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Review

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Percutaneous catheter-based repeat revascularization in patients with previous PCI or CABG: a comprehensive review of the evidence

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Abstract

Repeat revascularization after percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is one of the most common long-term complications which warrants continuous clinical follow up. Re-interventions negatively impact long-term survival in patients with coronary artery disease. The repeat revascularization after PCI can be either a target lesion revascularization (stent thrombosis/in-stent restenosis) or a revascularization of native coronary artery after PCI (target vessel revascularization/non-target vessel revascularization). The EVENT registry reports that repeat revascularization rates in patients undergoing PCI is 12% in the first year of follow up. Repeat revascularization with additional stent deployment increases the rate of stent thrombosis and restenosis, thereby leading to recurrent ischemic events. Repeat revascularization after CABG can be either in the early postoperative period or later due to native disease progression or late graft stenosis. The need for re-intervention after surgical or percutaneous revascularization is inevitable and is dependent on modifiable and non-modifiable risk factors.

Keywords: Revascularization, percutaneous cardiac intervention, coronary artery, coronary artery bypass grafting

INTRODUCTION

The evolution of PCI techniques and tools has been tremendous in the last few decades, which has enabled the interventional cardiologist to treat increasingly complex lesions with fewer complications. Repeat revascularization after PCI is one of the most devastating long-term complications which warrants continuous clinical follow up. Re-interventions negatively impact long-term survival in patients with CAD. Newer generation DES with thinner stent struts and biodegradable polymers have reduced restenosis rates to a considerable extent as compared to the bare metal stent era[1]. Re-intervention following CABG is equally morbid and is indicated with early or late graft failures or progression of disease in the native coronaries. Early graft failure in CABG is often due to technical factors and harvest injuries sustained to the conduits. Atherosclerosis in SVG and competitive flow with arterial grafts are the major determinants of the long-term conduit patency. SVG failures have the propensity to cause ischemic symptoms and frequently necessitate re-intervention after CABG (about 6% of total PCI volume)[2,3]. The disease progression in the native coronaries after CABG is retarded by guideline-directed medical therapy[4]. However, the progression to occlusion of native CAD in the grafted target vessels would result in recurrence of symptoms requiring re-interventions. PCI is the primary choice of re-intervention in repeat revascularizations after index PCI or CABG, as evident from the recent literature[5], and this review focuses on the evidence supporting the approach.

REPEAT REVASCULARIZATION AFTER PCI [Table 1]

The EVENT registry reports that repeat revascularization rates in patients undergoing PCI is 12% in the first year of follow up. Repeat revascularizations can be broadly divided into planned (staged PCI for multi-vessel CAD) or unplanned re-interventions. Nearly three quarters of the patients in the EVENT registry had unplanned re-interventions and nearly half of them were for restenosis of index lesions and the rest for non-target lesions[6]. The unplanned re-interventions can be classified as follows.

[I] Target lesion revascularization (TLR): re-intervention to address restenosis within the previous stent which includes 5 mm proximal and distal margin from the stent. This can be due to: (1) stent thrombosis (within the first 30 days after index PCI); or (2) in-stent restenosis (reduction in the lumen diameter of the stent following PCI).

[II] Revascularization of Native coronary artery after PCI. The revascularization of the native coronary artery can be either: (1) target vessel revascularization (TVR), i.e., revascularization of the target epicardial vessel containing the stent or its branches; or (2) non-target vessel revascularization, i.e., re-interventions on ischemia producing lesions unrecognized during index PCI or due to progressive atherosclerotic disease.

The risk predictors for mortality after repeat revascularization were post PCI myocardial infarction or stent thrombosis, age, diabetes, male sex, PCI in a STEMI setting, and previous CABG[6]. Patients requiring repeat revascularization of target lesion had increased mortality compared to those not requiring revascularization[7]. Repeat revascularization with additional stent deployment increases the rate of stent thrombosis and restenosis, thereby leading to recurrent ischemic events[8].

