Review Article

Off-Pump All Arterial Coronary Artery Bypass Grafting

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There is growing acceptance of the long-term durability of using coronary artery bypass grafting (CABG) for the treatment of coronary artery disease (CAD). The idea is to give an antegrade flow to the coronary artery circulation, thereby relieving angina. CABG as used in clinical practice since the 1960s, is arguably the most intensively studied surgical procedure ever, while percutaneous coronary intervention (PCI), used for over three decades, has been subjected to more randomized clinical trials (RCTs) than any other interventional procedure. In comparison with CABG, PCI unfortunately has a higher rate of reintervention. In 2009, the American College of Cardiology (ACC), Society for Cardiovascular Angiography and Interventions (SCAI), Society of Thoracic Surgeons (STS), American Association for Thoracic Surgery (AATS), American Heart Association (AHA), and the American Society of Nuclear Cardiology (ASNC) jointly launched appropriateness criteria for revascularization.[1] Appropriateness criteria are based on current understanding of the technical capabilities and potential patient benefits of the procedures examined. Coronary revascularization is appropriate when the expected benefits, in terms of survival or health outcomes (symptoms, functional status, and/or quality of life) exceed the expected negative consequences of the procedure. The methods of revascularization depend mainly on symptoms, clinical presentations and coronary artery anatomy. Generally, surgery is mostly appropriate except for certain situations, for example, prior bypass surgery with native triple vessel disease, and failure of multiple bypass grafts with patent left internal thoracic artery (LITA) to the native coronary artery, depressed left ventricular ejection fraction. Percutaneous coronary intervention (PCI) has many uncertainties and may be inappropriate in the following conditions: left main (LM) coronary artery disease; multivessel coronary artery disease associated with diabetes, and depressed left ventricular function.

In 2010, the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI) developed a new guideline for myocardial revascularization.[2] Some of the recommendations were (1) Non-emergent high-risk PCI procedures, (including those performed for distal LM disease, complex bifurcation stenosis involving large side branches, single remaining coronary artery, and complex chronic total occlusion recanalization) should be performed by adequately experienced operators at centers that have access to circulatory support and intensive care treatment, and have cardiovascular surgery on site. (2) For patients with stable CAD and multivessel or LM disease, all relevant data should be reviewed by a clinical/noninvasive cardiologist, a cardiac surgeon, and an interventional cardiologist to determine the likelihood of safe and effective revascularization with either PCI or CABG. PCI is more preferential for one or double vessel disease - non-proximal LAD. The recommended risk stratification score to be used in candidates for percutaneous coronary intervention is the SYNTAX score. The SYNTAX score was derived from the combined angiographic anatomic classifications of each significant lesion from the SYNTAX (SYNergy between PCI with TAXUS and Cardiac Surgery) trial.[3] The SYNTAX score has been shown to be an independent predictor of major adverse cardiac events in patients treated with PCI. For example, patients with triple vessel complex lesions, incomplete revascularization achievable with PCI and SYNTAX score >22 should have CABG rather than PCI. Patients with LM and double vessel or triple vessel disease and SYNTAX score ≥33 should also have CABG in preference to PCI.

The most common risk models for CABG are The Society of Thoracic Surgeons (STS) score and the European System for Cardiac Operative Risk Evaluation (EuroSCORE). In contrast with the SYNTAX score, STS score and EuroSCORE were calculated from clinical variables rather than angiographic anatomy. STS risk models are based upon clinical data from The Society of Thoracic Surgeons National Adult Cardiac Surgery Database, one of the oldest and largest of all specialty registries.[4] The EuroSCORE, developed in 128 centers in eight European states, aims to predict 30-day mortality of patients undergoing cardiac surgery.[5] It has been validated with good results in European, North American and Japanese populations.[6-8] It has also been used to predict other useful endpoints including long-term mortality[9], intensivecare unit stay,[10] complications and costs of cardiac surgery.[11] Both the STS and EuroSCORE risk algorithms are good predictors of early mortality from offpump coronay artery bypass grafting (OPCAB) or Onpump coronary artery bypass grafting (ONCAB).

Compared with PCI, however, CABG presents a greater immediate risk of mortality and morbidity, as well as higher initial costs. When these 2 procedures have been compared longitudinally over several years, however, the total costs become similar, due to the greater need for reintervention after PCI. Off-pump coronary artery bypass grafting (OPCAB) has been developed and re-popularized over the past decade, in order to reduce morbidity and mortality due to conventional CABG or on-pump coronary artery bypass grafting (ONCAB), which cardiopulmonary bypasses and cardioplegic arrests require. Cardiopulmonary bypass (CPB) is associated with an acute phase reaction of protease cascades, leucocyte, and platelet activation that result in tissue injury.[12] This largely manifests as subclinical organ dysfunction, which produces a clinical effect in those patients that exhibit an excessive inflammatory response, or in those with limited functional reserve. The risks of myocardial ischemia/reperfusion, (otherwise associated withaortic crossclamping, and cardioplegic arrest), and systemic inflammatory response or wider organ dysfunction, are known to be elicited by cardiopulmonary bypass (CPB). OPCAB was developed precisely in order to alleviate and minimize complications from CPB and cardioplegic arrest; therefore complete revascularization can be achieved with excellent long-term results and reduction of morbidity and/or mortality.

In addition to the CPB, the quality of conduits for CABG also determines the clinical outcome and more importantly, patients' long-term survival after CABG. The objectives of this review are to (1) compare the rationale and outcome of OPCAB and ONCAB, and (2) compare the results of arterial conduits and vein grafts.

