim to enhance its outcomes.

Current guidelines for off-pump coronary artery bypass grafting

The current US and European guidelines do not explicitly mention OPCAB [26,27]. The US guidelines recommend that, in patients with significant aortic calcification, techniques that avoid aortic manipulation (off-pump or beating-heart approaches) are reasonable to decrease the incidence of perioperative stroke, provided they are performed by experienced surgeons. In contrast, the European guidelines offer a slightly more specific recommendation: OPCAB and/or no-touch on-pump techniques on the ascending aorta should be considered in patients with significant atherosclerotic disease of the ascending aorta to prevent perioperative stroke, particularly for high-risk patients treated in high-volume off-pump centers [27]. These guidelines reflect the fact that OPCAB is not as common as on-pump CABG, and that excellent results are difficult to achieve when the procedure is performed by inexperienced surgeons due to its technical demands. Furthermore, there is limited data showing that OPCAB leads to better survival or lower rates of major adverse cardiovascular events than on-pump CABG. While outcomes are indeed superior when OPCAB is performed by experienced surgeons, this advantage may not be observed with less experienced operators. Therefore, surgeons may choose their technique based on experience and judgment in elective surgeries; however, accumulating experience with OPCAB remains essential. As the guidelines indicate, certain patients absolutely require OPCAB based on their condition, so even surgeons who primarily perform on-pump CABG should be capable of performing OPCAB when necessary.

Randomized trials of off-pump coronary artery bypass grafting

The landmark randomized trials related to OPCAB and their significance are summarized in Table 1. Even in the 2000s, OPCAB outcomes were mostly based on retrospective data. Most early studies showed results that were similar to or better than those of on-pump CABG, although a few studies reported poorer outcomes. As a result, the number of OPCAB cases gradually increased. However, the Randomized On/Off Bypass (ROOBY) trial in 2009 reported disappointing outcomes for OPCAB at early, 1-year, and 5-year follow-ups [28,29]. This trial played a significant role in the subsequent decline in OPCAB adoption, despite its growing use. The ROOBY trial found similar initial surgical outcomes between the techniques, but noted a statistically significant increase in 1-year cardiac deaths and lower graft patency for OPCAB patients. At 5-year follow-up, there were no differences in cardiac death, nonfatal MI, or repeat revascularization between the groups; however, the on-pump CABG group had better outcomes in terms of acute MI, repeat CABG, and 5-year survival. The 10-year follow-up revealed no difference in overall survival between the techniques, with only a slight advantage in revascularization-free survival for on-pump CABG [30]. Notably, the trial's limitations included a study population that was more than 99% male, excluding women who are at higher risk with CABG. Moreover, most male participants were veterans and did not represent general patient characteristics. Over 50% of the surgeons in the study were trainees with limited OPCAB experience, calling the reliability of the results into question. Although the authors claimed that outcomes from trainees were comparable to those from staff surgeons, the study's setting—a Veterans Hospital—suggests that even the staff surgeons may have had limited OPCAB experience. Consequently, the ROOBY trial negatively influenced OPCAB adoption, leading to a decline in its use not only in the United States but also in Europe. In the United States, the proportion of OPCAB cases peaked at 23% in 2002 and declined to 17% by 2012, 5 years after the ROOBY trial. Despite reports of no signif-

Table 1. Landmark randomized trials related to off-pump coronary artery bypass surgery