TARGET LESION REVASCULARIZATION

The clinical impact of TLR is not well studied. Data from a pooled analysis of 21 randomized trials show

Table 1. The specifics of re-intervention with PCI following PCI

	Incidence	Risk factors	Pathophysiology	Prevention
Native vessel significant CAD	6% of patients develop significant CAD in non stented vessel by 1 year	- Increased baseline glucose levels - Increased TGL levels - Small decrease in Apolipoprotein B - Elevated preprocedural Hs CRP - Vulnerable plaque by VH-IVUS or OCT	Similar to native CAD	Life style changes/pharmacological means
Stent thrombosis	< 1% - more common in the first week after PCI	Patient factors - smokers, DM, CKD, reduced LVEF Lesion related - small vessel disease, complex interventions, stenting in PPCI setting Technical factors - stent underexpansion, malapposition, stent fractures, residual dissection	Highly thrombogenic mileu in PPCI, high thrombus burden, slow flow due to microvascular dysfunction	Newer generation DES, potent antiplatelets like prasugrel and ticagrelor Routine aggressive post dilatation, imaging guided PCI optimization
In stent restenosis	< 10%	Patient factors - smokers, DM, CKD, genetic polymorphism Lesion related - longer stent, ostial and bifurcation lesions, tortuous and calcific anatomy, small vessel disease Technical factors - stent under expansion, mal-apposition, geographic miss	Vessel wall injury and endothelial dysfunction by stent induces neo intimal hyperplasia	Proper bed preparation, adequate post dilatation, imaging guided PCI optimization and proper stent landing

CAD: Coronary artery disease; CRP: C-reactive protein; CKD: chronic kidney disease; DM: diabetes mellitus; DES: drug-eluting stent; LVEF: left ventricular ejection fraction; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; TGL: triglyceride; VH-IVUS: virtual histology intravascular ultrasound.

that 7.2% of the patients had a TLR procedure at a median time of 271 days after PCI. TLR was an independent predictor of mortality compared to target vessel and non-target vessel revascularization[7]. Target lesion restenosis may present as acute coronary syndrome in 40% of cases, which increases mortality[9].

Stent thrombosis

Incidence

Stent thrombosis is a potential complication following PCI resulting in sudden death or non-fatal MI (STEMI) in most cases. It usually occurs within the first 30 days after index PCI, with higher incidence in the first week. Stent thrombosis has decreased from 4% in the BMS era to < 1% with the current generation DES with concomitant and prolonged use of DAPT[10]. Despite successful revascularization, the outcomes following angiographically confirmed ST was associated with an increased risk of death when compared to the matched controls (27.3% *vs.* 11.3%, *P* log rank < 0.001), as reported by Rozemeijer *et al.*[11].

Risk factors

The predictors of stent thrombosis (STh) are related to the following. Patient factors include smoking, diabetes mellitus, CKD, and reduced left ventricular ejection fraction (LVEF). Anatomical factors include complex coronary interventions, small vessel disease interventions, and stenting in the primary PCI setting have higher risk of stent thrombosis. Stent under expansion, malposition, residual dissection, and stent fractures are common technical and procedure-

related risk factors.

Pathophysiology

The amplified risk of early stent thrombosis in ACS is due to its pro-thrombotic milieu. High thrombus burden, impaired distal TIMI flows due to microvascular obstruction by thrombotic debris, plaque prolapse through stent struts, incomplete stent apposition due to dissolution of jailed thrombus, and impaired LVEF all lead to high rates of early STh in the setting of ACS. The rupture of the vulnerable plaque allows direct contact of the exposed highly thrombogenic necrotic material to platelets resulting in platelet recruitment, activation, and aggregation, as well as activation of the coagulation cascade especially thrombin. However, the direct thrombin inhibitor bivalirudin failed to show an additional protective effect compared to heparin plus GPIIb/IIIa in the ACUITY trial[12].