Off-Pump Coronary Artery Bypass Grafting (OPCAB) vs. On-Pump Coronary Artery Bypass Grafting (ONCAB)

"Only the man who is familiar with the art and science of the past is competent to aid in its progress in the future"

Theodor Billroth

Concepts of surgical treatment of CAD have been developed since 1880.[13] Interestingly, the idea of surgical revascularization was first suggested when Langer observed the interconnections within the coronary system, and between coronary vessels and surrounding extracardiac structures such as the diaphragm, bronchi, and the pericardium. In 1898, Pratt suggested that coronary sinus blood flow could be reversed by the insertion of an artery into the myocardial venous system thereby enhancing myocardial blood flow. Much of the early surgical treatment of CAD however, was primarily concerned with relieving the discomfort of angina, rather than with revascularizing the myocardium. In 1899 for example, Parisian Professor of Physiology, Charles Emile Francois Franck, suggested treating angina by performing sympathetic ganglionectomy of the upper thoracic ganglia to divide the afferent pain fibres.[14] Another palliative approach for treating angina, namely thyroidectomy, emerged from Kocher's observation in 1902 that a patient with angina became asymptomatic after total thyroidectomy.[15] Finally, Wearn, who had found connections between the cardiac chambers and the myocardial sinusoids, suggested in 1928 that "if coronary flow was occluded, flow in the Thebisian vessels could be reversed, thus supplying blood from the ventricular cavities to the myocardium". Many surgeons experimented with these ideas. In 1930, Claude Beck championed early attempts at increasing the blood supply to the myocardium by inducing pericardial scarring and thereby encouraging neovascularization.

Several other operations (cardiopneumopexy, cardio-jejunopexy, cardiogastropexy, cardiolienopexy) and revascularization of the heart by tubed pedicle graft of skin and subcutaneous tissue were also developed. Other indirect coronary revascularizations were (1). coronary sinus arterialization using brachiocephalic, subclavian, and innominate arterial grafts, (2) increasing left heart volume by created a surgical communication between the pulmonary artery and left atrium in patients in an effort to increase left heart volume and thus antegrade coronary artery blood flow, (3) increasing coronary collateral by the bilateral ligation of the distal internal thoracic arteries would shunt flow through branches of the pericardiophrenic arteries back through the heart via vascular anastomoses within the epicardium, (4) increasing pulmonary collaterals by ligating the lingular vein and then suturing the lingula to the epicardium. However none of these gave good clinical outcomes. Transmyocardial laser which was clinically employed in 1983 was also developed by indirect revasculaization concept. In 1946, Vineberg developed a procedure involved tunneling of the internal thoracic artery (ITA) into the left ventricular myocardium as a form of indirect myocardial revascularization.

The idea of operating directly on the coronary arteries was conceived as early as the first decade of the twentieth century when Alexis Carrel's experiments grafting both arteries and veins in animals paved the way for the development of direct CABG in humans. He developed a technique of vascular anastomosis (applicable to either small or large arteries and veins) which achieved a watertight suture without narrowing the caliber of the vessel. His experimental results of anastomosing the innominate artery of one dog into the distal coronary artery of another were reported in 1910. He also performed the first CABG using a free carotid artery graft anastomosed between the descending thoracic aorta and left coronary artery. In addition, he first performed vein bypass grafting by anastomosing a vein into a transected aorta. At this time, this operation was performed with difficulty and carried a high mortality rate. In 1912, Carrel was awarded the Nobel Prize in Medicine or Physiology for his work on transplantation and vascular grafting.[16] Myocardial revascularization by anastomosing the ITA to the coronary artery was advocated by Demikhov[17], who undertook a canine study of this technique in 1952; 4 of his dogs survived for more than 2 years with patent grafts. Robert H. Goetz performed the first successful clinical CABG on May 2, 1960.[18] He used a non-suture technique to connect the right ITA to the coronary artery by means of a modified Payr's cannula made of tantalum.[19] The patency of the anastomosis was demonstrated angiographically and the patient remained free of angina pectoris for 1 year. Kolessov, a Russian surgeon, performed the first successful human CABG in 1964 when he anastomosed an ITA to a coronary artery through a left thoracotomy without the use of CPB.[20,21] (Table 1) This was achieved almost simultaneously and independently by Gordon Murray in Canada.[22]

The development of coronary arteriography by Sones[23] in the early 1960s at the Cleveland Clinic enabled for the first time accurate identification of the location and degree of coronary stenoses to help direct CABG, and work there subsequently focused on direct endarterectomy with patch-graft reconstruction.[24] Several years later, Favaloro at the Cleveland Clinic refined the technique of CABG using the greater saphenous vein (SV) as a conduit, the operation became more widely accepted and appreciated.[25]

Table 1: The First Clinical Coronary Artery Bypass Operations

Date	Surgeon	Graft	Technique	Follow-up
May 2, 1960	Goetz	RITA	Tantalum ring	No angina at 1 year Pt. died of AMI 1.5 years later
April 4, 1962	Sabiston[26]	SV	Suture	Pt. died 3 days later (This case first reported in 1974)
Feb 25, 1964	Kolesov	LITA	Suture	No angina at 3 years' follow-up
Nov 23, 1964	Garrett Dennis DeBakey[27]	SV	Suture	No angina at 7 years' follow-up (This case first reported in 1973)
Mar 22, 1967	Kolesov	LITA	Stapling	No angina at 3 years' follow-up
May 9, 1967	Favaloro[25]	SV	Suture	Successful
Feb 29, 1968	Green[28]	LITA	Suture	Successful

AMI = acute myocardial infarction; LITA = left internal thoracic artery; RITA = right internal thoracic artery; SV = saphenous vein.

