Complete Versus Incomplete Revascularization With Coronary Artery Bypass Graft or Percutaneous Intervention in Stable Coronary Artery Disease

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In patients who have multivessel but stable coronary artery disease (CAD), the perceived advantages of complete revascularization (CR) over incomplete revascularization (IR) are intuitively logical and have been the impetus to perform CR whenever feasible. These advantages were suggested by early studies in patients with 3-vessel CAD who underwent coronary artery bypass graft (CABG) demonstrating a survival benefit of patients with CR compared with those with IR.\(^1\)\(^-\)\(^4\) Nonetheless, in practice, the variations in severity of the coronary anatomy as well as the patient’s clinical status often precludes CR resulting in a higher frequency of IR in patients with multivessel disease. For example, in the SYNTAX (SYnergy between PCI with TAXus and Cardiac Surgery) trial, patients randomized to percutaneous intervention (PCI)\(^5\) had CR in only 56.7% even when CR was intended and in Bypass Angioplasty Revascularization Investigation (BARI) this was 56%.\(^6\) A critical review of the literature demonstrates the complexity of the issues and poses several unanswered questions (Table 1).

In the current era of significantly improved medical therapy (primary and secondary prevention) of CAD as well as the increasing use of sophisticated invasive and noninvasive testing of the physiological significance of coronary artery stenoses, both surgeons and cardiologists have an arsenal of diagnostic tools at hand that may guide decisions in selecting revascularization strategies. This review provides a contemporary overview of the currently available literature in the field and proposes an evidence-based approach for patients with severe CAD and stable angina undergoing revascularization.

Frequently Encountered Difficulties in Reviewing Data on CR

The Missing Universal Definition

The dilemma of comparing outcomes after CR and IR begins with the lack of universal definitions. There are considerable differences between complete/incomplete anatomic and functional/physiological revascularization. Ong and Serruys\(^8\) reviewed comprehensively past definitions of CR used in different trials (Table 2).

As seen, some definitions are based on anatomy, some on the extent of ischemia, and some on other preset criteria. Conceivably, a comparison of studies using such different definitions is difficult, if not impossible. In most trials, completeness of revascularization has been determined on anatomic basis because of lack of data on myocardial viability and jeopardy.\(^18\) To improve future comparability, Zimarino et al\(^9\) recently proposed a contemporary definition of 3 different types of revascularization as follows: (1) complete anatomic revascularization, defined as treatment of all coronary artery segments >1.5 mm in diameter and ≥50% diameter stenosis; (2) incomplete anatomic but functionally adequate revascularization (ie, reasonable IR or functionally CR),\(^19\) defined as treatment of all coronary segments with ≥50% diameter stenosis supplying viable myocardium; and (3) incomplete functional revascularization consequentially, defined as the inability to treat all coronary segments that supply viable myocardium and have a >50% diameter stenosis.\(^18\)

Influence of Confounding Variables

In both trials and registries, there are multiple reasons underlying the decision not to perform CR in an individual patient and differences in baseline variables appear to play a major confounding role, which could bias the data in favor of CR by selecting the healthier patient for CR rather than IR. Multivariate analyses tend to adjust for differences in baseline variables but cannot eliminate these nor adjust for unmeasured confounders/variables and no amount of propensity matching can evaporate the bias introduced when one group of patients is sicker than the other.

The clinical presentation influences the decision to perform CR; for example, the presence of hemodynamic instability at the time of the procedure may have an impact on procedural performance, in both CABG and PCI.\(^20\) Other patient characteristics also influence the decision such as older age, comorbidities, and the development of a procedural complication. In general, sicker patients with...
Table 1. Unanswered Questions

Unanswered Questions
1. Are there standardized definitions for CR/IR available?
2. Is CR a fundamental tenet or is it just a worthwhile objective, for which benefits outweigh the risks? Does it have the same implications for surgeons vs interventional cardiologists?
3. Should CR become the standard for comparison of the efficacy of different procedures, eg, should the ability to achieve CR vs IR be used as a criterion to select specific therapeutic options such as PCI vs CABG?
4. Do we perform CR in those patients in whom we can, and only perform IR when CR is not feasible?
5. Has the FAME7 study reframed the issues with regard to CR vs IR?
6. Does the effect of CR vs IR depend on the specific arterial segment involved, eg, is CR more important when the LAD is involved?

