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REVIEW

Off-pump coronary artery bypass grafting: Misperceptions and misconceptions

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Abstract

Coronary artery bypass grafting (CABG) continues to be one of the most commonly performed cardiac surgical procedures worldwide. Conventional CABG performed on cardiopulmonary bypass termed on-pump CABG is regarded as the gold standard. However, on-pump CABG results in several physiologic derangements including but not limited to thrombocytopenia, activation of complement factors, immune suppression, and inflammatory responses leading to organ dysfunction. Furthermore, manipulating an atherosclerotic ascending aorta during cannulation and cross-clamping can predispose to embolization and stroke risk. Recognition of these detrimental effects of on-pump CABG resulted in resurgence of off-pump CABG nearly two decades ago. Off-pump CABG since its resurgence has been a subject of intensive scrutiny and speculation. Despite numerous retrospective nonrandomized studies, prospective randomized trials, and meta-analyses validating the safety and efficacy of off-pump CABG, opponents of the technique have persistently demanded abandonment of off-pump CABG. Several misconceptions and misperceptions are used as an excuse for such demands. This review article examines published scientific evidence to evaluate these misperceptions and misconceptions about off-pump CABG.

Key words: Coronary artery bypass grafting; Cardiopulmonary bypass; Off-pump coronary artery bypass grafting; Surgical myocardial revascularization; Coronary artery surgery

Core tip: There is reluctance to adopt off-pump coronary artery bypass grafting owing to concerns about incomplete revascularization, poor graft patency, and long-term mortality. These concerns are the result of misperceptions and misconceptions rather than reality. This manuscript attempts to tackle these misperceptions and misconceptions.

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INTRODUCTION

Conventional coronary artery bypass grafting (CABG) is characterized by performance of delicate coronary anastomoses on cardiopulmonary bypass (CPB). However, the price of a still and bloodless operative field is ultimately paid by the patients in the form of negative effects of CPB including blood trauma, activation of a series of inflammatory responses, nonpulsatile flow, and possible embolization of air or debris-most particularly embolization of atherosclerotic debris from the aorta[1]. Off-pump CABG was rediscovered with the primary objective of avoiding these deleterious effects of CPB.

Since its resurgence nearly two decades ago off-pump

CABG has been extensively investigated and scrutinized. It has been compared with the gold standard on-pump CABG in numerous randomized controlled trials[2-10] as well as large retrospective observational studies[11-15]. Majority of the published evidence comparing on-pump and off-pump CABG has shown comparable outcomes for these two techniques. However, inability of small, prospective, randomized controlled trials that have lacked sufficient sample size to demonstrate differences in early and long-term outcomes coupled with misperceptions and misconceptions about incomplete revascularization, reduced long-term graft patency and increased need for repeat revascularization resulting in inferior long-term survival have prompted opponents of off-pump CABG to demand abandonment of this technique. Those who question the feasibility and utility of off-pump CABG completely ignore the fact that larger observational studies that are better powered to statistically compare outcomes have shown more favorable in-hospital outcomes and equivalent long-term outcomes with off-pump and on-ump CABG[11-16].

In the current era increasing number of patients with high-risk profile are being referred for CABG. The benefits of off-pump CABG are apparent for patients at high risk for complications associated with CPB and aortic manipulation. Recent studies have demonstrated improved outcomes in higher-risk patients undergoing off-pump CABG[6,17-19]. In view of changing patient profile it will be prudent to acknowledge that off-pump CABG is a valuable technique in the armamentarium of cardiac surgeons and is here to stay. Misleading the cardiac surgical community by using misperceptions and misconceptions and in the process denying patients, particularly those at high-risk for complications due to use of CPB, the opportunity to have safe and effective myocardial revascularization off-pump is not a wise move. This review article examines published scientific evidence to evaluate these misperceptions and misconceptions about off-pump CABG and attempts to allay unnecessary apprehension about the safety and efficacy of off-pump CABG.

Completeness of revascularization

The criticism regarding completeness of revascularization is no longer valid in the current era as technology to safely perform multivessel off-pump CABG has improved tremendously over the past decade. Grafting of vessels on the lateral and inferior aspects is no longer impossible. In fact, the majority of evidence from randomized trials suggests at least equivalent completeness of revascularization[2-7,9,10] (Table 1). Furthermore, it is equally important to understand that completeness of revascularization and number of grafts should not be used synonymously. A more logical way to address the issue of completeness of revascularization is to use the index of completeness of revascularization [number of grafts performed divided by the number of grafts needed (number of graftable vessels with angiographically significant stenoses)][20].