Prevention

Potent and predictable platelet inhibition with thienopyridines, especially prasugrel and ticagrelor, has shown significant reduction in STh: TRITON TIMI 38 trial, prasugrel (1.1%) *vs.* clopidogrel (2.4%)[13]; and PLATO trial, ticagrelor (1.3%) *vs.* clopidogrel (1.3%)[14]. Duration of DAPT is another important factor, with the optimal duration after deployment of the new generation DES being 12 months, which may be extended beyond for patients at increased risk for late STh while balancing the bleeding risk[15]. Improved stent design with thinner struts and thinner, durable, biocompatible polymer offers protection against STh. Newer generation DESs with everolimus, zotaralimus, and biolimus have significantly lower STh rates compared to first-generation DESs[16]. Routine aggressive post-dilatation and intra-vascular imaging with intravascular ultrasound (IVUS) and optical coherence tomography (OCT) helps in PCI optimization and identifying residual dissection, stent mal-apposition, and stent fractures, which are potential risk factors for STh.

In stent restenosis

Incidence

In stent restenosis (ISR) is defined as reduction in the lumen diameter following PCI, and it is an important factor for repeat TLR. The incidence of ISR has dropped from 32%-55% in the pre-stent era to 17%-41% in BMS era to < 10% with new generation DESs. It is more common with multi-vessel disease compared to single vessel disease[17]. Taniwaki *et al.*[18] reported a neo-atherosclerosis rate of 40.9% at five-year follow up by OCT analysis with extension of fibroatheroma to at least 1.0 mm in length.

Risk factors

The predictors of ISR are related to the following factors[19,20]:

Patient factor: apart from diabetes mellitus, smoking, and CKD, certain genetic polymorphisms involving the inflammatory markers predispose certain individuals for increased restenosis rates. The increased blood viscosity, enhanced platelet aggregation, and decreased biological activity of anti-thrombin II and fibrinogen increase the pro-thrombotic effect characteristic of diabetic vessel, leading to increased ISR.

Anatomical factor: ostial and bifurcation lesions, tortuous and calcific anatomy, and smaller vessel size < 3 mm predispose to increased ISR.

Technical factors: longer stent implantation (> 32 mm), stent mal-apposition, stent under expansion, and geographical miss are important technical factors. Proper bed preparation with adequate pre-dilatation and de-bulking with cutting and scoring balloons and routine post dilatation help in adequate stent expansion.

Pathophysiology

NIH is a non-specific inflammatory response leading to excessive tissue proliferation and vascular remodeling in the lumen of a stented vessel, as evidenced by increased C-reactive protein and MCP-1 levels in patients at increased risk for restenosis[21]. NIH is induced by vessel wall injury and endothelial dysfunction caused by mechanical stretch and medial dissection during PCI. Persistent vascular insult by stent struts is reduced by thin strut cobalt chromium platform compared to thick strut stainless steel platforms. Excessive neointimal proliferation is counteracted by the anti-proliferative drug in DES and carried by the polymer that stays on the vessel surface and delivers the drug.

Prevention

Newer generation DESs with drugs (zotarolimus and biolimus A9) and thinner, biodegradable or bio-absorbable polymers have been designed to reduce the ISR rates[22,23]. Intravascular imaging with IVUS and OCT helps in plaque characterization, identifying stent mal-apposition and under expansion, and choosing the ideal site for stent deployment, and it helps reduce the restenosis rates. Repeat revascularization is mandated in ISR with ischemia driven symptoms. IVUS and OCT help in identifying the pathology of ISR and guide the treatment strategy in repeat revascularization[24]. However, the results of re-intervention in ISR remain poorer, as documented in the pooled analysis from the RIBS (Restenosis Intra-stent: Balloon Angioplasty Versus Elective Stenting) IV and V randomized trials, in patients with ISR treated with everolimus-eluting stents reporting mortality, MI, and MACE rates of 2.6%, 1.0%, and 10.0%, respectively[25], at one-year follow up.