CR indicates complete revascularization; IR, incomplete revascularization; PCI, percutaneous intervention; FAME, Fractional Flow Reserve vs Angiography for Multivessel Evaluation; and LAD, left anterior descending coronary artery.

Table 2. Summary of Definitions for Complete Revascularization After Ong and Serruys et al

Revascularization Definition

Complete anatomic/numeric revascularization All stenotic vessels are revascularized, irrespective of size and territory supplied.
- Unconditional 2,10
- Conditional 11–15

Complete functional revascularization All ischemic myocardial territories are repurposed; areas of old infarction with no viable myocardium are not required to be repurposed.
14,15

Complete revascularization by a predetermined scoring cutoff value Scoring of stenoses in different vessels at different locations (weightings may be used). The overall extent of disease is a continuous variable, the treatment is another variable, and the posttreatment score determines completeness of revascularization.
16

Functional Jeopardy score: The postrevascularization score is calculated on the basis of the amount of remaining myocardium at risk.
17

have an inherent methodological disadvantage. Procedural success is assessed with postprocedural coronary angiography, whereas for CABG trials the review of completeness of revascularization often relies on the operative report to determine (1) which vessels were bypassed and (2) the status of early graft patency (assessed by flowmeters and occasionally fluorescein angiography). In addition, angiographic evaluations often lack the use of quantitative coronary angiography, which significantly increases inter- and intraobserver variability.

IR Versus CR in Chronic Stable Angina: Trials, Registries, and Single-Center Experiences

CR Versus IR in Coronary Artery Bypass Grafting Alone or In Direct Comparison With PCI

There are several studies that suggest a survival benefit of CR over IR in patients with severe multivessel CAD undergoing CABG. A large study from Emory showed that survival at 5 years was significantly greater in patients with CR (88.5%) than in those with IR (83.5%). In addition, more patients were free of angina after CR (70%) than after IR (58%). Similarly, Klei et al demonstrated that CR was associated with better survival (5-year unadjusted survival rate 82.4% versus 52.6%), only limited by major baseline differences between the 2 groups favoring patients who underwent CR, and a lack of adjustment in the survival analysis. Another large series from the Cleveland Clinic showed that CR compared with IR with ungrafted high-grade left circumflex or right CAD was associated with a substantially increased 10- and 20-year survival (91.1% CR versus 81% IR at 10 years and 70% versus 53% at 20 years). Finally, a more recent substudy of the SYNTAX trial including registry and randomized data demonstrated, after multivariate analysis, that IR and not the complexity of the coronary anatomy to be an independent predictor of adverse 2-year outcomes (P=0.002).

The difference, however, was mainly driven by the need for repeat revascularization and not by survival (Tables 3 and 4).

In contrast to the above, several other studies failed to demonstrate convincing benefit of CR over IR for multivessel CABG. In an important but retrospective study, using the CASS Registry data, Bell et al showed that in stable patients (group I, Canadian Cardiovascular Society I–II), the number of vessels bypassed failed to significantly influence event-free survival. In patients who had severe symptoms (Canadian Cardiovascular Society classes III–IV [group II]), however, bypassing ≥3 vessels independently improved long-term survival, specifically in patients with left ventricular dysfunction (ejection fraction <35%; Figure 1). Similar conclusions were drawn from the BARI. Vander Salm et al concluded that after 7 years of follow-up, the construction of ≥1 venous graft to any system other than the left anterior descending coronary artery (LAD) appeared to confer no long-term advantage and could actually be deleterious if multiple non-LAD insertion sites were chosen (ie, >1 graft to right coronary artery, circumflex, or ramus system). In addition, the subsequent subanalysis of Bourassa et al within the nondiabetic group with a priori intended IR failed to show a difference in the 5-year overall and cardiac mortality. More data supporting noninferiority of IR were
recently published by Rastan et al. In this analysis of 936 consecutive patients undergoing reasonable IR (with a left internal mammary artery to the LAD but without bypasses to the right coronary artery or circumflex vessels), there was no difference in hospital mortality (3.3% CR versus 3.2% IR) or in cumulative survival at 1 year (93.1% CR versus 93.6% IR) and 5 years (82.2 CR versus 80.9% IR). Further indirect support for the concept of reasonable IR comes from older data by Lytle et al, where reoperation of a late graft stenosis conveyed no survival benefit, unless performed on an LAD vein graft, in patients with moderate-to-severe decrease in LV function, older age, 3 vessels or left main disease, and classes I and II symptoms.