The heart-lung machine was developed at the same time as indirect and direct coronary revascularization techniques became established. Initial investigations into systemic hypothermia and inflow occlusion began at the University of Minnesota. Such a heart-lung machine would first require a safe method of anticoagulation that could be reversed at the end of the operation; second, it would require a method of pumping blood without destruction of red blood cells; and third, there would have to be a method to oxygenate blood and dissipate carbon dioxide during the time that the heart and lungs were temporarily at rest. The first 2 requirements were easily met. Heparin and protamine were readily available, and there were several pumps being used in the dairy and food industry that could be adapted. The real problem was to develop an artificial oxygenator. This turned out to be difficult. Then, in 1937, Dr John Gibbon began work on a pump oxygenator that he finally put into clinical practice on May 6, 1953.[29] His technical achievements were astounding; however, when compared with today's knowledge and technology, they appear rudimentary, and indeed, after having only 1 survivor in his first 6 cases, he essentially abandoned its use. Although during the same period, C. Walton Lillehei at Minnesota was poised to begin a clinical trial in which the oxygenator would be either the mother or father of the patient, a technique called cross circulation. He did 45 operations using cross circulation and had 28 survivors. Although there was great interest in this technique, it was not adopted by other surgical groups. The risk of injury of the parent acting as the donor was a major concern.[30]

Finally, at the Mayo Clinic, John Kirklin and his colleagues were building a heart-lung machine based on the Gibbon design that used a vertical film oxygen-ator and roller pumps. It was called the Mayo-Gibbon heart-lung machine. This is the first truly commercial heart-lung machine, which was used in 1950s and early 1960s. The heart-lung machine was used routinely in operations for ischemic heart disease in the late 1960s. In 1959 Dubost et al. became the first to perform a coronary artery operation in a human using heart-lung machine or cardiopulmonary bypass (CPB) when they performed coronary ostial reconstruction on a patient with syphilitic aortitis.[31] On April 4, 1962, David Sabiston, Jr, performed the first saphenous vein–coronary artery bypass grafting procedure without using CPB in the world.[32] After 1968, CABG with CPB was widely adopted. Favaloro et al. at The Cleveland Clinic subsequently popularized the use of autologous saphenous vein segments as bypass grafts.[25, 33] The major advance of 1968 was the implementation of ITA grafting by several groups. Though Goetz and Kolesov had performed the first such human operations, it was only in 1968 that broad use of the procedure began. Bailey was the first to perform the procedure that year[34], followed soon by Reed, who became the first to perform the operation using CPB and fibrillation. Further application of the ITA occurred with the work Spencer[35] and Green, of the group at New York University. During the next 10 years, after the first operation using CPB, the operative mortality for open heart surgery rapidly decreased each year. Better oxygenators, better surgical techniques, better cardiology, and many other improvements brought the risk of death down to single-digit levels. The current heart-lung machine is now simplified and adoption of its use is widespread (Figure 1).

Figure 1: *Heart-Lung Machine at the Bangkok Heart Hospital*

CPB however does have some specific drawbacks, with several potentially harmful effects on normal homeostatic physiology which include (1) the effects of hypothermia, (2) the physiologic derangements caused by contact of blood with artificial surfaces, (3) the need for anticoagulation, and (4) the alterations in perfusion mechanics to organ systems. Hypothermia during CPB causes alterations in drug metabolism and distribution, and adverse effects on coagulation through both the intrinsic and extrinsic pathways and inhibition of platelet function. Enzymatic reactions are delayed, and vasomotor changes result in reduced organ perfusion and redistribution of blood away from the heart. When blood comes into contact with artificial surfaces, several inflammatory responses are initiated through activation of the complement cascade, coagulation pathways, and the kallikrein cascade.[36] The coagulation cascade is activated and clotting occurs. Therefore the anticoagulant, heparin needs to be given during CPB. Despite the reversal of the heparin effect by using protamine at the end of CPB, postoperative bleeding occasionally occurs because of platelet dysfunction and fibrinolysis. Neutrophil activation plays a major role in the systemic inflammatory response and organ dysfunction. At the beginning of CPB, neutrophil counts measured in both atria increase. Once blood flow is restored to the lungs, however, neutrophil counts continue to increase only in the right atrium, as opposed to a decline in the left atrium, due to trapping within the pulmonary capillaries. Proteolytic enzymes are released and free oxygen radicals are produced, both of which lead to extensive endothelial cell damage, increased vascular permeability, and capillary leak. For many patients, it is a subclinical event, but in some it may advance to a life threatening, fulminant condition, similar to adult respiratory distress syndrome (ARDS), otherwise known as noncardiogenic pulmonary edema. Both fluctuations in arterial pressure and the absence of pulsatile blood flow with CPB may lead to transient hypoperfusion to the organs. The kidneys in particular are susceptible, and impairments in baseline (or preoperative) renal function may lower the threshold for postoperative renal dysfunction or failure. In addition, it is thought that splanchnic hypoperfusion, resulting in circulating endotoxins, causes activation of macrophages and monocytes, and is responsible for the direct relationship between the duration of CPB and the level of tumor necrosis factor-alpha (TNF-α) in the blood. The side effects of CPB are summarized in Table 2.

Table 2: The side effects of cardiopulmonary bypass

Inflammatory responses
• Plasma protease cascades
• Cellular response and tissue injury
• Cytokine response
Clinical organ dysfunction
• Myocardial injury
• Renal injury
• Pulmonary injury
• Neurological injury

The clinical benefits possible in avoiding the CPB's side effects became the driving force for many of cardiac surgeons to develop OPCAB techniques. Furthermore techniques of myocardial protection during induced temporary cardiac arrest and types/ routes of cardioplegic solution delivery play also important roles for outcome of ONCAB. While the basic pathobiology of myocardial ischemic injury and reperfusion has been determined over the last 50 years, there are important, unresolved, or at least not completely elucidated, issues in the field. These include the relative contributions of different modes of cell injury and death to evolving myocardial infarcts; interactions of phenomena produced by reperfusion including stunning and preconditioning. Promising new cardioprotective strategies for reducing lethal reperfusion injury are discussed, including ischemic postconditioning, activators of the reperfusion injury salvage kinase pathway, inhibitors of protein kinase c-delta, and inhibitors of the mitochondrial membrane permeability transition pore.[37] Complex multiple coronary reconstructions in high risk patients requiring long periods of aortic cross-clamping are particularly associated with high rates of morbidity and mortality because of damage to the myocardium.[38]