Trial	Study period	Patients (off-pump/ on-pump)	Centers	Surgeon experience	Patient profiles	Key findings	Significance
BHACAS	1997–1999	200/201	Single center (UK)	Not specified	Excluded high-risk patients: LVEF <30%, recent MI, prior CABG, renal or respiratory impairment	Off-pump surgery significantly reduced in-hospital complications (AF, infections, transfusion needs, ICU stay) without compromising midterm outcomes (1–3 years)	Demonstrated the advantages of OPCAB in early outcomes, addressing initial concerns about incomplete revascularization and graft patency.
ROOBY	2002–2008	1,104/1,099	18 US Veterans Affairs centers	Minimum 20 off-pump cases; average experience: 120 cases (median: 50); many operations performed by trainees	Predominantly male veterans; excluded severe comorbidities or urgent surgery cases	Off-pump group had worse 1-year graft patency and higher cardiac deaths. Long-term outcomes showed no significant survival differences.	Played a major role in the decline of OPCAB adoption due to disappointing results and study design limitations. Raised concerns about surgeon experience and reliability of outcomes.
SMART	2000–2001	100/100	Single center (Emory, USA)	Single experienced surgeon	Included multivessel coronary disease without exclusion criteria	Similar long-term survival and graft patency (7.5 years) between groups; off-pump reduced transfusion needs and hospital stay.	Highlighted the importance of surgeon experience, addressing concerns about long-term graft patency and survival. Supported OPCAB as a viable alternative to on-pump CABG.
GOPCABE	2008–2011	1,271/1,268	12 German centers	Off-pump: average 514 cases (median: 322); On-pump: average 1,378 cases (median: 578)	Patients aged ≥75 years; excluded urgent surgeries and prior pericardiotomies	No significant differences in major outcomes (death, stroke, MI) at 30 days and 1 year; slightly higher revascularization rates in the off-pump group.	Demonstrated that OPCAB outcomes can be comparable to on-pump CABG when performed by experienced surgeons, alleviating concerns raised by earlier trials like ROOBY.
CORONARY	2006–2011	2,375/2,377	Multicenter (worldwide)	Minimum 2 years of experience and >100 cases in both techniques	Included patients with relatively high-risk profiles; surgeons avoided off-pump for severe aortic disease	Similar major outcomes (death, MI, stroke) at 30 days, 1 year, and 5 years; the off-pump group had fewer respiratory complications and reoperations.	Addressed many negative perceptions from the ROOBY trial. Highlighted OPCAB's potential in high-risk patients and its comparability to on-pump CABG when performed by experienced surgeons.

BHACAS, Beating Heart Against Cardioplegic Arrest Studies; ROOBY, Randomized On/Off Bypass; SMART, Surgical Management of Arterial Revascularization; GOPCABE, German Off-Pump Coronary Artery Bypass Grafting in Elderly Patients; CORONARY, CABG Off or On Pump Revascularization Study; LVEF, left ventricular ejection fraction; MI, myocardial infarction; CABG, coronary artery bypass grafting; AF, atrial fibrillation; ICU, intensive care unit; OPCAB, off-pump coronary artery bypass.

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icant differences in heart failure, angina, atrial fibrillation, or 10-year survival, most hospitals, including the Veterans Hospital, continued to favor on-pump techniques. This trend was observed in both low- and high-volume CABG centers in the United States and Europe. Thus, the decline in OPCAB volume is attributed to randomized trials like ROOBY that failed to demonstrate clear advantages for OPCAB, the inherent technical difficulty of the procedure, and the potential for incomplete revascularization when performed by less experienced surgeons [31]. Although the ROOBY trial did not significantly influence surgeons who specialize in OPCAB, its results may have affected those including young surgeons who prefer to avoid the technically demanding procedure.

The clinical outcomes of OPCAB have been consistently reported since its inception. Early reports were produced during a period when commercial stabilizers or intracoronary shunts were not available to minimize ischemia during anastomosis, and when anesthetic agents and expertise were limited. Moreover, most early data were based on single-center retrospective studies rather than randomized trials, resulting in heterogeneous outcomes that varied with surgeon competence. While surgeons experienced in OPCAB generally reported better early postoperative results than on-pump CABG at the same institution, there were occasional exceptions. Overall, most results were either similar to or better than those of on-pump CABG. However, initial data also highlighted issues with incomplete revascularization and midterm or long-term graft patency, often due to inaccurate anastomoses caused by a lack of appropriate instruments, insufficient OPCAB experience, and limited anesthesia expertise. These challenges have made many surgeons hesitant to adopt OPCAB.

In 2002, Angelini et al. [23] reported the Beating Heart Against Cardioplegic Arrest Studies (BHACAS) trial, a randomized controlled study comparing OPCAB and on-pump CABG. This study, conducted when the surgical risks of OPCAB were partly mitigated by the use of a stabilizer and an intracoronary shunt, demonstrated several advantages of OPCAB. The trial found that OPCAB reduced the need for inotropes, the incidence of atrial fibrillation and arrhythmias, chest infections, and blood transfusions. Additionally, OPCAB was associated with shorter ventilator times, reduced intensive care unit (ICU) stays, and shorter overall hospital stays, indicating excellent early outcomes. However, the differences between the 2 techniques did not significantly affect midterm outcomes. This important trial confirmed that OPCAB had a positive impact on early outcomes and achieved comparable midterm results (at least 3 years postoperatively), thereby alleviating concerns about incomplete revascularization and poor graft patency [23,32].