Some studies investigated differences in CABG and PCI completeness of revascularization in a direct comparison. Both Arterial Revascularization Therapies Study (ARTS) and ARTS II revealed no significant difference between CR and IR (for both CABG and PCI) for death, myocardial infarction (MI), and cerebrovascular accident during 1 and 5 years of follow-up. Repeat revascularization in ARTS was statistically more frequent in IR-PCI versus CR-PCI (Figure 2) and in ARTS II more frequent in IR-PCI than CR-CABG, suggesting that the more complex the coronary anatomy (ie, higher SYNTAX score), the more benefit the patient had from CR in the PCI group.

A large, recent study by Kim et al analyzed 1914 consecutive Asian patients with multivessel coronary disease undergoing drug-eluting stents (DES) implantation (n=1400) or coronary artery bypass graft surgery (n=514). Over a 5-year follow-up, the authors did not find a significant difference in outcomes between CR and IR for both percutaneous and surgical revascularization, except in those patients with multivessel

### Table 3. Summary Data From Studies of CABG

<table>
<thead>
<tr>
<th>Trial/Study/Registry</th>
<th>Year(s)</th>
<th>No. of Patients/Follow-Up</th>
<th>Definition of CR</th>
<th>End Points</th>
<th>Benefit of CR vs IR/Caveats</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASS, Bell⁴</td>
<td>1974–1979</td>
<td>3372 with 3-vessel disease/annually for a mean of 4.9 y (maximum 8.1)</td>
<td>Unconditional (≥3 vessels bypassed)</td>
<td>Freedom from death, myocardial infarction, reoperation, or development of definite angina</td>
<td>Only in CCS III/IV (in particular, those with EF &lt;35%)</td>
<td>Observational</td>
</tr>
<tr>
<td>Emory, Jones³</td>
<td>1978–1981</td>
<td>1238 with 3-vessel disease/5 y</td>
<td>Unconditional</td>
<td>5-y survival, hospital mortality, myocardial infarction, employment, and angina status</td>
<td>Survival difference small (88.5% vs 83.5%), freedom from angina more significant</td>
<td>Observational</td>
</tr>
<tr>
<td>Lytle²⁶</td>
<td>1972–1989</td>
<td>1117/10 y</td>
<td>IR ≥20% graft stenosis</td>
<td>Survival</td>
<td>Re-CABG beneficial especially in LAD territory, also in reduced EF, elderly, 3-vessel/LM disease</td>
<td>Observational</td>
</tr>
<tr>
<td>Scott²⁵</td>
<td>1971–1997</td>
<td>2067/5, 10, and 20 y</td>
<td>IR ≥50% stenosis in LCX or RCA</td>
<td>All-cause mortality and reintervention</td>
<td>Ungrafted RCA and LCX (≥50%) and particularly high-grade (&gt;70%) L CX, prox. RCA, and any left main disease reduced long-term survival</td>
<td>Observational</td>
</tr>
<tr>
<td>BARI, Vander Salm²⁷</td>
<td>1988–1991</td>
<td>1507/7 y</td>
<td>Multiple (see Table 2)</td>
<td>Death, cardiac death, MI, repeat revascularization, angina, composites of death/MI, and cardiac death/MI</td>
<td>None; multiple non-LAD bypass grafts may increase risk</td>
<td>Observational</td>
</tr>
<tr>
<td>Kleiśli¹¹</td>
<td>1998–2000</td>
<td>1034/5 y</td>
<td>Conditional (grafs to every primary coronary artery &gt;50% stenosis)</td>
<td>All-cause death and cardiac death</td>
<td>Survival benefit of CR over IR/undisputed Kaplan-Meier curves only despite significant baseline differences</td>
<td>Observational</td>
</tr>
<tr>
<td>Rastan²⁸</td>
<td>2000–2007</td>
<td>936 (of 8806)/1 and 5 y</td>
<td>Reasonable IR (LIMA to LAD only)</td>
<td>Cumulative survival and hospital mortality</td>
<td>No difference</td>
<td>Observational</td>
</tr>
<tr>
<td>Mohr¹²</td>
<td>2005–2007</td>
<td>1541/2 y</td>
<td>Conditional, grafting all lesions ≥50% with a vessel diameter &gt;1.5 mm</td>
<td>MACCEs = all-cause death, VCA, MI, and repeat revascularization</td>
<td>IR (driven by repeat revascularization) predictor for adverse 2-y outcome</td>
<td>RCT/Registry</td>
</tr>
<tr>
<td>Kozower²⁰</td>
<td>1986–2003</td>
<td>500/5 and 8 y</td>
<td>Conditional (≥1 graft to all major territories with ≥50% stenosis)</td>
<td>Survival</td>
<td>CR improved mean survival by 25% (only patients 80–94 y old)</td>
<td>Observational</td>
</tr>
<tr>
<td>Aziz²³</td>
<td>1986–2007</td>
<td>580/5 and 8 y</td>
<td>Unconditional and conditional (≥1 graft to all major diseased vessels ≥50% stenosis)</td>
<td>Survival</td>
<td>CR improved mean survival by 18% (only patients 80–94 y old)</td>
<td>Observational</td>
</tr>
</tbody>
</table>