In the late 1980s, general surgeons began to develop and expand the practice of less invasive surgical techniques. The trend established by laparoscopic removal of the gallbladder rapidly spread to other abdominal and retroperitoneal operations, encouraged by the reports of faster recovery without sacrificing quality outcomes. In the present time, the laparoscopic cholecystectomy has become a standard surgical procedure for gallbladder surgery. For cardiac surgery, several North American surgeons became interested in using the coronary stabilizer for OPCAB in 1997. In 1998, Jansen et al. reported the design, experimental evaluation, and the first clinical use of this novel suctionbased mechanical coronary artery stabilizing system. After federal approval of the device, they began clinical application of this stabilizer. Early experience with the device was limited to vessels on the anterior surface of the heart, which were easily bypassed with excellent stabilization. Lateral and posterior vessels presented technical challenges because hemodynamic tolerance to the cardiac displacement necessary for exposure was poor. After experimental evaluation of the hemodynamic consequences of vertical cardiac displacement, techniques were developed and shared and gradually more surfaces of the heart could be approached safely. In the early 1990s, another sternotomy-sparing approach was used for CABG. A short, transversely placed, several-centimeter left anterior thoracotomy incision was used to access to the anterior surface of the heart which the LITA could be harvested and anastomosed to the LAD. This minimally invasive direct coronary artery bypass (MIDCAB) operation accomplished the goal of avoiding a sternotomy; however, CPB could also be avoided, and the concept of an off-pump approach gained greater acceptance. Most surgeons believed that avoiding of

CPB was the major advantage of minimally invasive surgery rather than changing skin incision. Three major developments that make multivessel OPCAB possible are (1) cardiac displacement/ exposure, (2) stabilization and (3) instruments for clearing surgical view for coronary artery anastomosis (Figure 2). The sequence of steps, anastomotics techniques, pharmacologic manipulations need to be changed from the traditional ONCAB. Dr. Visudharom K. (Kit Arom), former director of the Bangkok Heart Hospital and Chief of Cardiovascular & Thoracic Surgery, was one of the pioneers in USA who developed the OPCAB techniques. OPCAB was later adopted well as a standard CABG at the Bangkok Heart Hospital.[39-46] One of the concerns in adopting off-pump techniques is abandoning the safety net provided by CPB. Crashing in the middle of an OPCAB procedure is particularly difficult, both because of the lack of planning, as well as the often-dangerous hesitancy to use CPB and abandon one's goal of performing the operation offpump. Therefore, it is important for surgeons to know how to prevent rapid hemodynamic deterioration and how to respond when it occurs. The conversion rate from OPCAB to ONCAB at the Bangkok Heart Hospital has decreased year by year. The conversion rate in the past year was close to zero even the OPCAB had been used in 99% of cases.

The numbers of OPCAB patients and surgeons who perform OPCAB are increasing over the years. The potential benefits of OPCAB are (1) zero mortality, (2) less morbidity, (3) less blood transfusion, (4) reduced inotropic requirements, (5) reduced myocardial injury, (6) faster recovery, (7) short hospitalization, and finally (8) reduction of costs. The evidence of improvement are several, both at the molecular level and with regard to clinical outcomes.[47-53] Monocyte activation plays a key role in amplifying both inflammatory and coagulopathic sequelae in patients undergoing ONCAB. Greilich PE. et al. showed that activationdependent increases in monocyte surface changes (CD11b expression and monocyte-platelet conjugate formation)

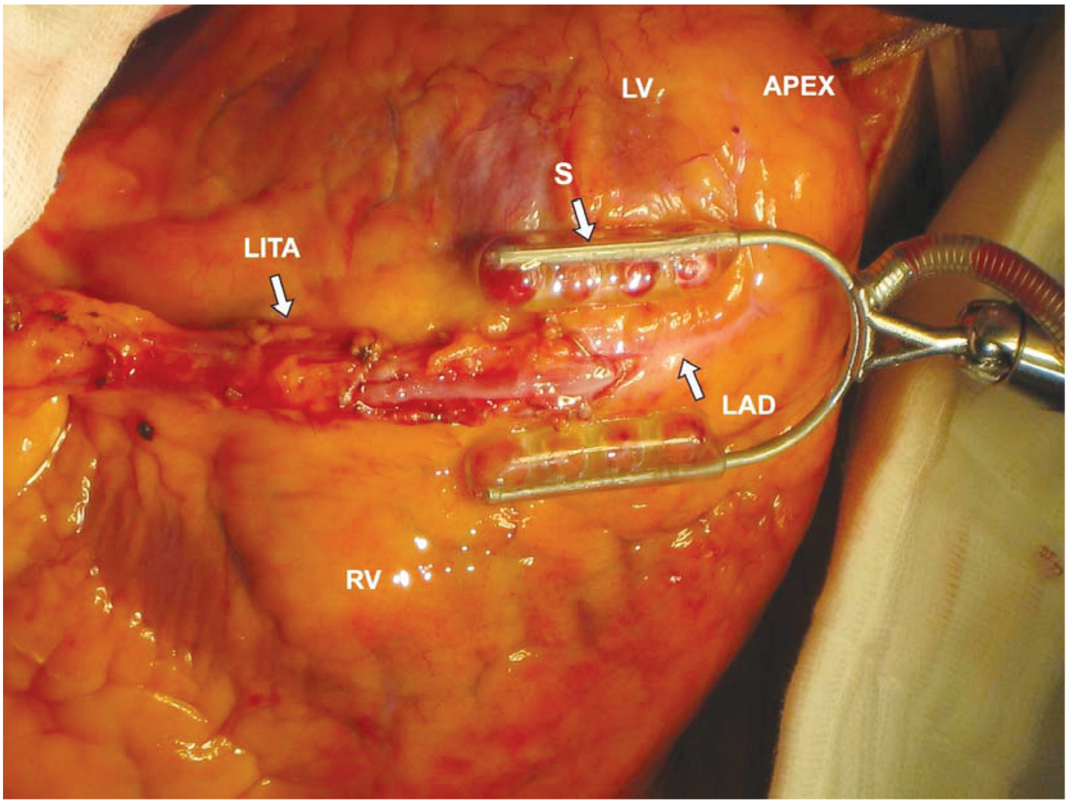

Figure 2: *The left internal thoracic artery was anastomosed to the left anterior descending artery with off-pump technique. Stabilizing arm with suction foot is on the area of anastomosis of the left anterior descending artery.*