In 2011, Puskas et al. [33] reported the Surgical Management of Arterial Revascularization (SMART) trial, which evaluated graft patency and long-term survival—factors previously cited as drawbacks of OPCAB in the ROOBY trial. Although a single-center study, the SMART trial was significant because it compared graft patency and long-term survival in consecutive patients with multivessel coronary disease, without exclusion criteria. The number of grafts was similar between OPCAB and on-pump CABG, and most patients underwent preoperatively intended complete revascularization. Early outcomes showed that OPCAB was associated with shorter hospital stays, reduced transfusion requirements, and lower cardiac enzyme release, while early mortality, stroke, MI, and in-hospital and 30-day major adverse cardiac events were similar between the groups. Graft patency, evaluated before discharge, at 1 year, and at 7.5 years postoperatively, was similar for both techniques across different coronary territories. Long-term survival was comparable at 1 year, but a favorable trend for OPCAB emerged at 3 years, though it was not statistically significant. By 5 years, a statistically significant survival advantage for OPCAB was observed, which persisted at 7 years. Unlike the ROOBY trial, the SMART trial was conducted by an experienced surgeon, making it a significant contribution to the debate over long-term graft patency and survival with OPCAB [33].

The German Off-Pump Coronary Artery Bypass Grafting in Elderly Patients (GOPCABE) study was another multicenter randomized trial that focused on elderly patients aged over 75 years. The participating surgeons had performed more than 500 OPCAB or on-pump CABG procedures. Although both methods involved fewer than 3 graft anastomoses—raising concerns that complete revascularization might not have been achieved in many cases—the study found no differences between the 2 techniques at 30 days and 1 year postoperatively regarding death, stroke, MI, repeat revascularization, or the need for new renal replacement therapy. These results from experienced surgeons suggest that OPCAB can yield outcomes that differ from those reported in the ROOBY trial, which involved less experienced operators. While OPCAB did not demonstrate a clear advantage over on-pump CABG, it also did not show inferior outcomes, thereby alleviating concerns about long-term graft patency and survival [34].

Concerns regarding the long-term survival of OPCAB were further alleviated by the CABG Off or On Pump Revascularization Study (CORONARY) trial, a large multicenter, multinational randomized study involving over 4,000 patients. In this study, surgeons with at least 2 years of experience and over 100 cases in each technique participated. Although the number of grafts was similar between the techniques, the OPCAB group had a slightly lower average (3.0 versus 3.2), which resulted in higher rates of incomplete and early revascularization. However, there were no differences in major outcomes—such as mortality, MI, stroke, and renal failure—at postoperative day 30. Minor outcomes, including reoperation, respiratory complications, and acute kidney injury, were lower with OPCAB. One-year follow-up results showed no significant differences in major outcomes, including the repeat revascularization rate, and there were also no differences in quality of life or neurocognitive function between the groups. The 5-year follow-up similarly revealed no differences between the 2 techniques. An unexpected finding was the lack of difference in stroke incidence, which was anticipated to favor OPCAB. The authors noted that surgeons often chose OPCAB over on-pump CABG when the condition of the ascending aorta increased the risk of stroke. Although this represents a limitation of the trial, it also implies that patients at risk for stroke may benefit from OPCAB. Despite this drawback, the CORONARY trial successfully addressed many negative perceptions of OPCAB generated by the ROOBY trial, and it highlighted the potential for OPCAB to be effectively used in high-risk patients, particularly when performed by experienced surgeons [35-37].

Meta-analyses of off-pump coronary artery bypass grafting

A recent meta-analysis comparing the 10-year mortality outcomes of OPCAB and on-pump CABG found no significant difference between the 2 techniques, despite OPCAB patients being older and having a lower left ventricular ejection fraction. The authors emphasized that successful OPCAB results depend on surgeon experience, the ability to manipulate the heart without causing hemodynamic instability, technical proficiency in performing multiple distal anastomoses, and the anesthesiologist's expertise in intraoperative management [38].