CABG indicates Coronary Artery Bypass Graft; CR, complete revascularization; IR, incomplete revascularization; CASS, Coronary Artery Surgery Study; CSS, Canadian Cardiovascular Society; LAD, left anterior descending coronary artery; RCA, right coronary artery; LCX, left circumflex; BARI, Bypass Angioplasty Revascularization Investigation; and MI, myocardial infarction.
IR (≥2 diseased vessels incompletely revascularized); among there was a trend in favor of CR for the composite end point of death, myocardial infarction, stroke, and repeat revascularization (30.3% versus 22.1%).

With the advent of DES and decreasing rates of restenosis and intensified medical secondary prevention, the need for repeat revascularization has declined, closing the former gap between CABG and PCI, but with the caveat that this applies to patients judged suitable for either procedure during the process of eligibility for randomization. More importantly, unless multiple vessels (≥2) are left unrevascularized, IR patients survive as long as CR patients.

Commonly, elderly patients (≥80 years of age) are underrepresented in large clinical trials. It is therefore interesting to note that in 2 studies focusing on octogenarians, Kozower et al29 and Aziz et al30 found that after adjustment for baseline variables, complete CABG revascularization carried a survival benefit over IR. This is in contrast to a subset of data by Kleisli et al11 who found no clinically significant benefit of CR in their octogenarians.

In conclusion, data from the last 3 to 4 decades show a rather consistent trend toward survival benefit of a CR over an IR strategy for patients with multivessel disease undergoing CABG who are older and have severe anginal symptoms or reduced left ventricular ejection fraction. Of note, there are no current studies in patients with reduced LV function or severe anginal symptoms directly comparing CABG versus PCI with respect to completeness of revascularization. Traditionally, these patients undergo CABG surgery as recommended by the current national guidelines.