It is important to emphasize that the frequency of complete revascularization reported by various studies comparing off-pump and on-pump CABG is always influenced by relative experience with each technique of the reporting center(s) and surgeon(s). For example, centers where on-pump CABG is used for most cases, and off-pump CABG is used for only a few cases the rates of complete revascularization in the late *vs* early off-pump experience will remain the same highlighting the importance of learning curve as well as case load. Such centers can also have an impact on the final completeness of revascularization achieved by multicentre randomized trials. This fact is exemplified by the Veterans Affairs (VA) Randomized On/Off Bypass (ROOBY) trial[21]. Every year, approximately 4000 isolated CABG procedures are performed in the VA system at 42 cardiac surgery facilities[22]. During the recruitment period of the ROOBY trial only 7 of the 42 centers qualified as high-volume off-pump CABG centers performing at least 50 off-pump cases per year[23]. Since the recognized learning curve for off-pump CABG is between 50 and 75 cases[24] it is not surprising that the ROOBY trial reports incomplete revascularization with off-pump CABG.

Several additional caveats exist regarding reporting of incompleteness of revascularization with off-pump CABG. First, none of the trials or studies reporting incomplete revascularization provides an explanation for failure to completely revascularize the off-pump CABG cohort. Second, from these trials, it is difficult to determine the significance of the ungrafted territory for a

Table 1 Comparison of number of grafts performed and completeness of revacsularization off-pump and on-pump in randomized controlled trials

Ref.	No. of grafts off-pump CABG	No. of grafts on-pump CABG	*P*	Completeness of revascularization
Coronary trial, Lamy *et al*[2] 2012	3.0	3.2	< 0.001	Yes[1]
GOPCABE trial, Diegeler *et al*[3] 2013	2.7	2.8	< 0.001	No
ROOBY trial, Shroyer *et al*[4] 2009	2.9	3.0	0.002	No
DOORS trial, Houlind *et al*[5] 2012	2.9	3.1	0.007	Yes
On-off study, Lemma *et al*[6] 2012	3.0	3.3	0.001	Yes
The Best Bypass Surgery trial, Møller *et al*[7] 2010	3.2	3.3	0.11	Yes
SMART trial, Puskas *et al*[9] 2003	3.39	3.4	NS	Yes
BHACAS trial, Angelini *et al*[10] 2002	2.23	2.31	NS	Yes

[1]Rate of incomplete revascularization (as assessed by the surgeon at the time of surgery) was higher, though the *P* value for the difference was only marginally significant (11.8% *vs* 10.0%, *P* = 0.05). NS: Not significant; BHACAS: Beating Heart Against Cardioplegic Arrest Studies; GOPCABE: German Off-Pump Coronary Artery Bypass Grafting in Elderly Patients; ROOBY: Randomized On/Off Bypass; DOORS: Danish On-pump *vs* Off-pump Randomization Study; SMART: Surgical Management of Arterial Revascularization Therapies; CABG: Coronary artery bypass grafting.

number of reasons. Foremost, it is impossible to determine myocardial viability in the territory left ungrafted, because myocardial viability studies were not used in these trials; thus, the significance of a reduced number of grafts in the off-pump CABG cohort is impossible to predict. Likewise, none of the trials used a myocardium at risk score, which is a potentially valuable tool to aid in determining the true significance of the non revascularized territory because there is a recognized hierarchy of effect, depending on which vessels are left ungrafted and how much myocardium is at risk[25]. Synnergren *et al*[26] examined the effect of incomplete revascularization over a 5-year period in a nonrandomized cohort of 9408 patients. Leaving 1 diseased vascular segment without a bypass graft resulted in no increased risk of death. However, leaving 2 vascular segments ungrafted significantly increased the risk for mortality ($P = 0.01$). Finally, it is important to mention that majority of the trials reporting incomplete revascularization with off-pump CABG report similar early mortality and morbidity rates for the two cohorts[2-5].

Graft patency

Graft failure is one of the major determinants of clinical prognosis after CABG. There has been considerable concern among surgeons and cardiologists that the greater technical difficulty of off-pump coronary revascularization might translate into less precise anastomoses and subsequently diminished graft patency[27]. With conventional on-pump CABG, the 15-year patency rate is > 97%. This is the gold standard that any new revascularization method must compete against[28]. A steep learning curve, distractions caused by cardiac motion or pulmonary insufflations, and construction of anastomoses on a moving target have been implicated as factors responsible for inferior graft patency after off-pump CABG[28].