NATIVE VESSEL DISEASE PROGRESSION POST PCI

Data from a pooled analysis of 21 randomized trials show that 2.5% of the patients had a TVR procedure at a median time of 537 days after PCI[7].

Incidence

PCI does not have the potential for overall disease modification in CAD as the effect of stent is limited to a particular segment of the artery where it is deployed and offers no modification of the progressive atherosclerotic process of the remaining coronary arterial tree. Progression of coronary atherosclerotic plaque in non-stented segments may lead to stable ischemic symptoms or ACS secondary to plaque rupture. This would necessitate repeat revascularization with long-term morbidity after PCI. Progression of coronary atherosclerosis is defined as a new stenosis of at least 50% in an arterial segment previously considered normal or an increase in the grade of previous stenosis by > 20%. Insignificant non-critical lesions detected during index PCI may evolve into clinically significant lesions requiring revascularization, in approximately 6% of patients by one year[26]. The PROSPECT study attributed clinical events to progression of vulnerable plaque as assessed by IVUS-virtual histology and estimated that 12% of patients developed MACE during the three-year follow-up period from the non-stented lesions[27].

According to Alexopoulos *et al.*[28], among the survivors of late MI after PCI, disease progression in non-stented arteries is observed in half of the cases. MI secondary to disease progression presented later compared to stent related MI (mean times of 27 months *vs.* 9 months in ST and 19 months in ISR). Furthermore, MI resulting from disease progression presented as ST-segment elevation myocardial infarction (STEMI) in 38.1% of patients, whereas, in ST- and ISR-related MI, the percentages of STEMI occurrence were 60% and 20%, respectively[28].

Risk factors

High baseline glucose levels, increased levels of triglycerides, and small decrease in Apo lipoprotein B are considered as important residual risk factors for re-intervention even in patients with LDL levels < 70 mg/dL[29]. Elevated pre-procedural high sensitivity C-reactive protein is associated with an increased all-cause mortality in the long term but does not predict stent-related complications[30]. Determination of the plaque characteristics such as thin cap fibroatheroma and plaque composition may give insights into the long-term progression of atherosclerosis and predict future clinical events[31]. Intravascular ultrasound-virtual histology and OCT helps in assessing these vulnerable plaques[32]. According to Taniwaki *et al.*[18] and Palmerini *et al.*[33], the incidence of native vessel atherosclerosis in non-stented arteries is higher in patients who had neointimal proliferation within the stented segments. Whether common risk factors predispose to both in-stent restenosis and native atherosclerosis or endothelial dysfunction due to PCI accelerates atherosclerosis in non-stented arteries is unknown. Intensive global risk modification with emphasis on effective secondary prevention strategies post-PCI (lifestyle and pharmacological interventions) may result in halting the progression of atherosclerosis. This might translate into reduced major cardiac events and repeat revascularization rates in post-PCI patients.

REPEAT REVASCULARIZATION AFTER CABG [Table 2]

PCI in early post op CABG

Incidence

The reported incidence of perioperative myocardial ischemia (PMI) after isolated CABG ranges between 2% and 10%[34]. PMI adds to considerable in-hospital morbidity/mortality and adverse long-term survival. Most published series have reported PMI within the first 72 h after CABG, although it might occur at any time in the postoperative period. The reason for early graft failures would be mostly technical: harvest injury, kinking, anastomotic stenosis, or graft spasms/thrombosis. Coronary angiography can accurately detect the cause of PMI, enabling immediate implementation of corrective measures (i.e., emergent PCI or revision CABG) and limiting the extent of myocardial damage in patients with graft-related problems[35,36]. Thielmann *et al.*[37] demonstrated that 1%-3% of grafts fail within 24 h after CABG, with consequent early PMI and irreversible myocardial cell damage. This translated to higher in-hospital mortality and major adverse events. Myocardial damage early after CABG might result from graft- or non-graft-related mechanisms during the immediate perioperative period[37].