However, in younger and overall more stable patients with preserved left ventricular ejection fraction, reasonable IR (provided that the LAD is revascularized)26,28 appears feasible and safe without compromising survival but accepting a potentially higher need for future repeat revascularization. Survival benefits of CR over IR shown in earlier studies in this group of patients are likely due to less aggressive medical therapy before and after surgery, and the powerful potential impact of confounders does not allow for definitive conclusions with regard to the benefits of CR versus IR.

### Table 4. Data From Subset Analyses From PCI vs CABG Trials

<table>
<thead>
<tr>
<th>Trial/Study/Registry</th>
<th>Year(s)</th>
<th>No. of patients/Follow-Up</th>
<th>Definition of CR/End Points</th>
<th>Benefit of CR vs IR/Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td>BARI, Bourassa14</td>
<td>1988–1991</td>
<td>1829/5 y</td>
<td>Functional mortality, cardiac mortality, repeat CABG, repeat angioplasty, and any repeat revascularization</td>
<td>PTCIRA in nondiabetics does not compromise long-term survival</td>
</tr>
<tr>
<td>ARTS I10</td>
<td>1997–1998</td>
<td>1143/1 y</td>
<td>Unconditional (all lesions with ≥50% stenosis)/death, MI, and CVA</td>
<td>IR-PCI with reduced event-free survival/only with inclusion of repeat revascularization</td>
</tr>
<tr>
<td>ARTS II13</td>
<td>567/5 y</td>
<td>Conditional (all lesions with ≥50% stenosis ≥1.5 mm/death, CVA, MI, and any revascularization</td>
<td>IR-PCI confers higher event rate only in highest SYNTAX score tertile/major driver of statistics was repeat revascularization</td>
<td></td>
</tr>
<tr>
<td>Kim31</td>
<td>2003–2005</td>
<td>1914/5 y</td>
<td>Multiple/death, composite of death, MI, CVA, and composite of death, MI, CVA, and repeat revascularization</td>
<td>No clear benefit of CR, only trend toward increased composite of death, MI, CVA, and repeat revascularization with multivessel (≥2) IR-PCI</td>
</tr>
</tbody>
</table>

PCI indicates percutaneous intervention; CABG, coronary artery bypass graft; CR, complete revascularization; IR, incomplete revascularization; BARI, Bypass Angioplasty Revascularization Investigation; PTCA, percutaneous transluminal coronary angioplasty; ARTS, Arterial Revascularization Therapies Study; MI, myocardial infarction; and CVA, cerebrovascular accident.

### Figure 1.
Selected graphs from Bell et al9 showing event-free survival stratified by several vessels grafted overall (upper left graphic), survival in patients with an ejection fraction (EF) <35% (upper right graphic), and event-free survival for the combined end point of death/myocardial infarction (MI)/reoperation and recurrence of angina (lower graphic).
The impact of CR in percutaneous interventions has been investigated for >2 decades. Within this time frame, interventional techniques have significantly and rapidly improved including the implementation of bare metal and subsequently DES over balloon angioplasty alone (Table 5).

Several earlier studies and registries, some reaching into the BMS era, failed to show a clear long-term survival benefit of CR over IR in percutaneous interventions. Bourassa et al23 investigated the long-term outcomes of 757 patients in the National Heart, Lung, and Blood Institute (NHLBI) Percutaneous Transluminal Coronary Angioplasty (PTCA) Registry, 83% of who had IR. In-hospital emergency and elective CABG rates were higher for IR; the 9-year data, however, showed no significant difference in adjusted freedom from death, MI, recurrent angina, or repeat revascularization between CR and IR. Data from Mayo Clinic in the early PTCA era demonstrated that CR was achieved in only 41%.32 After 26 months of follow-up, adjusted event-free survival of death or MI, necessity for CABG surgery, and the occurrence of severe angina were similar between IR and CR.

