



# Does it pay to be indecisive when considering revascularization during percutaneous coronary intervention?

*"...CR should not necessarily be performed during either PCI or CABG in patients with multiple lesions. Rather, ischemia-guided procedures, using invasive and noninvasive functional evaluations, should be carried out."*

## KEYWORDS: carotid artery stenosis ■ endarterectomy ■ stenting

Angiographic complete revascularization (CR) has been associated with better long-term clinical outcomes after percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery [1,2]. In real world practice, however, diseased segments are often incompletely revascularized in patients undergoing PCI, due to technical complexity, low ejection fraction or safety concerns regarding the implantation of multiple drug-eluting stents. Furthermore, even in patients undergoing CABG, incomplete revascularization (IR) has occasionally been adopted to reduce operation-related complications, particularly when minimally invasive or off-pump surgery is attempted. Although several previous studies have demonstrated the benefit of CR after PCI or CABG, those results had limited application to current practices due to recent updates in the use of drug-eluting stent (DES), left internal mammary artery grafting, off-pump surgery and current medications. Therefore, a critical review evaluating the clinical impact of angiographic CR is appropriate at this time.

### Definitions of angiographic CR

Definitions of CR have varied in previous studies, depending on the patient population and the types of treatment, either PCI or CABG. Although the traditional definition of CR was total revascularization of lesions >1.5 mm in diameter and with >50% stenosis [3,4], several studies have defined CR relative to vessels with >70% stenosis [1]. In addition, practical definitions were applied to proximal segments or vessels >2.5 mm in diameter because the stent sizes available were >2.5 mm [5,6].

The prevalence of CR was found to differ between PCI and CABG procedures. When the traditional definition of CR was applied to all coronary segments, its success rate among all patients was <50% [6]. However, using the definition for

larger vessels (>2.5 mm) or tighter stenosis (>70%), the success rate of CR was >60% [1,2,6,7]. Since CR was attempted during most CABG operations, it was more frequently achieved after CABG, with a success rate >70% [3,5,6,8–10]. Therefore, it is noteworthy that IR was not uncommon following either PCI or CABG [11].

### Outcomes of CR

In the era of bare-metal stents (BMS), the Arterial Revascularization Therapies Study group investigated the prevalence of CR, defined as revascularization of lesions >1.5 mm in diameter and with >50% stenosis, in 1205 patients randomized to either PCI with BMS or CABG [3]. They reported that the prevalence of CR was 71% after PCI and 98% after CABG. Over 1 year, the incidence of major adverse cardiac and cerebrovascular events (MACCE), including death, myocardial infarction, stroke or repeat revascularization, was lower following PCI in the CR than in the IR group (23.4 vs 30.6%;  $p < 0.05$ ), but was similar in these two groups after CABG (10.1 vs 12.2%). This finding was supported by the results of the New York State PCI Registry, which enrolled 21,945 patients who received BMS [2]. CR for lesions with >50% stenosis was performed in 69% of patients, with different hospitals reporting rates ranging from 52 to 88%. Over 3 years, the adjusted survival rate was 91.4% in the CR group, and 89.5, 88.8 and 88.7% in the groups of patients with  $\geq 2$  vessel IR, total occlusion, and  $\geq 1$  vessel IR plus total occlusion, respectively. Therefore, the adjusted hazard ratio (HR) of IR for survival was 1.15 (95% CI: 1.01–1.30) compared with CR. After PCI with DES, CR was still an important predictor of favorable long-term prognosis. For example, of the 11,394 patients in the New York State Registry who underwent DES implantation, 39% underwent CR [1]. The risk-adjusted survival rates were 93.8% in the IR



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group and 94.9% in the CR group (HR: 1.23; 95% CI: 1.04–1.45). Therefore, these investigators recommended that patients with multivessel disease undergo CABG if CR was not expected to be successful by PCI. Regarding the impact of CR in CABG, a Swedish hospital registry reported that IR in >1 diseased vessel was associated with an increased risk of 5-year mortality (HR: 1.82; 95% CI: 1.15–2.85) [9]. However, the vast majority of registries showed that anatomical CR was not associated with long-term outcomes in patients undergoing CABG [3,5,8].