Interestingly, all concerns about suboptimal graft patency over the years have been predominantly attributed to 2 randomized controlled trials[4,29]. Shroyer *et al*[4] demonstrated that the patency rate of the off-pump arm was lower than that of the on-pump arm on 12-mo angiography, and the 1-year composite adverse outcome rate (death from any cause, nonfatal myocardial infarction, and any reintervention procedure) was higher for off-pump than for on-pump CABG. Such findings do not come as a surprise since the 53 participating surgeons enrolled on average only eight patients per year during the study period and had unacceptably high conversion rates to on-pump surgery (12%) and incomplete revascularization (18%). Moreover, in 60% of the cases a resident was the primary surgeon again raising concerns about the relative inexperience translating into poor graft patency. Another unrecognized confounder that contributed to poor graft patency in the ROOBY trial[4] was the concomitant use of endoscopic vein harvesting (EVH) in 1471 patients (on-pump = 907 and off-pump = 564). The incidence of a patient having 1 or more occluded saphenous vein grafts on follow-up angiography was 41.3% in the EVH group, compared with 28.0% in the open vein harvesting (OVH) group ($P < 0.0001$). Overall saphenous vein graft patency in the EVH group was 74.5%, which was significantly worse than the 85.2% rate in the OVH group ($P < 0.0001$)[30]. Since ROOBY trial was recruiting at a time when EVH was not being widely practiced the poor vein graft patency secondary to EVH can be attributed to learning curve and relative inexperience of the vein harvesters. Poor conduit quality, a consequence of the learning curve for EVH, has been shown to be a predictor of early graft failure, blunted positive remodeling, and greater negative remodeling[31].

The other frequently cited randomized trial supporting the argument of poor graft patency after off-pump CABG is the trial by Khan *et al*[29] reporting decreased patency at 3 mo in the off-pump group. However, closer analysis of this reveals that limited experience of the operating surgeons, consisting of only 98 off-pump procedures, which require a different skill set, during the two years before the study (an average of 25 procedures per surgeon per year) coupled with the relatively low dose of intraoperative heparin, the absence of aggressive antiplatelet therapy with clopidogrel postoperatively, and the failure to use new suction devices to optimize exposure were perhaps some of the confounding factors for poor graft patency[32,33].

Long-term survival

The negative impact of incomplete revascularization and lower graft patency on late mortality rates is well-recognized[34]. Takagi *et al*[35] recently published a meta-analysis of 11 randomized trials demonstrating a statistically significant increase in ⩾ 1 year all-cause mortality by a factor of 1.37 with off-pump relative to on-pump CABG (RR = 1.373; 95%CI: 1.043-1.808). It is extremely important to highlight that the sensitivity analysis in this meta-analysis revealed that the ROOBY trial[4] strongly contributed to the pooled estimate. The aforementioned criticisms of this trial provide an explanation for the inferior survival of off-pump cohort. Furthermore, majority of the recently conducted trials reporting 30-d mortality[2,3,5,6] have not yet reported outcomes for long-term follow-up.

It is expected that once longer follow-up data is available for recently conducted randomized trials, that utilized newer technology for stabilization and exposure and had similar index of completeness of revascularization for off-pump and on-pump CABG, this controversy will be resolved.

CONCLUSION

Although there are numerous clinical studies attesting to the benefits of off-pump CABG[36-38], skepticism, fuelled by misperceptions and misconceptions, persists regarding the safety, efficacy, and equivalence of revascularization with off-pump CABG compared with on-pump CABG[39]. It is extremely important to highlight that off-

pump CABG is a technically demanding strategy and central to all the concerns associated with this technique is the issue of learning curve[1]. The learning curve in off-pump surgery can be safely negotiated with appropriate patient selection, individualized grafting strategy, peer-to-peer training of the entire team, and graded clinical experience (preoperative planning, adequate exposure, proximal anastomoses to the aorta, and distal anastomoses initially to anterior wall vessels, followed by inferior wall vessels and then lateral wall vessels)[40].

Contrary to the proponents and opponents of off-pump CABG, the authors' view is that both on-pump and off-pump CABG have their place in the field of myocardial revascularization. Present day cardiac surgeons must adopt off-pump CABG rather than condemn and castigate it. The rational for this view is the changing profile of patients that are being referred for surgical revascularization. At the same time, technical precision, anastomotic quality, and completeness of revascularization should not be compromised in an attempt to avoid the deleterious effects of CPB unless these short-term risks outweigh any potential long-term benefit.

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