Ijsselmuiden et al34 followed 219 patients with MVD in the bare-metal stent era of which 108 underwent CR and 111 culprit vessel PCI (CVR). Within a 1- and 5-year follow-up, there was no statistically significant difference in MACE between CVR and CR. Data from the BARI trial showed that within 5 years after PTCA, there was no significant difference between patients receiving CR versus IR with angioplasty with regard to cardiac death, MI, need for CABG, or angina.14 By pooling data from 2047 patients undergoing PTCA in the BARI

This has had major implications for the comparability and applicability of studies performed before the era of routine use of DES and current improvements in postinterventional medical therapy, including more advanced antiplatelet therapy and aggressive risk factor reduction.

Percutaneous Intervention

**Table 5. Summary Data From Studies of PCI**

<table>
<thead>
<tr>
<th>Trial/Study/Registry</th>
<th>Year(s)</th>
<th>No. of patients/Follow-Up</th>
<th>Definition of CR/End Points</th>
<th>Benefit of CR vs IR/Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHLBI PTCA, Bourassa23</td>
<td>1985–1986</td>
<td>757/9 y</td>
<td>Residual stenosis ≤50%/freedom from death, MI, CABG, and PTCA</td>
<td>CR reduced late occurrence of CABG only</td>
</tr>
<tr>
<td>BELL22</td>
<td>1979–1988</td>
<td>867/26 mo</td>
<td>Dilation of all stenoses ≥70%/event-free survival of death, MI, CABG, and angina</td>
<td>No difference after adjustment for baseline variables</td>
</tr>
<tr>
<td>BARI, Kip33</td>
<td>1988–1991</td>
<td>2047/5 y</td>
<td>All clinically relevant lesions/cardiac death, death/MI, and CABG</td>
<td>CR reduced the need for CABG</td>
</tr>
<tr>
<td>Ijsselmuiden34</td>
<td>1995–1998</td>
<td>219/1 and 5 y</td>
<td>All vessels ≥50% stenosis/composite of cardiac and noncardiac death, CABG, and re-PCI</td>
<td>No difference</td>
</tr>
<tr>
<td>NYS31</td>
<td>1997–2000</td>
<td>21 945/3 y</td>
<td>All lesions ≥50% in major vessels/survival</td>
<td>IR increased adjusted mortality by 15% (absolute survival differences small, baseline characteristics favoring CR/CTO patient population</td>
</tr>
<tr>
<td>APPROACH15</td>
<td>1995–2001</td>
<td>1956/3 y</td>
<td>Functional (Duke jeopardy score ≤2)/death, repeat PCI, and CABG</td>
<td>CR reduced the need for CABG, no survival benefit</td>
</tr>
<tr>
<td>Hannan21</td>
<td>2003–2004</td>
<td>11 294/18 mo</td>
<td>All lesions ≥70% in major vessels /mortality, death/MI, CABG, and repeat PCI</td>
<td>CR with 1.1% survival benefit/ baseline characteristics again favoring CR/CTO patient population</td>
</tr>
<tr>
<td>Valenti18</td>
<td>2003–2006</td>
<td>486/2 y</td>
<td>TIMI 3 with residual stenosis ≤30% in major vessels and branches (&gt;2 mm)/cardiac survival</td>
<td>10% survival benefit with CR/CTO patient population</td>
</tr>
<tr>
<td>Lehmann16</td>
<td>2000–2008</td>
<td>679/2.5 y</td>
<td>3 different definitions, unconditional and conditional/long-term all-cause mortality</td>
<td>Only CR of all segments (unconditional) predictor of survival/R patients with more comorbidities</td>
</tr>
<tr>
<td>Géneréux16</td>
<td>2003–2005</td>
<td>2686/1 y</td>
<td>Residual SYNTAX score=0/MACE and death or MI after 30 days and 1 y</td>
<td>Residual SYNTAX score &gt;8 associated with poor prognosis/ACS patient population</td>
</tr>
</tbody>
</table>

PCI indicates percutaneous intervention; CR, complete revascularization; IR, incomplete revascularization; MI, myocardial infarction; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; CTO, chronic total occlusion; and APPROACH, Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease.
randomized trial and the BARI observational registry, Kip et al.\textsuperscript{33} investigated the differential impact of a pre-PTCA strategy of IR versus CR because of initial lesion outcome. Despite unfavorable baseline characteristics of the IR group, a pre-PTCA strategy of IR or CR because of unsuccessful but intended CR was unrelated to 5-year risk of cardiac death or death/myocardial infarction compared with CR, but were all independently related to the need for CABG.\textsuperscript{33} In contrast, more recent data in the later BMS and DES era, especially in patients with CTO, suggest that CR has a small but statistically significant survival benefit over IR.