LV = Left ventricle, **S** = Stabilizer, **LITA** =Left internal thoracic artery,
LAD = Left anterior descending artery, **RV** = Right ventricle

associated with ONCAB are abolished when performed OPCAB. The plasma increases in the monocyte-secreted cytokines IL-6, IL-8 and IL-10 were both delayed, and their amounts diminished when CABG was performed off pump.54 The use of CPB in ONCAB contributes to the postoperative inflammatory response. The molecular chaperone heat-shock protein (HSP) 70 may be induced by ischemia, and has been detected both in the myocardium and in the circulation after CABG. In vitro, extracellular HSP70 may activate both innate and adaptive immunity. Dybdahl B. et al. demonstrated that significantly more HSP70 is released after ONCAB than after OPCAB, possibly indicating a difference in inflammatory responses, cellular stress or damage, between the two procedures.[55]

Talpahewa SP. et al. studied the changes in cortical cerebral oxygenation during ONCAB using the Near infrared spectroscopy.[56] They found that ONCAB is responsible for deterioration in [O_2Hb], and cerebral blood volume, which peaks at 40-60 min following initiation of CPB. The changes in [O_2Hb] are reversible whereas the reduction of cerebral blood volume persists to the end of the surgery. This suggests a transient impairment in the autoregulatory mechanisms controlling cerebral blood flow following discontinuation of CPB. Lee et al. performed a prospective RCT, demonstrating that ONCAB was associated with more cerebral microemboli and significantly reduced cerebral perfusion (post-op) to the bilateral occipital, cerebellar, precunei, thalami, and left temporal lobes than was the case with OPCAB.[57] Compared with base line, OPCAB patients performed better on the Rey Auditory Verbal Learning Test (total and recognition scores) at both 2 weeks and at 1 year whereas ONCAB performances were statistically unchanged for all cognitive measures.

One major concern for OPCAB is graft patency, which may be compromised because of poor visualization during anastomosis. Angelini GD. et al. compared long-term outcomes in patients randomized to OPCAB or ONCAB, who were followed up for 6 to 8 years after surgery.[58] Patency was studied in 199 of 349 survivors. There was no evidence of attrition bias. The likelihood of graft occlusion was no different between OPCAB (10.6%) and ONCAB (11.0%) groups (odds ratio, 1.00; 95% confidence interval, 0.55-1.81; $p > .99$). In addition to concern about the graft patency, surgeons who use ONCAB might be worried by evidence that surgeons perform fewer grafts with OPCAB compared with ONCAB. However, the absolute difference reported by a systemic review of 22 RCTs was only 0.2 grafts fewer with OPCAB. Incomplete coronary revascularization is not a problem in our experience, even with small coronary arteries in diabetic patients.[59] The advantages of OPCAB perhaps demonstrate better in high risk patients with several comorbidities. Generally for OPCAB experienced surgeons, the outcomes are excellent comparable to the ONCAB (Table 3).[60-62]

However, there were also negative studies that did not demonstrate the benefit of OPCAB; even those showing worse outcomes than ONCAB.[63-65] Several problems were raised in these studies. General limitations of the randomized controlled trials include study design, patient selection, and inadequate sample sizes. For example, a prospective randomized study detecting statistically significant differences in 30-day mortality (2.9% ONCAB versus 2.4% OPCAB) requires the randomization of 15598 patients in each treatment group ($\alpha = 0.05$, power = 0.8). Meta-analysis is a useful tool for formally summarizing the available information and creating hypotheses that may be tested in future trials. However limitations are flawed methods of each study, publication bias, variation of concomitant treatments (co-interventions) and heterogeneity of studies. The other common factor is surgical experience.[58] OPCAB is a new technique and it requires a lot of practice to be able to do an efficient coronary anastomosis in all areas of the left ventricle.

Arterial Grafts vs. Venous Grafts

Long-term patency of a bypass graft is an important determinant in reducing morbidity and increasing survival after CABG. Problems in graft patency study include (1) lack of uniform definitions of graft failure, (2) most studies were of symptomatic angiogram (many graft failures cause no symptom), (3) exact time of graft failure was unknown, and (4) the use of appropriate statistical models for analysis. The traditional conduits are left internal thoracic artery (LITA) and saphenous vein graft (SV). Kaplan–Meier (K-M) estimates of patency suggest that about 85–92% of LITA grafts are patent at 15 years. Unfortunately K-M estimates of patency of SV at 10 and 20 years are only 60% and 20% respectively.[76, 77] Mechanisms of SV graft failure could be divided into (1) intrinsic causes and (2) extrinsic causes. The intrinsic causes include poor vein quality, missed valve/ branch (in situ), branch ligature placement, intimal flaps, intimal hyperplasia, accelerated atherosclerosis, aneurysmal dilatation. The extrinsic causes are anastomotic problems, inflow tract stenosis or occlusion outflow tract stenosis or occlusion, thromboembolism and mechanical compression of graft. The pathology of SV graft disease consists of thrombosis, neointimal hyperplasia, and atherosclerosis. Therapeutic strategies to prevent SV graft disease include external stenting, pharmacotherapy, and gene therapy. However the successes of laboratory studies have not been replicated in the clinic yet.[78, 79] Because of the growing evidence of the benefits of arterial grafts, the right internal thoracic artery (RITA), right gastroepiploic artery (RGEA) and radial artery (RA) have been investigated and used more frequently. There was a survival benefit and a lower reintervention rate in favour of bilateral over single ITA grafting in a wide range of patients that continued into the third decade after surgery.[80]

Table 3: Summary of the randomized controlled trials comparing off-pump (OPCAB) and on-pump (ONCAB) surgery