Another study summarized the advantages and disadvantages of these 2 approaches. Operative mortality was similar between the techniques, although small randomized controlled trials (RCTs) indicated reduced mortality among patients with ST elevation undergoing urgent or emergent OPCAB. Mid- and long-term survival outcomes were also comparable, except in the ROOBY trial, which has been criticized for its surgeon selection. Studies by experienced surgeons have reported no significant differences in graft patency at 30 days or 1 year postoperatively; however, some investigations noted lower graft patency with OPCAB, particularly for vein grafts. This disparity may partly result from more pronounced postoperative thrombocytosis following OPCAB compared to on-pump CABG, underscoring the importance of postoperative antiplatelet therapy—especially to prevent early occlusion of vein grafts. Notably, many studies were conducted before the adoption of optimal medication protocols (e.g., dual antiplatelet therapy for vein grafts), which may have adversely affected reported patency rates. Yet, a long-term follow-up over 6–8 years reported no significant difference in graft patency between the techniques. While several studies have noted fewer graft anastomoses and consequently higher repeat revascularization rates with OPCAB, research conducted by experienced surgeons found no differences in these parameters. Regarding stroke and neurocognitive outcomes, OPCAB may offer advantages due to reduced aortic manipulation; however, aside from a few reports, it has not consistently demonstrated a clinical benefit over on-pump CABG. This lack of benefit may be partly due to the limited use of an-aortic techniques in OPCAB procedures. Moreover, OPCAB has been reported to benefit renal preservation and reduce bleeding, transfusion requirements, and respiratory complications—especially in high-risk patients [39].

Another meta-analysis of 51 RCTs reported similar advantages and disadvantages for the 2 techniques. In this analysis, short- and mid-term rates of MI and mortality were similar between OPCAB and on-pump CABG. However, OPCAB was associated with fewer graft anastomoses and higher rates of mid-term graft failure and repeat revascularizations. On the other hand, the incidence of postoperative stroke, low cardiac output, and renal dysfunction was lower in patients undergoing OPCAB. Furthermore, OPCAB reduced ventilation time, ICU stay, hospital stay, transfusion requirements, and overall hospital costs [40].

A separate meta-analysis comparing graft patency between the techniques reported disappointing outcomes for OPCAB, though the analysis was affected by biases related to surgeon experience, perioperative medications, and heterogeneous follow-up durations. The findings indicated poorer graft patency with OPCAB, particularly for vein grafts and for grafts bypassing the LAD and circumflex territories. In contrast, patency rates were comparable for arterial conduits and for grafts bypassing the RCA territory. In summary, the lower graft patency rate observed with OPCAB was mainly due to occlusion of SV grafts rather than arterial grafts. These results suggest that the future of OPCAB should emphasize total arterial revascularization using BIMA and the radial artery, alongside dual antiplatelet therapy for vein grafts [41].

Off-pump coronary artery bypass grafting in high-risk patients

Most studies comparing OPCAB and on-pump CABG have primarily included low-risk patients, with few high-risk cases. This has made it challenging to demonstrate a clear clinical benefit of OPCAB over on-pump CABG, even though guidelines suggest that OPCAB's advantages are more pronounced in high-risk patients. Although studies in high-risk patients have typically been conducted by experienced surgeons due to the complexity of these cases, it remains uncertain whether OPCAB can consistently yield better outcomes than on-pump CABG. One study, however, may offer insights into this issue. Puskas et al. analyzed data from over 7,000 patients undergoing either OPCAB or on-pump CABG, using the Predicted Risk of Mortality (PROM) from the STS database. They found no mortality difference between the groups among low-risk patients with a low PROM, but OPCAB was associated with lower mortality in high-risk patients with a high PROM. These differences appeared to widen as the PROM increased, suggesting that OPCAB should be actively considered for high-risk patients [42].

Perioperative stroke can arise from various causes, including postoperative atrial fibrillation, thromboembolic events due to a hypercoagulable state, and cerebral ischemia during surgery. However, the most common cause is atheroma embolization resulting from intraoperative aortic manipulation. A meta-analysis of 100 RCTs examining stroke within 30 days post-surgery demonstrated that OPCAB reduced stroke incidence by 28% and improved outcomes for all-cause mortality or MI [43]. Another meta-analysis reported that OPCAB without aortic clamping achieved a 56% reduction in mortality and a 44% reduction in the composite endpoint of death and stroke compared with on-pump CABG [44]. These findings suggest that OPCAB—especially an-aortic OPCAB—offers significant advantages in reducing postoperative stroke compared to on-pump CABG. In the 5-year follow-up of the SYNTAX trial, a landmark study comparing PCI and CABG, CABG showed lower risks of death, MI, and repeat revascularization compared to PCI. Moreover, a higher SYNTAX score, indicating greater complexity and risk, amplified the advantage of CABG over PCI. However, regarding stroke, the early postoperative incidence was significantly lower in PCI patients, though the rates became comparable at 5 years [45]. It is noteworthy that only 13.9% of CABG patients in the SYNTAX trial underwent OPCAB. This finding was unexpected, as the BEST trial—where 64.3% of CABG patients received OPCAB—reported no difference in early postoperative stroke incidence between CABG and PCI groups [46]. Additionally, a direct comparison of OPCAB and PCI revealed that the initial stroke incidence was lower in OPCAB patients (0.5% versus 1.2%) [47].