Data from the New York State Registry during the BMS era tend to support the concept of CR by demonstrating that the 3-year adjusted mortality was increased by 15% when revascularization was incomplete.\textsuperscript{22} In detailed analyses of the IR group, a single unopened CTO increased the risk of late death by 35% and ≥2 incompletely revascularized arteries including ≥1 CTO increased the risk by 36%. Despite statistical significance, the magnitude of the benefit was small and of uncertain clinical significance. In addition, there were multiple unfavorable patient characteristics and a variety of comorbidities associated with IR that all favored the CR arm reflecting the limitations of multivariate analysis as eluded to above.

Comparable data with similarly CR-favoring baseline characteristics were obtained by the same group during the DES era.\textsuperscript{21} In this large cohort, 18-month survival was slightly, but still statistically significantly higher in the CR group (93.8 versus 94.9%; \( P=0.01 \)). When stratified further, patients with 2 vessels not revascularized and total occlusions were at highest risk.

Additional support for performing CR in severe CAD with at least 1 CTO came from Valenti et al.\textsuperscript{35} The 2-year cardiac survival rate was higher in the CTO-PCI success group compared with CTO-PCI failure group and overall in patients with CR when compared with patients with IR.

The investigators of the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH)\textsuperscript{13} reported that independent predictors of IR were the presence of a total occlusion, a higher pre-PCI Duke jeopardy score,\textsuperscript{14} aged >65 years, and renal failure. After correcting for baseline characteristics, complete multivessel PCI was associated with a reduced need for future CABG but not repeat PCI and only a nonsignificant trend toward better survival.

More recently, Lehmann et al.\textsuperscript{36} demonstrated that CR was associated with a survival benefit of ≈50% over IR. When STEMI patients (26% of the population) were excluded, however, there was no longer a statistically significant difference.

In a meta-analysis of 26 studies and a total of 46,260 patients by Bangalore et al.,\textsuperscript{37} there was an overall trend of favoring CR. CR was associated with a 35% lower risk of all-cause death, significantly lower cardiac mortality, nonfatal myocardial infarction (OR=0.79; 95% CI, 0.70–0.89) and the need for CABG (OR=0.51; 95% CI, 0.39–0.65) compared with patients undergoing IR. CR was also associated with 31% less angina with no difference in repeat PCI. The results were mainly driven by the BARI and NYS-PCI registry data.\textsuperscript{37}

Most recently, a novel approach of calculating the residual SYNTAX score in patients with IR after PCI for moderate- to high-risk acute coronary syndromes demonstrated a poorer 30-day and 1-year prognosis for patients with a residual SYNTAX score of >8.\textsuperscript{16} Future studies in patients with stable CAD will have to show whether a higher residual SYNTAX score is also associated with a poorer prognosis in a stable patient population.

In conclusion, the sicker the patient as defined by the presence of multivessel disease, CTO and impaired LV function combined with the evidence of viable myocardium, the greater the apparent survival benefit from CR with PCI but with the caveat that in almost all the studies baseline variables and demographics tended to favor patients receiving CR. In addition, only ≈50% of patients could be completely revascularized largely because of the presence of CTO. In studies where CR is obtainable, outcomes are better when it is achieved. The actual differences in survival are small, and the major benefit may be on a lower rate of repeat revascularization in the DES era. Irrespective of whether the patient is completely or incompletely revascularized, optimal medical therapy including aggressive risk factor reduction plays a crucial role in reducing the rates of late repeat revascularization.