Study	No. of Patients		Results
	OPCAB	ONCAB	
van Dijk[66, 67]	142	139	No. of anastomosis - no diffference Blood products and Release of creatine kinase muscle-brain isoenzyme - less in OPCAB Complications - no differences Survival free cardiovascular events - no differences OPCAB - no effect on 5-year cognitive or cardiac outcomes
Angelini[68]	200	201	OPCAB significantly lowers in-hospital morbidity without compromising outcome in the first 1-3 years after surgery compared with ONCAB.
Puskas[69]	100	100	OPCAB achieved similar completeness of revascularization, similar inhospital and 30-day outcomes, shorter length of stay, reduced transfusion requirement and less myocardial injury.
Muneretto[70]	88	88	OPCAB could be successfully used for total arterial grafting without compromising the completeness of revascularization. Avoidance of CPB significantly decreased mechanical ventilation support and length of intensive care unit and postoperative stay.
Khan[71]	54	50	OPCAB was as safe as ONCAB and caused less myocardial damage. The graft-patency rate was lower at three months in the OPCAB than in the ONCAB.
Legare[72]	150	150	There were no significant differences between the OPCAB and the ONCAB in mortality, transfusion, perioperative myocardial infarction, permanent stroke, new atrial fibrillation, and deep sternal wound infection. The mean time to extubation was 4 hours, the mean stay in the intensive care unit was 22 hours, and the median length of hospitalization was 5 days in both groups.
Al-Ruzzeh[73]	84	84	OPCAB showed similar patency of grafts, better clinical outcome, shorter hospital stay and better neurocognitive function than ONCAB.
Fattouch[51]	63	66	OPCAB reduced early mortality and morbidity in patients with STsegment elevation myocardial infarction in respect to the ONCAB. OPCAB showed better results than ONCAB in patients who underwent surgery within 6 hours from the onset of symptoms and in patients with cardiogenic shock.
Moller[74]	176	163	No significant difference was found in the composite primary outcome (i.e., all-cause mortality, acute myocardial infarction, cardiac arrest with successful resuscitation, low cardiac output syndrome/cardiogenic shock, stroke, and coronary reintervention) after 30 postoperative days, nor were any of the individual components of the primary outcome significantly different.
Hueb[75]	155	153	No difference was found between groups in the primary composite end point (death, myocardial infarction, further revascularization or stroke) at 5-years follow-up.

Buxton B. et al. advocated the use of RITA for grafting coronary arteries with a high grade stenosis or occlusion, for grafting left rather than right coronary arteries, and using in situ rather than free ITA grafts. Passing the RITA to the left, either anterior to the aorta or through the transverse sinus, did not influence patency.[81]

The RA initially was used as a conduit for coronary artery bypass grafting by Carpentier and associates in 1973.[82] In contrast to other arterial conduits, the RA appeared to offer a highly promising alternative for a number of technical reasons. It is easily harvested and handled during the surgery. It is similar in length and size to the ITA, its diameter is closer to the size of the coronary artery than that of the SV. However, despite these potential advantages, Curtis and colleagues reported in 1975 that the failure rate of RA grafts in a group of 79 patients was 64.7% at 6 to 12 months after operation.[83] This represented a significantly higher failure rate than that of the SV and ITA grafts used in the same patients. Furthermore, one of the histologically normal RA grafts removed at reoperation revealed marked concentric intimal hyperplasia. This shed considerable doubt upon the viability of the RA as an alternative graft. In 1976 Chiu suggested that the thick-walled RA appeared to depend more on vasa vasorum for its integrity than the thin-walled vein. The vasa vasorum of free RA graft, which disrupted at both ends, cannot regenerate readily from the adjacent tissue and may have been more vulnerable to intimal hyperplasia and occlusion than either SV or ITA grafts.[84] In 1976 Fisk and colleagues reported results from 48 RA grafts. After 1 to 24 weeks, only 50% of RA grafts were patent compared with 77% of SV grafts. These authors suggested that the RA should not be used. As a result of these poor results the RA fell out of favor, and only recently has been rediscovered as a viable conduit.

The early 1990s witnessed a revival of interest in the RA. During this period, Carpentier and associates were contacted by a patient who had been part of their trial conducted in the 1970s. This patient's RA graft was thought to have occluded soon after surgery. However, to their surprise, an angiogram 18 years later indicated that the RA was in fact patent and free from disease. This discovery led to Acar and colleagues to reinvestigate the use of the RA for CABG.[86]

Several studies confirmed its suitability. Ruengsakulrach P., et al. studied cadaver's hand and found that a complete (classic) superficial palmar arch was found in 10% of hands, and a classic complete deep palmar arch was found in 90% of hands.[87] Although the superficial palmar branch of the ulnar artery was continuous with the radial artery in only 34% of hands, every hand had at least one major branch connecting the radial and ulnar arteries. Therefore in the absence of vascular disease, harvesting the radial artery should be regarded as a safe procedure.

Intimal hyperplasia which was thought to be cause of graft failure occurs as a consequence of physiologic stimuli, constituting an attempt by the tissue to maintain normal conditions of flow and/ or wall tension. Regions of the intima with adaptive increases in thickness differ functionally from adjacent, thinner regions. Excessive lipoprotein in the plasma tends to accumulate preferentially in the hyperplastic intima causing atherosclerosis.[88] From the histopathology study, the RA is more likely to have atherosclerosis, intimal hyperplasia, and medial calcification than the ITA.[89] The ITA is elastic artery as compared to the RA which is muscular artery and the ITA has more internal elastic lamina layers than the RA. This may be one of the reasons that the RA has higher incidence of atherosclerosis than does the ITA.[90] Since the RA is a muscular artery therefore it is a vasoreactive conduit which has high tendency of vasospasm than the ITA and is reason that the ITA and is reason that postoperative calcium blocker may be indicated. The incidence of medial calcification (Monckeberg's calcinosis) in the RA was 13.3%.[89] Medial calcification of an artery, even when extensive, is not necessarily associated with extensive intimal changes and the lumen of the artery is not to be compromised by the medial change. On the contrary, vessels with marked calcification often show less intimal involvement than is average for that age. The degree of intimal hyperplasia in the RA was due to increasing age, diabetes, history of smoking, and peripheral vascular disease.[89] The use of RA in these patients should be carefully considered.

The prevalence of the RA calcification (intimal or medial) detected by preoperative assessment of the RA by ultrasound in patients who were scheduled for CABG was 24.7%. Echogenic plaques were found in 6.8% and the overall incidence of RA abnormality (calcification or echogenic plaques) was 31.5%.[91] Older or male patients or those with carotid artery disease are at a high risk for RA calcification alone; those who have carotid disease or peripheral vascular disease tend to have a higher risk of any RA abnormality.