A study comparing OPCAB and on-pump CABG in octogenarian patients reported excellent outcomes for OPCAB. The procedure was associated with a lower risk of stroke and atrial fibrillation. The authors concluded that OPCAB might be a valid option to reduce procedure-related morbidity in high-risk patients, particularly those at elevated risk for cerebrovascular events [48]. These findings underscore the potential of OPCAB to reduce stroke incidence and support the use of an-aortic OPCAB when stroke risk is a concern.

A study comparing 3 techniques—OPCAB, on-pump CABG, and on-pump beating-heart CABG—in patients with acute coronary syndrome demonstrated excellent outcomes for OPCAB. Although rates of stroke, renal dysfunction, and ICU stay did not differ significantly among the groups, OPCAB had the highest probability of being the most effective treatment regarding 30-day mortality, showing a 72% reduction in the likelihood of 30-day mortality [49].

Registry data on OPCAB in emergency situations—including patients with cardiogenic shock (36.3%) and PCI complications (15.9%)—demonstrated favorable outcomes. In this study, only 4.4% of cases required conversion to on-pump CABG even in emergencies, 98.2% utilized LIMA, and 79.6% achieved complete revascularization, with an average of 3.04 grafts per patient. Consequently, the overall mortality rate was 5.3%. These findings indicate that OPCAB can be effectively and safely employed in high-risk patients requiring emergency surgery [50].

Uncertainty remains regarding why OPCAB appears more advantageous for high-risk patients compared to on-pump CABG. The improved surgical outcomes related to stroke reduction can be attributed to OPCAB employing a no-touch aortic technique. However, other benefits of OPCAB in high-risk patients are less clearly supported by evidence. It may be that patients with low or intermediate risk can better withstand the adverse effects—such as multi-organ injury, oxidative stress, abnormal fluid shifts, and myocardial reperfusion injury—associated with CPB and its inflammatory response, whereas high-risk patients cannot as effectively recover from these insults.

Crossover of off-pump coronary artery bypass grafting

One reason surgeons hesitate to attempt OPCAB is the potential need for emergent conversion to on-pump CABG, which can seriously adversely affect surgical outcomes. Although conversion from the planned technique is uncommon, it can occur for various reasons, and its incidence can be minimized with increased experience.

During crossover, elective conversion that occurs before starting the graft bypass is generally not problematic, as it does not significantly affect heart function. In contrast, urgent or emergent conversions during anastomosis or heart verticalization can lead to severe hemodynamic instability, resulting in increased perioperative morbidity and mortality due to myocardial damage. Intraoperative conversion rates have been reported to range up to 19.4% (with an average of 4.9%), and STS data in the United States reported a rate of 2.2%. In the CORONARY trial, emergent conversion occurred in 3.2% of cases due to intraoperative hypotension and ischemia, while elective conversion occurred in 4.7% of cases, typically due to small or intramuscular coronary arteries. The report identified chronic atrial fibrillation, urgent surgery, a planned high number of graft anastomoses, and limited surgeon experience in OPCAB as risk factors for emergent conversion. Furthermore, the conversion rate varied depending on the inclusion of high-risk patients, such as those with myocardial dysfunction or ischemic mitral regurgitation [51].

Elective conversion does not significantly affect surgical outcomes; however, emergency conversion exacerbates myocardial damage and prolongs surgical time, leading to increased bleeding, extended ventilation time, and higher inotrope requirements. Furthermore, emergent conversion raises the risk of respiratory failure, renal failure, perioperative MI, stroke, and the need for intra-aortic balloon pump support and extracorporeal membrane oxygenation, thereby increasing postoperative complications and mortality.