Despite the aforementioned studies showing the superior benefits of CR, the most recent study from the Asan Multivessel Registry failed to show an association of CR with long-term clinical outcomes [6]. Of 1914 patients with multivessel disease undergoing DES implantation (1400 patients) or CABG surgery (514 patients), 917 (47.9%) underwent angiographic CR for lesions with >50% stenosis and >1.5 mm in diameter, including 573 (40.9%) of the patients who underwent PCI and 344 (66.9%) of those who underwent CABG. Over 5 years, the incidence of MACCE was similar in patients with CR and IR (22.4 vs 24.9%; adjusted HR: 0.91; 95% CI: 0.75–1.10;  $p = 0.32$ ). Even when CR was defined for lesions >2.5 mm in diameter or proximal lesions, CR remained a nonsignificant predictor of 5-year MACCE. The 368 (19.2%) patients with multivessels left unrevascularized, however, showed a tendency toward a higher rate of MACCE (30.3 vs 22.1%; adjusted HR: 1.27; 95% CI: 0.97–1.66;  $p = 0.079$ ). The discrepancy between the results of the Asan registry and those of other studies may be caused by differences in patient characteristics and procedural techniques. Nonetheless, what these studies consistently indicate is that a ‘reasonable incomplete revascularization’ is a more reliable strategy for patients with multivessel disease [6,8,11].

### Ischemia-guided revascularization

The limitations of angiography-guided CR were already suggested by studies assessing functional outcomes, including myocardial perfusion image or fractional flow reserve (FFR). In the studies using myocardial perfusion imaging, almost one-half of patients underwent multivessel revascularization without objective evidence of inducible ischemia [12]. A substudy of the Flow Reserve versus Angiography for Multivessel Evaluation (FAME) study found that only 14% of patients with anatomical three-vessel disease were functionally abnormal, as assessed by FFR [13]. These studies indicate that angiographic stenosis is

often misleading in determining the need for revascularization. Therefore, guidelines have recommended that ischemia-guided revascularization should be based on the functional assessment of inducible ischemia [14].

Unnecessary revascularization for nonischemic coronary vessels may lead to increased medical costs and deterioration in clinical prognosis. The safety of deferring stenotic, but nonischemic, vessels has been confirmed in several studies. For example, during 5-year determination of FFR in patients in the Determine Appropriateness of Angioplasty in Moderate Coronary Stenoses (DEFER) study, deferred patients with FFR  $\geq 0.75$  had a similar event rate as stented patients. Paradoxically, in the FAME study, the 2-year incidence of death or myocardial infarction was significantly lower in FFR- than in angiography-guided patients (8.4 vs 12.9%;  $p = 0.02$ ) [15], although the increased event rate in the latter group may be due to the use of more complex procedures using more stents. Consequently, cost-utility analysis showed that FFR-guided stenting significantly decreased 1-year medical costs with the same risk of events [16]. This finding is in line with the lack of clinical benefit of routine revascularization, compared with provisional use, in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial for stable coronary patients [17].

### Conclusion & future perspective

Because of the disadvantage of anatomic evaluation and advantage of functional evaluation, adherence to guidelines should be repeatedly emphasized by physicians. It is not reasonable to revascularize all coronary lesions without functional assessment. For example, when a patient presents with unstable symptoms and has a flow-limiting right coronary stenosis on emergency angiography, attempted CR with ad-hoc simultaneous PCI for a nonflow-limiting stenosis in the left anterior descending artery is not reasonable in the absence of FFR assessment. If FFR cannot be performed, a noninvasive functional evaluation followed by a staged procedure is needed after urgent PCI for the right coronary stenosis. In patients with stable coronary symptoms, functional assessment before revascularization should be considered mandatory.

This article highlights that angiographic CR should not necessarily be performed during either PCI or CABG in patients with multiple lesions. Rather, ischemia-guided procedures, using invasive and noninvasive functional evaluations, should be carried out.

### Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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