Risk factors and pathophysiology

A sudden graft occlusion with PMI might be implicated when events such as acute ST-segment elevation, rise of cardiac biomarkers, hemodynamic instability, or sustained ventricular arrhythmia occur during the early postoperative stay. Graft-related PMI and myocardial damage after CABG could be attributed to graft occlusion, subtotal or hemodynamic relevant anastomotic stenosis, graft kinking or overstretching, and postoperative graft spasm[38]. The resultant myocardial hypo- and/or malperfusion with subsequent regional myocardial dysfunction often leads to a wave front of myocardial damage extending from the sub-endocardium to the sub-epicardium in a time-dependent fashion. Although reversible if identified and intervened earlier, it might lead to irreversible myocardial damage if left untreated with eventual loss of cardiac myocytes and necrosis.

PCI has the advantage of being quicker and less invasive than an early re-do CABG without compromising the completeness of repeat revascularization in this situation. Risk of mediastinal bleeding with fibrinolysis is quite significant in the early phase after CABG, and it does not effectively tackle the problem of compromised anastomosis. Conservative treatment of patients with early graft failure with a large area of "at risk myocardium" would surely lead to myocardial pump failure and a progressive and lethal low cardiac output syndrome. Thus, PCI is the choice of intervention in these patients for optimal myocardial salvage.

Table 2. The specifics of re-intervention with PCI following CABG

	Incidence	Risk factor	Time to intervene with PCI
Native disease progression	· 9.2%-34.6% at 5 years	· Diabetes · Smoking · Hyperlipidemia · Hypertension · Heart failure · Graft compromise · Lack of aspirin /statin use · ACE inhibitor therapy · Use of SVG · PVOD · Male gender · High grade base line stenosis	· Median time to intervention - 559 days[52]
Early graft failure	· 1%-3% in first 24 h · 8%-12% before discharge	· Technical factors-Kinks, harvest injury, anastomotic stenosis · Poor target vessels · OPCAB · Lack of antiplatelet use	· Emergent PCI · Poorer results with intervention > 30 h
Late graft stenosis	· SVG-50% · LITA-95% · RITA-91% · RA-88% (patency rate at 10 years)	· Extent of distal run off in the target vascular bed · Diabetes · Hyperlipidemia · Factors causing accelerated atherosclerosis · Competitive flow in grafted territory for arterial grafts · Poor compliance to statin/anti-platelet therapy · Endarterectomy	· From 6 months after index CABG[56]

ACE: Angiotensin-converting enzyme; CABG: coronary artery bypass grafting; PVOD: peripheral vascular occlusive disease; LITA: left internal mammary artery; OPCAB: off pump coronary artery bypass grafting; PCI: percutaneous coronary intervention; RITA: right internal mammary artery; RA: radial artery; SVG: saphenous venous graft.

Time interval to early repeat revascularization with PCI after CABG

A time interval between primary CABG and postoperative angiography of > 30 h was not only associated with higher in-hospital mortality but was also independently predictive of late mortality; hence, close vigilance, a high degree of suspicion, early postoperative angiography, and expeditious treatment of PMI may be essential components of optimizing patient outcomes post-CABG[39].

Davierwala *et al.*[38] observed in their report that the shortening of the time interval between PMI and postoperative coronary angiogram might have a positive bearing on the early and late mortality by reversing extensive myocardial ischemia and the consequential myocardial damage. According to them, one method of reducing this time interval would be by reducing the threshold levels for performing a postoperative angiogram via strict adherence to a predefined protocol. Although such an approach may increase the risk of cardiac catheterization-associated complications, the rate and severity of such complications are lower than the risks associated with a delayed diagnosis and treatment of PMI[38].

Emergency re-interventions for early graft failure using a catheter-based revascularization strategy for acute thrombolysis or PCI have been reported to have favorable results[39]. In a study of 45 patients, early postoperative PTCA was reported to be successful 49 days after CABG with re-intervention in 95% of the native coronary artery lesions, 89% of vein graft stenoses, and 100% of LITA graft lesions[40]. Patent grafts were observed in 25%-34% of the patients in these three series, suggesting that repeat coronary angiography should be applied whenever PMI due to acute graft failure is suspected (with the exception of hemodynamically unstable patients) rather than performing a "blind" redo-CABG[40].