There were two randomized trials regarding the RA patency namely "the radial artery patency and clinical outcomes (RAPCO) trial" [92, 93] and "the radial artery patency study (RAPS) trial".[94] The RAPCO demonstrated that there are no clinical or angiographic differences between RA and free RITA or the SV graft at 5 years follow up. The RAPS found the failure rate of RA was 8.2% versus failure rate of SVG 13.6% ($p = 0.009$). They concluded that the RA was superior to the SV. However if the seven RA conduits which had the "string-sign" were considered failures, instead of patent, the results were almost identical. The trials need to be followed for another 5 years, since vein graft disease rapidly progresses after 5 years of grafting. Table 4. summarizes the graft patency according to the 2010 recommendations by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS).[2]

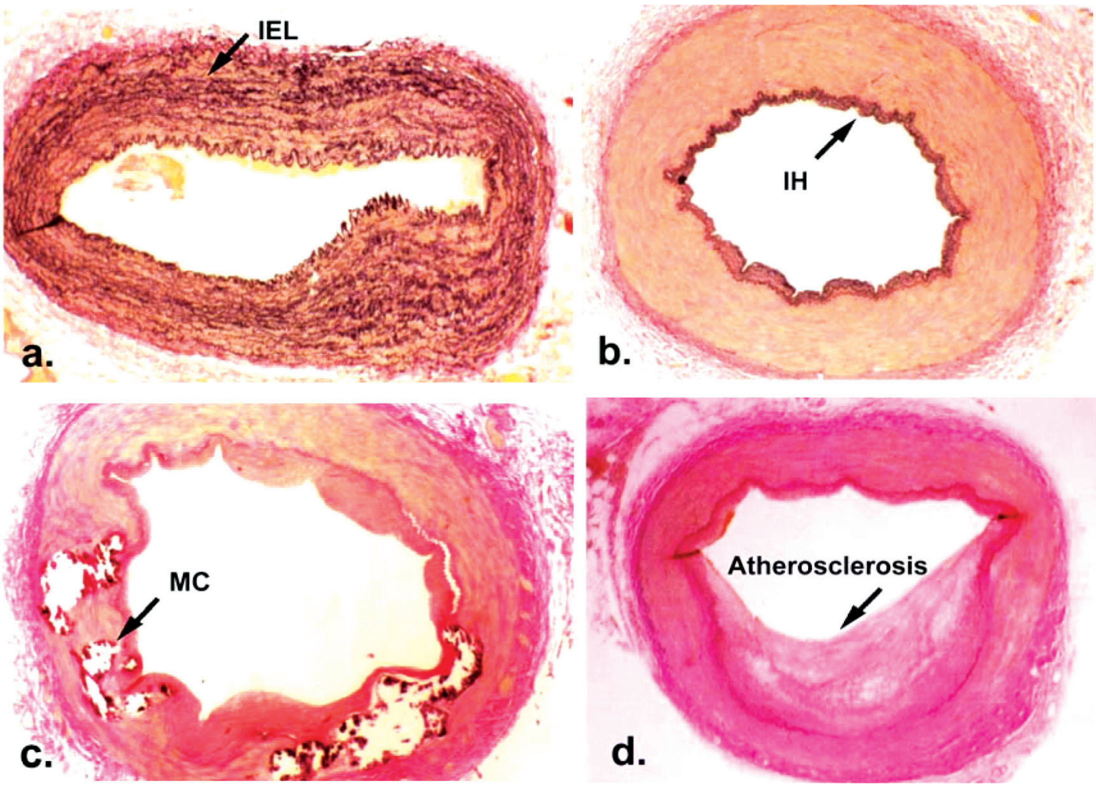

Figure 3: *Histopathology of the internal thoracic artery (ITA) and radial artery (RA), (a.) The ITA demonstrates internal elastic lamina (IEL). [Verhoeff Van Gieson's elastin ´ 20 (original magnification)] (b.) The RA demonstrates intimal hyperplasia (IH). [Verhoeff Van Gieson's elastin ´ 20 (original magnification)] (c.) The RA demonstrates medial calcification (MC) in the media of the arterial wall. [Haematoxylin-eosin´25 (original magnification)] (d) The RA demonstrates atherosclesosis. [Haematoxylin-eosin´25 (original magnification)]*

ITA = internal thoracic artery; RA = radial artery; IEL = internal elastic lamina; IH = intimal hyperplasia; MC = medial calcification

Table 4: Graft patency after coronary artery bypass grafting (%)

Graft	Patency at 1 year	Patency at 4-5 years	Patency at 10-15 years
SV 95, 96	>90	65-80	25-50
Radial artery 94, 96	86-96	89	Not reported
Left ITA 96, 97	>91	88	88
Right ITA 96	Not reported	96	65

ITA = internal thoracic artery; SV = saphenous vein.

To expand the use of the RA and avoid aortic cross clamping during proximal inflow graft anastomosis, composite graft (T or Y graft) has been introduced. (Figure 4) Muneretto C. et al. performed a prospective randomized study compared composite arterial graft (LITA-RA, n=80) with a standard aortocoronary graft with SV (LITA and SV, n = 80).[98] They found a lower incidence of stroke, graft occlusion and recurrent angina in the composite arterial graft group.

For RGEA, two large studies of about 1000 cases have indicated 5-year patencies of 62% and 86%.[99, 100] A current reviews indicated RGEA performance was similar to that of the SV. Low-grade stenosis of the target coronary artery proximally or competitive flow is a major cause of early RA and RGEA graft failure.

