



Mini Review

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# Clinical Review of Coronary Revascularization in Special Subgroups in the Current Era

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## Abstract

Coronary artery bypass grafting (CABG) and Percutaneous coronary intervention (PCI) revascularization strategies have undergone significant advancements in recent years, creating the need to reexamine data from clinical studies and critically scrutinize existing guidelines in order to determine the optimal care for each individual patient. In this review, we aim to address the current data available for the treatment of patients with multi vessel disease, focusing on special population subgroups based on advanced age, gender, previous CABG, renal failure and diabetes mellitus. This synthesis of information is necessary and timely as it will provide an essential framework for physician dialogue and evidence-based approach of coronary revascularization in the current and beyond in the management of these selected patients.

**Keywords:** Coronary Artery Bypass Grafting; Percutaneous Coronary Intervention; Diabetes Mellitus; Aged; Female; Renal Failure

**Abbreviations:** PCI: Percutaneous Coronary Intervention; DES: Drug-Eluting Stent; MVD: Multi-Vessel Coronary Artery Disease; CABG: Coronary Artery Bypass Grafting; ARTS I: Arterial Revascularization Therapies Study Part I; MASS II: Multi vessel Coronary Artery Disease; ERACI-II: Patients with Multiple Vessel Disease; SOS: Stent on Surgery; ASCERT: American College of Cardiology Foundation and the Society of Thoracic Surgeons Collaboration on the Comparative Effectiveness of Revascularization Strategies; DM: Diabetes Mellitus; HCR: Hybrid Coronary Revascularization

## Introduction

Multivessel coronary artery disease (MVD) is defined by significant atherosclerosis (>70% occlusion) involving at least two or three of the major coronary arteries, and it occurs in 40-65% of patients with acute myocardial infarction [1]. MVD is associated with a higher burden of comorbidities and left ventricular dysfunction, and it significantly increases the risk of morbidity and mortality after interventional therapy, as observed in previous studies [1,2]. Numerous additional studies on MVD have contrasted coronary artery bypass grafting (CABG) with the various methods of Percutaneous coronary intervention (PCI), from balloon angioplasty and bare metal stents, to first- and second-generation drug-eluting stents, and conclusions have fluctuated with time. Several factors contribute to this discrepancy, including but not limiting to the size and nature of the patient population, the type of technology utilized as well as experiences of the clinicians performing those procedures. To incorporate multiple trials and draw empirical conclusions

with enough statistical power and confidence, it is beneficial to conduct a meta-analysis of randomized controlled trials or refer to large clinical registries or other observational datasets.

Clinical trials investigating bare metal stent PCI versus CABG in multi vessel CAD include the Arterial Revascularization Therapies Study Part I [ARTS I], the Medicine, Angioplasty, or Surgery Study for Multi vessel Coronary Artery Disease [MASS II], the Argentine Randomized Study of Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease [ERACI-II]. In these studies, negligible difference was noted in long-term survival rates [3,4]. Secondary outcomes from these trials revealed an increased need for revascularization after 5 years with bare metal stenting [3,4]. However, when comparing first generation drug-eluting stents to CABG in the Stent on Surgery (SOS) trial, Booth and colleagues showed a continuing survival advantage after 6 years for patients who had a CABG [5]. Notably, PCI consistently reduced hospital mortality in all age groups [6].

CABG patients experienced greater relief from angina than those undergoing PCI, though the difference was minimal [7]. The ASCERT (American College of Cardiology Foundation and the Society of Thoracic Surgeons Collaboration on the Comparative Effectiveness of Revascularization Strategies) published in the *New England Journal of Medicine* showed that even though CABG had better outcomes over a period of four years (16.4% versus 20.8%; risk ratio 0.779), it did so with a higher financial burden than PCI [8]. More recently, in 2015, an observational registry study in New York compared second-generation DES to CABG (n=9223 matched pairs). PCI with everolimus-eluting stents had a lower risk of death and stroke within 30 days of the procedure, though there was no difference long-term (>30 days) [9]. However, PCI was found to be associated with greater risk of myocardial infarction in patients with incomplete revascularization, and a need for future revascularization.

Likewise, authors of this study propose weighing the short-term risk of death and stroke with CABG against the long-term need for additional revascularization and the risk of myocardial infarction if complete revascularization cannot be achieved. Importantly, specific patient subgroups with multi vessel coronary disease must be evaluated and assessed critically in order to determine the most optimal treatment strategy i.e. CABG or PCI. These subgroups include patients with advanced age, gender, previous CABG, renal failure and diabetes mellitus.

### Choice of coronary revascularization strategy in special subgroups

**a) Patients aged 65 and older:** The elderly patient population requires special attention, because of increased risk of mortality and perioperative complications with revascularization in the setting of multiple comorbidities and overall frailty. Weintraub et al. [10] investigated elderly patients and determined that after 4 years there was lower mortality as well as a long term survival advantage with CABG than with PCI in patients 65 years and older with two- or three-vessel coronary artery disease without acute myocardial infarction. A 2009 meta-analysis of 10 clinical trials also reported lower mortality rated with CABG intervention than PCI for those greater than 65 years [11]. In a population of octogenarians, Singh et al also determined that the mortality rate was five times higher in comparison to the younger population and actually represents thirty percent of all deaths after PCI [6]. In fact, in a cohort of previous studies, age was actually an independent predictor of outcomes after Percutaneous revascularization overall [6].