The exact time of graft failure and onset of symptoms is debatable in most cases. There are data available from randomized clinical trials which have demonstrated the benefits of even a "delayed" re-perfusion (12-

48 h after onset of symptoms) of infarcted myocardium in reducing infarct size, with myocardial salvage and prevention of arrhythmias[41]. The concept of delayed reperfusion might apply differently in a postoperative case of CABG where the myocardial perfusion dynamics are not solely determined by an "infarct-related artery" with or without graft failure in contrast to that in primary PCI where this solely forms the supply to the myocardium at risk[42].

Native disease progression after CABG

Incidence

Although considered to be a lesser endpoint when compared to death, myocardial infarction (MI) or stroke, the need for repeat revascularization due to distal disease progression in native coronaries, or graft failure *per se* after CABG can significantly affect the quality of life and have significant economic implications. Sergeant *et al.*[43] reported that 62% of patients undergoing CABG would have recurrent ischemia with 36% having MI and 28% requiring either redo CABG or PCI for symptom relief at 15-year follow up after index CABG. In another study, Sabik *et al.*[44] reported that fewer than 50% of patients undergoing CABG remained free from some form of re-intervention at 25-year follow up. The reason for this might be the progression of disease in the native coronaries and graft failure in the long term[45].

Risk factors for native disease progression and re-intervention after CABG

The long-term results of CABG may be limited by the extent of progression of disease in the native coronary arteries. There are reports citing up to six times faster progression of native proximal disease in targets grafted with SVG[46]. In the recent study by Jabagi *et al.*[47], native vessel disease progression was a common event with 34.6% of vessels upstream to a bypassed conduit and 16.3% of left main stem disease showing significant disease progression at five-year follow up. The same study reported the risk factors for native disease progression after CABG to be age ($P = 0.034$), previous PCI ($P = 0.002$), angiotensin converting enzyme (ACE) inhibitor drug use ($P < 0.001$), CAD severity ($P < 0.001$), and angina severity of Canadian Cardiac Society Class III/IV ($P = 0.016$) and NYHA Class III/IV ($P < 0.001$). Progression of lesions to total occlusion correlated with the use of SVG ($P = 0.019$), previous PCI ($P = 0.007$), and the use of ACE inhibitors ($P < 0.001$)[47]. The presence of PVOD has been reported to be consistently associated with LM disease progression[48].

In another study by Yoon *et al.*[49], the disease progression to occlusion after CABG in LAD and non-LAD targets were 9.2% and 13.9%, respectively, at mid-term follow up with CT coronary angiography. Upon multivariate analysis, heart failure, graft compromise, and failure to use aspirin after CABG were significantly associated with new native vessel occlusion in LAD targets, whereas male gender, high-grade baseline stenosis, left main disease, and lack of statin use were found to correlate with occlusion in non-LAD targets[49].

In a retrospective data analysis by Inci *et al.*[50], the primary risk factors for re-intervention after CABG included diabetes, active smoking, family history of CAD, hypertension, ECG changes in the follow up period, and LVEF > 50% for PCI or repeat CABG. The factors contributing to accelerated arteriosclerosis (diabetes, elevated total cholesterol, and triglyceridemia) have been previously reported to predict re-intervention rates after CABG[43].

Arterial grafts have been reported to slow the downstream progression of disease in the grafted native coronaries by means of the vasoactive cytokines and NO production by arterial endothelium. Consequently, multiple arterial grafting strategies have been reported to return better patency rates with lower re-intervention rates[50,51]. Studies have reported slower disease progression in vessels receiving arterial grafts

when compared to SVG grafts[49,50].