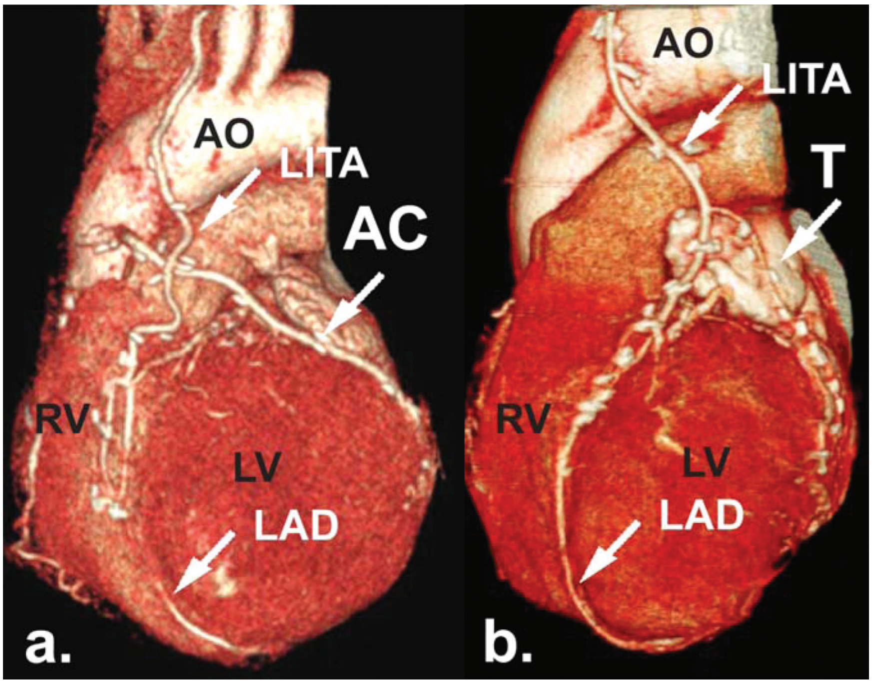

Figure 4: 256 slice computed tomography volume-rendering image in the left anterior oblique projection. (a.) the radial artery (aortocoronary graft) to the obtused ***marginal branch of the left circumflex artery (b.) the radial artery (T graft from the left internal thoracic artery) to the obtused marginal branch of the left circumflex artery.***

T	=	T graft	LV	=	Left ventricle
AO	=	Aorta	LITA	=	Left internal thoracic artery
AC	=	Aortocoronary graft	LAD	=	Left anterior descending artery
RV	=	Right ventricle			

Table 5: Technical recommendations for coronary artery bypass grafting

Technical	Class [a]	Level [b]
Procedures should be performed in a hospital structure and by a team specialized in cardiac surgery, using written protocols.	I	B
Arterial grafting to the left anterior descending artery system is indicated.	I	A
Complete revascularization with arterial grafting to non-LAD coronary systems is indicated in patients with reasonable life expectancy.	I	A
Minimization of aortic manipulation is recommended.	I	C
Graft evaluation is recommended before leaving the operating theatre.	I	C

[a]**Class of recommendation.**

Class I = Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.

[b]**Level of evidence.**

Level A = Data derived from multiple randomized clinical trials or meta-analyses.

Level B = Data derived from a single randomized clinical trial or large non-randomized studies.

Level C = Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Off-Pump All Arterial Coronary Artery Bypass Grafting

Logical thinking: "if the CABG performs with off-pump and all arterial grafts, it should give both short and long-term excellent outcomes. Balacumaraswami L, et al. compared intraoperative transit-time flow measurements in all ITA, RA, and SV in patients undergoing OPCAB and ONCAB.[101] In comparison with OPCAB, the overall mean graft flow and flow/pressure ratio were significantly higher and mean arterial pressure significantly lower for all grafts in the ONCAB. These findings are probably a result of vasodilatation resulting from CPB and reactive hyperemia resulting from a period of ischemia. There was no difference in the mean graft flow and flow/pressure ratio of arterial grafts, which were significantly less than for SV. Therefore where unstable patients and graft flow are concerned, OPCAB with SV graft should be considered.

Kobayashi J. et al. randomly assigned patients to undergo multiple arterial OPCAB (n=81) or ONCAB (n=86).[47] The number of arterial grafts performed per-patient were 3.3±1.0 for OPCAB and 3.4±0.9 for ONCAB. The completeness of revascularization, hospital mortality, perioperative complications and early graft patency (within 3 weeks after the operation by angiography) were found to be similar in both groups. The operative was significant shorter in OPCAB group. Table 5. summarizes the technical recommendations for CABG from the 2010 guidelines on myocardial revascularization.[2]

Bangkok Heart Hospital Experiences

Between Jan 2005 and Dec 2010, 816 patients underwent isolated OPCAB at the Bangkok Heart Hospital. All arterial OPCAB was used in 581 patients (71%). LITA, RITA, RGEA, left RA and right RA were used in 97.4% (566/581), 18.2% (106/581), 20.5% (119/581), 85.9% (499/581) and 26.9% (156/581), respectively. Male was 84.0% (488/581). Mean age was 60.7±10.3 yrs. 68.7% (399/581) had hypertension and 41.8% (243/581) had diabetes. 29.6% (172/581) had significant left main coronary artery disease. Mean preoperative left ventricular ejection fraction was 57.1±13.2 %. Average number of grafts was 4.1±1.3. The clinical outcomes were improved over the year even for high risk patients. The 30-day mortality was 0% and there was no perioperative myocardial infarction, reoperation for bleeding, deep sternal wound infection and stroke in the year 2010 (Society of Thoracic Surgeons score: mean 1.09 ±0.94%, median 0.80% and European system for cardiac operative risk evaluation score: mean 2.13±1.81%, median 1.30%).

Conclusion

Patients may achieve an excellent outcome with either type of procedure. Older patients with more co-morbidities and more advanced atherosclerotic disease will probably derive greater benefit from OPCAB. The long-term benefit of CABG is maximized with the use of arterial grafts, specifically ITA. Using RA increases the number of arterial anastomoses beyond the use of both ITAs. The side-to-side anastomosis eliminates an aortic anastomosis, decreases amount of graft required, and increases total graft flow (a higher patency rate). All arterial conduits provide superior long term graft patency in general. However the choice of graft depends also on individual patient risk factors and coronary artery anatomy, target vessel size and degree of stenosis.

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