Fractional Flow Reserve in the Context of CR

In multivessel CAD, clinical and anatomic data can be supplemented by fractional flow reserve (FFR) as an invasive assessment of the physiological significance of a stenosis to guide deciding which vessel(s) can be left nonrevascularized. The results of the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trial\textsuperscript{7} showed that there was a 5.1% higher survival free of MACE in the FFR-guided group after 1 year (MACE=death, nonfatal MI, repeat revascularization). Of note, of all lesions between 70% and 90% in the FFR group, 80% had an FFR <0.80 but still 20% had an FFR >0.80. Of all lesions between 50% and 70%, only 40% had an FFR <0.80 but 60% had an FFR >0.80 (Figure 3).\textsuperscript{38} Indeed, the application of an FFR-guided functional SYNTAX score (versus a purely anatomic SYNTAX score) on patients with multivessel CAD undergoing PCI helps to better discriminate the risk of adverse events.\textsuperscript{39}
With this information, one has to question the common surgical revascularization threshold of 50% diameter stenosis, given that the FAME data suggest that 60% of such stenoses may not be hemodynamically significant. In fact, CR based on anatomic criteria alone may soon become obsolete, emphasizing physiology-driven coronary interventions.

Implications: Is Reasonable IR Clinically Reasonable?

In summary, many studies that support an approach of CR versus IR are inconclusive because of the multiplicity of confounding variables that in general favor patients who were completely revascularized. Although CR is a desirable goal, it is not mandatory and the concept of reasonable IR appears to offer comparable results. This assumes, however, that viable LAD territory is revascularized.26,28

In this respect, we should consider IR as part of a spectrum. At one end are patients with small vessels, less severe multivessel disease (eg, 2 vessel disease or low SYNTAX score), lesser degrees of ischemia, and myocardial jeopardy among whom no more than one major epicardial vessel is nonrevascularized; in this setting, IR would be considered reasonable. At the other end of the spectrum are patients with extensive ischemia, viable myocardium, and significant disease of all 3 vessels or a high SYNTAX score. Here, the approach of IR may be hazardous and associated with a substantial residual burden of angina, myocardium at risk, and adverse cardiac events.40

We here propose a reasonable, universal definition of CR/IR incorporating current evidence:

1. Complete anatomical revascularization defined as treatment of all coronary artery segments >1.5 mm in diameter and ≥50% diameter stenosis regardless of their functional significance.

2. Incomplete anatomical but functionally adequate revascularization (reasonable IR) defined as treatment of coronary segments with ≥50% diameter stenosis and an FFR ≤0.8, or ≥70% diameter stenosis without FFR supplying viable myocardium.

3. Incomplete anatomical and functional revascularization defined as the inability to treat all coronary segments that have a ≥50% to 70% diameter stenosis and an FFR ≤0.8 or >70% without FFR that supply a significant degree of viable myocardium.

The advent of hybrid coronary revascularization to treat multivessel coronary disease, that is, combining percutaneous techniques with minimal-access CABG, may unify the best of both revascularization techniques in 1 procedure. At least in small early-experience studies with short-term follow-up, hybrid revascularization appears feasible and safe.51-53 However, an increased need for early antiplatelet therapy with the risk for bleeding complications and repeat revascularization, driven by IR and in-stent restenosis, may reduce the overall benefit.53-54 In addition, Lichtenberg et al55 showed that multivessel disease was an independent risk factor for adverse outcome in patients undergoing minimally invasive revascularization of the LAD using the internal thoracic artery (n=149), with, however, acceptable midterm morbidity and mortality.

In decision making whether to attempt CR or to follow a reasonable IR strategy (for both PCI and CABG) in patients with stable multivessel coronary disease, clinical and demographic variables including patient’s age and life expectancy, the severity of symptoms at presentation, comorbidities (particularly diabetes mellitus), left ventricular function and myocardial viability, coronary anatomy (including the number of CTO vessels, ability to revascularize the LAD, 3- versus 2-vessel disease, and quality of distal vessels) as well as the physiological significance of coronary lesions ≥50% to 70% diameter stenosis should be considered.

Disclosures

None.

References


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