Re-intervention in patients who have undergone CABG is warranted in the presence of symptoms or if > 10% of LV myocardium is at risk in asymptomatic patients[5]. As the peri-procedural risk for re-do CABG in this subset of patients is higher, PCI is the preferred approach when there is amenable anatomy in the native coronaries. Re-intervention is recommended to treat the critically progressed native coronary lesion, and, if that is not feasible, intervention on the bypassed grafts should be considered[5].

Pathophysiology of native disease progression

The major mechanism of progression CAD in native coronary arteries following CABG is atherosclerosis with plaque formation and plaque rupture[52]. Negative disease remodeling due to decreased flow across the proximal lesion in grafted native coronaries has been reported as a cause of progression to occlusion by some investigators[53]. The risk factors for atherosclerosis (systemic factors such as diabetes, smoking, and hyperlipidemia as well as local factors such as increased oxidative stress, vascular inflammation, and endothelial dysfunction) result in accelerated native disease progression with or without graft failure and consequent re-interventions[52]. There are opposing views in the literature as regards to atherosclerosis and graft patency with a large angiographic series demonstrating no correlation between classic atherosclerotic risk factors and graft occlusion[54]. However, the sub-analysis of PREVENT IV trial data documented that the only consistent marker of graft failure in the long term was the presence of concomitant significant cerebrovascular disease, which is a proven surrogate for atherosclerotic disease burden[55].

Late graft stenosis after CABG

Incidence

About 8%-12% of SVG grafts fail before hospital discharge, whereas 15%-30% occlude by the end of first year after CABG. The annual occlusion rate of SVG grafts is about 2% in the first five years, which increases to 4% during Years 6-10 with only 50% remaining patent at the end of the first decade after CABG[56]. On the other hand, arterial grafts function much better than SVG grafts, and, once the initial phase of early graft failure secondary to technical factors is over, they return better patency rates in the long term (LITA, 98%; RITA, 91%; and RA, 88%) at ten-year follow up[52].

Risk factors for graft occlusion in the long term

One of the most important yet often overlooked determinants of long-term patency of grafts is the extent of distal run off in the vascular bed to which the conduit is grafted. The size of the target vessel (at least 1.5 mm diameter distal to the area of grafting), size of the target vascular bed, and the atherosclerotic disease burden in the distal vascular bed are the chief determinants of the long-term patency of bypass grafts, especially SVG grafts. Diabetes with concomitant hyperlipidemia and other risk factors for atherosclerosis[52] have been documented to cause long-term graft failure. Surprisingly, hypertension has not been associated with either NIH or accelerated SVG atherosclerosis in both human and experimental models[56].

Pathophysiology

SVG grafts have more collagen content when compared to arterial grafts and the NO and prostacyclin mediated relaxation response is quite compromised in SVG grafts when compared to arterial grafts. Once deployed in arterial circulation, SVG grafts develop NIH with subsequent atherosclerosis, which in turn is accelerated with a hyperglycemic-hyperlipidemic mileu. Vein wall thickening, varicosities, and post-phlebitic changes downgrade the long-term patency of SVG to less than half of that of a good quality vein graft[56].

Atherosclerosis of the conduit, progression of native coronary disease, and competitive flow in the grafted vascular territory are the common factors identified in the long-term failure of arterial grafts[2,52].

Time to intervention

SVG graft stenosis after CABG is the result of accelerated atherosclerosis and the "late catheter-based interventions" might be warranted as early as six months after the index CABG[56].

Results of PCI for late re-interventions after CABG

The primary indications for late re-intervention with PCI after CABG is to provide symptom relief and minimize the risk of graft failure and/or treat the culprit lesion in the graft or native coronary vessel. In the AWESOME trial (Angina With Extremely Serious Operative Mortality Evaluation), the three-year survival rates after index CABG were comparable and non-significant between PCI and repeat CABG (76% and 73%, respectively)[57]. PCI can thus be the treatment of choice in late revascularizations after CABG.