Emergent conversion should generally be considered if any of the following conditions are present: a cardiac index below 1.5 L/min/m^2, SVO_2 below 60%, mean arterial pressure under 50 mm Hg, systolic pulmonary artery pressure exceeding 50 mm Hg, ST-segment elevation over 2 mV, the occurrence of malignant arrhythmias, or significant new wall motion abnormalities on transesophageal echocardiography. In practice, these thresholds are not always definitive; therefore, the decision often relies on the experience and judgment of the surgeon and anesthesiologist. In emergent conversion, on-pump beating-heart CABG offers advantages regarding myocardial injury, blood loss, and renal complications compared to arrested-heart CABG. Some studies have reported early mortality benefits approaching 50% with on-pump beating-heart CABG. This outcome aligns with the theoretical premise that on-pump beating-heart CABG is less susceptible to global myocardial ischemia-reperfusion injury and systemic inflammation than arrested-heart CABG. Although this technique may increase the risk of incomplete revascularization if performed by inexperienced surgeons, it has demonstrated greater benefits in high-risk patients, particularly those with low ejection fractions, acute coronary syndrome, or requiring hemodialysis [52-54].

OPCAB is not uniformly practiced worldwide, and its prevalence varies significantly by country. This variation may stem from a greater emphasis on its disadvantages, despite its many advantages; however, the exact reasons for these differences remain unclear. In the United States and Europe, OPCAB is currently performed in less than 20% of all coronary bypass surgeries, and its use is declining. In contrast, OPCAB is the preferred technique in several Asian countries, such as Korea and Japan, where it is performed in over 60% of cases and continues to gain popularity.

Future of off-pump coronary artery bypass grafting

OPCAB is technically more demanding than on-pump CABG and may lead to lower graft patency and a reduced rate of complete revascularization. This concern often discourages surgeons from adopting OPCAB. Nevertheless, OPCAB offers several advantages over on-pump CABG. Notably, OPCAB has demonstrated superior outcomes in high-risk patients and in those with porcelain or severely atherosclerotic aortas, for whom on-pump CABG may not be viable. Moreover, for patients requiring aortic manipulation for various reasons, employing a proximal seal system rather than side-clamping may help reduce the risk of stroke and other complications [55].

Large-scale randomized trials have thus far failed to demonstrate a convincing advantage of OPCAB over conventional CABG. This is primarily because these studies were conducted predominantly in low-risk patients and of-

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ten by relatively less experienced surgeons. While some encouraging results have emerged, they are largely limited to outcomes from a few renowned surgeons at high-volume centers and are difficult to generalize. These factors have contributed to the stagnant adoption rate of OPCAB. Consequently, significant changes are required for OPCAB to evolve into the primary CABG technique and to prove its superiority in competing with PCI in the future [56,57].

An-aortic off-pump coronary artery bypass grafting with total arterial revascularization

The exclusive benefits of OPCAB should be fully leveraged. One major advantage of OPCAB is that it can be performed without manipulating the aorta, thereby lowering the incidence of postoperative stroke compared to on-pump CABG. To further prevent or reduce postoperative stroke, the no-touch aortic technique should be actively implemented. As reported in the SYNTAX trial, the risk of stroke was significantly increased in patients undergoing on-pump CABG or OPCAB with aortic manipulation compared to PCI. Consequently, the no-touch technique is essential. Achieving an aortic no-touch approach requires a composite graft strategy, regardless of the graft material used. Fig. 1 illustrates a grafting strategy for total arterial revascularization without aortic manipulation. A composite graft comprising the LIMA combined with either the right IMA or a radial artery can achieve total arterial revascularization and potentially improve long-term survival.

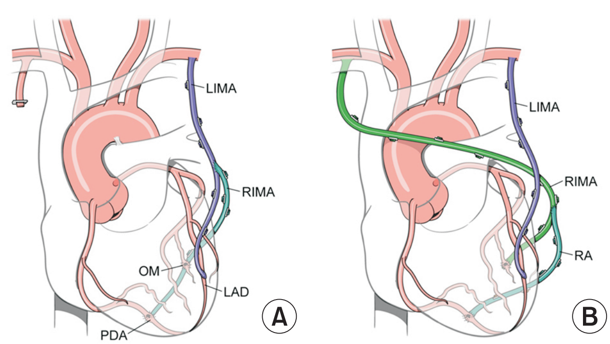

Fig. 1. A schematic illustration of an-aortic off-pump coronary artery bypass grafting with total arterial revascularization. (A) A composite graft using the left internal mammary artery (LIMA) and right internal mammary artery (RIMA); the RIMA was anastomosed to the *in-situ* LIMA, with the LIMA serving as the sole inflow source for the entire coronary bypass. (B) Bilateral *in-situ* internal mammary artery configuration; the radial artery (RA) was anastomosed to the *in-situ* RIMA, providing a dual inflow source without aortic manipulation. OM, obtuse marginal; LAD, left anterior descending artery; PDA, posterior descending artery.