**b) Gender:** While the majority of patients with coronary artery disease are men, CAD is also the leading cause of death in women [6,12,13], yet women receive less revascularization and evidence-based medications [14]. In a population-based cohort study that spanned a decade, Guru et al. showed that women have a more complex clinical preoperative presentation and unfortunately are more likely to be readmitted with unstable

angina and congestive heart failure after CABG, despite having similar survival to men [12]. In some studies, such as the one by Lempereur et al. [15] that examined the risk factors for in-hospital mortality following PCI, female sex remained an independent predictor of mortality. Furthermore, in evaluating DES versus BMS angioplasty, while there is a profound prognostic advantage for both genders, female patients reportedly had a higher benefit [16].

**c) Previous CABG:** In patients that have previously undergone a CABG procedure, additional PCI procedures for isolated disease is feasible but can be sometimes challenging. Weintraub et al. [10] showed that even though the initial mortality was higher for CABG, there was little difference long term, but more patients required additional procedures following a PCI. A five-year trial of patients who experienced graft failure established that repeat revascularization occurred more frequently after BMS PCI implantation than any other process [17].

**d) Renal Failure:** Kidney function is an important clinical parameter to assess when considering coronary revascularization. Chronic renal disease and renal failure are common sequela of CAD and increase patients' risk of procedure-related morbidity and mortality [18,19]. Additionally, patients with end stage renal disease have a much greater incidence of CAD and acute myocardial infarction [20,21]. Hemmelgarn et al. [22] evaluated survival in patients who received CABG, PCI or no revascularization for three stratifications of kidney function: dialysis-dependent kidney disease, non-dialysis-dependent kidney disease, and a group with serum creatinine above 2.3 mg/dL (reference group).

Based on their data, CABG was associated with increased survival in all groups of kidney disease, while PCI was superior to the no-revascularization group particularly in the reference group patients and the dialysis-dependent group [22]. This study was further validated by Krishnaswami et al. [23] in which CABG is more favorable than PCI with stenting, primarily due to a low re-operation rate, despite a higher level of invasiveness and longer recovery time. Despite these results, however, a recent assessment of nationwide trends in revascularization for patients with end stage renal disease showed that PCI intervention for a ST-elevation myocardial infarction has increased from 18.6% to 37.8% between 2003 and 2011; CABG had decreased slightly, 6.1% to 5.7% [24].

**e) Diabetes Mellitus:** Several trials have examined revascularization strategies in patients with diabetes mellitus (DM) and multi vessel coronary disease. The first large trial comparing CABG and PCI exclusively in diabetic patients was the FREEDOM trial, which showed superiority of CABG to PCI with drug eluting stents in terms of long-term mortality [25]. As many subsequent trials were too small to reach consensus, a recent meta-analysis by Verma et al. [26] examined eight randomized

control trials of patients with diabetes mellitus and multi vessel vascular disease to compare outcomes undergoing CABG or PCI [26]. At five years follow-up, all cause mortality was nearly one-third less in patients undergoing CABG.

There was no significant difference seen at 1-year, and no difference in incidence of non-fatal myocardial infarction between the two groups. However, the relative risk of stroke after CABG was 2.4 times that of PCI patients (PCI risk of 0.8%). While CABG currently appears to be a superior technique to PCI in the diabetic subgroup, the impact of covariates on this decision remains uncertain. Comparing patients with insulin-treated diabetes mellitus with non- insulin treated patients, a subgroup analysis of the FREEDOM trial study found minimal difference in PCI versus CABG [27]. Thus, factors of insulin use, gender, age, and comorbidities should be taken into consideration for treatment of CAD in patients with diabetes.

## Conclusion

Treatment patterns of coronary artery disease either through PCI or CABG have evolved significantly over the last decade, especially with the advent of moresophisticated stent technology such bio-absorbable vascular scaffolds, novel anti platelet agents, robust imaging and surgical platforms, as well as reliable extracorporeal circulatory support devices. Likewise, in recent years, institutional experiences have also grown resulting in better outcomes and improved efficacies of both these procedures. At the same time, there is also widespread interest among clinicians to minimize surgical trauma and improve techniques to further improve graft patency following CABG procedures. This has been achieved via standardization of routine surgical procedures, and use of buffered saline graft preservation solutions [28]. The field of hybrid coronary revascularization (HCR)- involving simultaneous or staged PCI/CABG procedures in select patients- has also emerged in recent years with comparable and promising outcomes to CABG alone [29]. In a recent survey among 200 cardiologists and cardiac surgeons from 100 top-ranked U.S. hospitals, more than 75% of responders felt that HCR is a reasonable alternative technique for coronary revascularization among suitable patients (including older and relatively healthy patient population without complex lesions).

Most predicted that the use of HCR would increase in the next decade [30]. While the current state of HCR is still limited to selected patients, with increasing engagement from and dialogue between the interventionists and surgical communities, as well as validated data from RCTs, HCR has the possibility of being a reliable revascularization strategy in the upcoming years. This review is by no means comprehensive, but rather serves as a framework in initiate physician dialogue on the optimal management of select, and in some ways at-risk patient subgroups. It also serves to synthesize existing literature with a goal of pointing out various knowledge gaps that could potentially be addressed through additional research studies.

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