Iqbal *et al.*[58] reported the one-year results after PCI on failed SVG grafts after CABG in the United Kingdom. They reported lower mortality (odds ratio: 0.60; 95% confidence interval: 0.51-0.71; $P < 0.001$) and MACE rates (odds ratio: 0.51; 95% confidence interval: 0.38-0.68; $P < 0.001$) with the use of second-generation DESs when compared with BMSs in these patients[58]. In a secondary analysis of EXCEL trial results, Giustino *et al.*[59] recently documented that repeat revascularizations in LMCA disease, PCI or CABG, resulted in increased cardiovascular mortality [adjusted hazard ratio (HR) = 4.22; 95% confidence interval (CI): 2.10-8.48; $P < 0.0001$] and adjusted all cause three-year mortality (adjusted HR = 2.05; 95%CI: 1.13-3.70; $P = 0.02$). The need for repeat revascularization following CABG was significantly lower than that for PCI as per this report (12.9% *vs.* 7.6%; HR = 1.73; 95%CI: 1.28-2.33; $P = 0.0003$)[59].

Locker *et al.*[60] recently reported the 10-year results of PCI after index CABG. Patients who received drug-eluting stent had better 10-year survival than BMS recipients (HR = 0.74; 95%CI: 0.59-0.91; $P = 0.001$). Repeat CABG fared better than PCI in this group of patients with improved late survival (48% *vs.* 33%). It is interesting to note that, in the subgroup analysis, PCI performed on native vessel disease had similar survival rate as that of repeat CABG (HR = 1.09; 95%CI: 0.75-1.59; $P = 0.65$), while those receiving intervention for occluded saphenous vein grafts had poorer late survival when compared to repeat CABG. (HR = 1.62; 95%CI: 1.10-2.37; $P = 0.01$)[60]. Thus, the conclusions of this study underscore the importance of the use of DES in re-interventions after CABG and equally highlight the need to tackle the native disease progression rather than the graft occlusion for optimal survival benefit.

PCI to SVG lesions

In the recent meta-analysis by Patel *et al.*[3], comparing DES *vs.* BMS for SVG interventions, with data derived from six RCTs, no difference was observed between the two groups in terms of all-cause/cardiovascular mortality, MACE rates, TVR, STh, or myocardial infarction with maximum follow up of 60 months. The introduction of thin strut BMS stents for SVG interventions and the high incidence of diabetes in the target population might have resulted in the comparable outcomes here[3]. This is in contrast to the re-interventions targeted at the native disease progression where DES fared better than BMS and is the recommended choice of intervention[5]. As the pathology of SVG occlusion is distinct from native disease progression, and SVG intervention with a second-generation DES is becoming commonplace, further RCTs testing the hypothesis will throw better light on this paradox.

CONCLUSION

The need for re-intervention after surgical or percutaneous revascularization is inevitable and is dependent on modifiable and non-modifiable risk factors. The current evidence favors PCI over other strategies for re-intervention after any form of index revascularization procedure (surgical, catheter based, or fibrinolytic). A second-generation DES is the preferred choice of stent in re-interventions after PCI, which is adequately backed by evidence. PCI to TLR has inferior results when compared to TVR or non-TLR re-interventions as per recent literature. A low threshold for early postoperative CAG to identify PMI would buy lead time for emergent re-interventions (ideally PCI) to optimize myocardial salvage and survival after CABG. Late re-interventions with PCI yield better results after CABG when performed for native disease progression than for SVG occlusions. As per the current evidence, DES is the preferred choice of stent in native disease progression, while DES or BMS could be utilized for SVG interventions when contemplating late catheter-based re-interventions after CABG. To conclude, the best insurance against future re-interventions lies in the optimization of the index procedure (PCI/CABG/medical management) to the patient and the heart team approach to decision making in CAD cannot be over-emphasized in achieving this end.

DECLARATIONS

Authors' contributions

Contributed equally to the conception, data collection and writing of the manuscript: Valooran GJ, Subbiah M, Idhrees M, Karuppannan M, Bashir M, Velayudhan B

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