One study on an-aortic OPCAB with total arterial revascularization demonstrated reductions in stroke, postoperative delirium, and early postoperative cognitive dysfunction compared with OPCAB involving aortic manipulation [58]. Therefore, the aortic no-touch technique should be widely adopted in the future. However, in the United States, only 4.1% of CABG procedures use BIMA, 5.5% utilize the radial artery, and multiple arterial grafting is performed in just 10%–15% of cases, indicating that CABG is losing ground in its competition with PCI.

To improve long-term survival and achieve superior results in major adverse cardiovascular events compared with PCI, an an-aortic total arterial revascularization strategy—uniquely feasible with OPCAB—should be prioritized, particularly in patients at risk for stroke. Therefore, OPCAB employing composite grafts composed exclusively of arterial conduits, along with the aortic no-touch technique, should become the primary surgical method in the future, especially in the absence of CPB.

Hybrid coronary revascularization

In the future, hybrid coronary revascularization (HCR) should be pursued. Current coronary revascularization guidelines emphasize the superiority of LIMA-to-LAD anastomosis as a key reason for preferring CABG over PCI. It is widely agreed among cardiologists and surgeons that LIMA-to-LAD is the most effective revascularization method. Based on this fact, HCR was designed to explore how LIMA-to-LAD CABG can be integrated with PCI in a complementary approach. This is because PCI techniques, including the qualitative development of stents, are more likely to develop faster than surgical techniques of CABG, and PCI is more likely to dominate over time. It is therefore necessary to study HCR, where LIMA to LAD bypassing is performed in a minimally invasive direct CABG approach, while other target vessels are treated with PCI in cases of multivessel coronary artery disease. Although this approach is not necessarily superior to total arterial revascularization using the aortic no-touch technique, it offers an attractive option for surgeons with less OPCAB experience. Additionally, HCR may appeal to patients who prefer a minimal incision and could serve as a promising strategy for future coronary revascularization.

Training in off-pump coronary artery bypass grafting

Training processes must be developed to make OPCAB more accessible to surgeons. However, training in OPCAB is more challenging than for on-pump CABG because performing anastomoses on a beating heart places a significant burden on novice surgeons. Even experienced surgeons may experience reduced accuracy when suturing on a moving target vessel. Moreover, the myocardium can only tolerate ischemia for a limited time—typically less than 15 minutes—necessitating rapid completion of the anastomosis. Consequently, extensive training time is not feasible. OPCAB training programs must be tailored to the circumstances of each surgeon or center. One beneficial approach is to develop suturing skills on a beating heart through animal experiments using pig hearts. Pig hearts are useful for training because their coronary anatomy closely resembles that of humans and their size is slightly larger. Thus, using pig hearts to teach techniques—such as the use of stabilizers, CO_2 blowers, and suturing on a beating heart—serves as an effective training method. However, not all surgeons have access to animal facilities for training.

Recently, commercial *in vitro* OPCAB training devices have been developed, providing an alternative for institutions without animal training resources. Ultimately, while institutional training methods and environments are important, it is paramount for surgeons to continuously practice suturing techniques independently, whether *in vivo* or *in vitro*.

Conclusion

OPCAB is currently performed in approximately 20% of all CABG procedures worldwide, except in Korea and Japan, where it is more common. This figure reflects the concentration of OPCAB cases in high-volume centers rather than indicating that 20% of surgeons routinely perform OPCAB. In fact, fewer than 20% of surgeons preferentially perform OPCAB. Consequently, most CABG procedures globally are performed using on-pump CABG—a trend influenced by improvements in cardiopulmonary pump devices and perfusion techniques. Moreover, on-pump CABG may facilitate complete revascularization and yield superior long-term graft patency in low-risk patients, a trend likely to persist in the near future. Nonetheless, as the number of high-risk patients unsuitable for on-pump CABG increases, the demand for OPCAB will rise. Therefore, surgeons must actively prepare for OPCAB. To remain competitive with PCI, it is imperative that surgeons develop proficiency in both techniques, tailoring their approach according to each patient's morbidity.

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