



Review

Novel Approaches to Define Outcomes in Coronary Revascularization

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ABSTRACT

Coronary revascularization is done to alleviate the patient symptoms or to improve prognosis. Despite these clinical indications, significant variability exists in the risk assessment tools used to select patients for coronary revascularization, to the extent of revascularization performed and, in our approaches to define “optimal” revascularization. The goal of this review is to evaluate novel approaches that can assess coronary artery disease before and after revascularization, define the thresholds of these approaches that have been shown to improve morbidity and mortality, and highlight future directions for research in this area. The novel approaches defining coronary revascularization described in this review are split among quality of life metrics, risk scores, noninvasive imaging outcomes, invasive imaging outcomes, and physiological measurements.

RÉSUMÉ

La revascularisation coronarienne est faite pour améliorer les symptômes des patients ou améliorer leur pronostic. Malgré ces indications cliniques, il existe des variations significatives dans les outils d'évaluations des risques utilisés pour sélectionner les patients pour une revascularisation coronarienne, l'ampleur de la revascularisation effectuée et la manière de définir une revascularisation optimale. Le but de cette revue est de décrire de nouvelles approches qui peuvent évaluer l'impact de la maladie coronarienne avant et après une revascularisation, définir les seuils associés avec ces nouvelles approches menant à une réduction de la morbidité et mortalité, et décrire les études à venir dans ces domaines. Les nouvelles approches déterminant la revascularisation coronarienne sont divisées en paramètres évaluant la qualité de vie, échelles de risque, résultats d'imagerie non invasive, résultats d'imagerie invasives et en mesures physiologiques.

Despite a decrease in the incidence and mortality of coronary artery disease (CAD) in the past 10 years, there are still 2.4 million Canadian adults with known ischemic heart disease, leading to significant mortality and morbidity.¹ The main goals of physicians treating adult patients with CAD is to initiate medical treatment and assess for revascularization. Currently, the latest Canadian Cardiovascular Society (CCS)

guidelines recommend revascularization therapy, either using percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), to improve quality of life and/or to reduce the risk of myocardial infarction (MI) and premature death.² Despite these clinical indications, significant variability exists in techniques used to measure the severity of coronary disease before and after revascularization, in the methods used to define the quality of revascularization, and in our ability to predict cardiovascular morbidity and mortality.

The goal of our report is threefold: (1) describe novel approaches that can be used to assess patients undergoing coronary revascularization; (2) define the thresholds of these novel approaches that can become an objective of coronary revascularization leading to the lowest cardiovascular morbidity and mortality; and (3) highlight future directions where research is leading these approaches.

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Patient-Centric Metrics

Most trials evaluating the relative effectiveness of coronary revascularization have focused on improving morbidity or mortality. However, when evaluating coronary revascularization indication or effectiveness from the patient’s perspective, especially when the patient is suffering from quality of life-limiting symptoms, the use of valid instruments that measure tangible improvements in these symptoms is essential (Fig. 1 and Table 1).

The Short Form 36 (SF-36) was designed as a general quality of life questionnaire³ and has been validated in patients undergoing revascularization using CABG or PCI.⁴ In patients referred for surgical revascularization, the SF-36 can be used to identify patients at worse prognosis who might warrant medical treatment instead of CABG. For example, a 10-point decrease in preoperative physical component score of the SF-36 had an odds ratio (OR) of 1.39 (95% confidence interval [CI], 1.11-1.77; *P* < 0.01) for extended hospital stay and 180-day mortality post-CABG, whereas the Mental Component Score was not predictive of mortality.^{5,6} The opposite relationship also exists for which baseline SF-36 can be used to predict improvement, assess coronary revascularization success, and determine the appropriate intensity of treatment in these patients.⁷ Post revascularization assessment is also important. In CABG patients, a deterioration of at least 10 points on the physical component scale after surgery had an OR of 1.61 (95% CI, 1.04-2.49; *P* < 0.01) of in-hospital mortality and increased the risk of prolonged length of stay by 33% (OR, 1.33; 95% CI, 1.13-1.57).⁷

CAD-specific questionnaires were developed, such as the Seattle Angina Questionnaire (SAQ).⁸ The SAQ is a 19-item

questionnaire that quantifies 5 subdomains: physical limitations due to angina, any recent change in the frequency or severity of angina, satisfaction with treatment, and quality of life.⁸ Although frequently used as an outcome in research, the SAQ is rarely used in clinics because of its length and lack of clear guidelines on how to treat patients on the basis of the values. Despite these limitations, the SAQ provides an accurate and objective way to assess the angina-related quality of life.⁹ A shorter version of the SAQ, the SAQ-7,¹⁰ has only 7 questions. It was developed to measure the physical limitations, angina frequency, and quality of life. The SAQ-7 was valid, highly reproducible, and was predictive of 1-year mortality and need for readmission. Moreover, the SAQ-7¹⁰ subdomains can be averaged to obtain a single value reflecting the full magnitude of the effect of revascularization. These methods could be integrated into practice when discussing revascularization and could provide an evidence-based risk prediction to the patient.

Questionnaires do not account for the inherent biases in assessing angina such as its: (1) cyclical nature; angina severity naturally fluctuates over time; (2) the adaptation to the ischemic threshold; a patient might decrease activity level to limit ischemic symptoms; and (3) the placebo effect; angina symptoms improve regardless of the treatment administered.¹¹ The latter was showcased in the Efficacy of a Device To Narrow the **C**oronary **S**inus in **R**efractory **A**ngina (COSIRA) trial, in which 40% of patients with refractory angina in the sham control group had an improvement of 1 CCS class in their symptoms, despite having no change in their treatment.¹² Similarly, in the **O**bjective **R**andomised **B**linded **I**nvestigation **W**ith **O**ptimal **M**edical **T**herapy of **A**ngioplasty

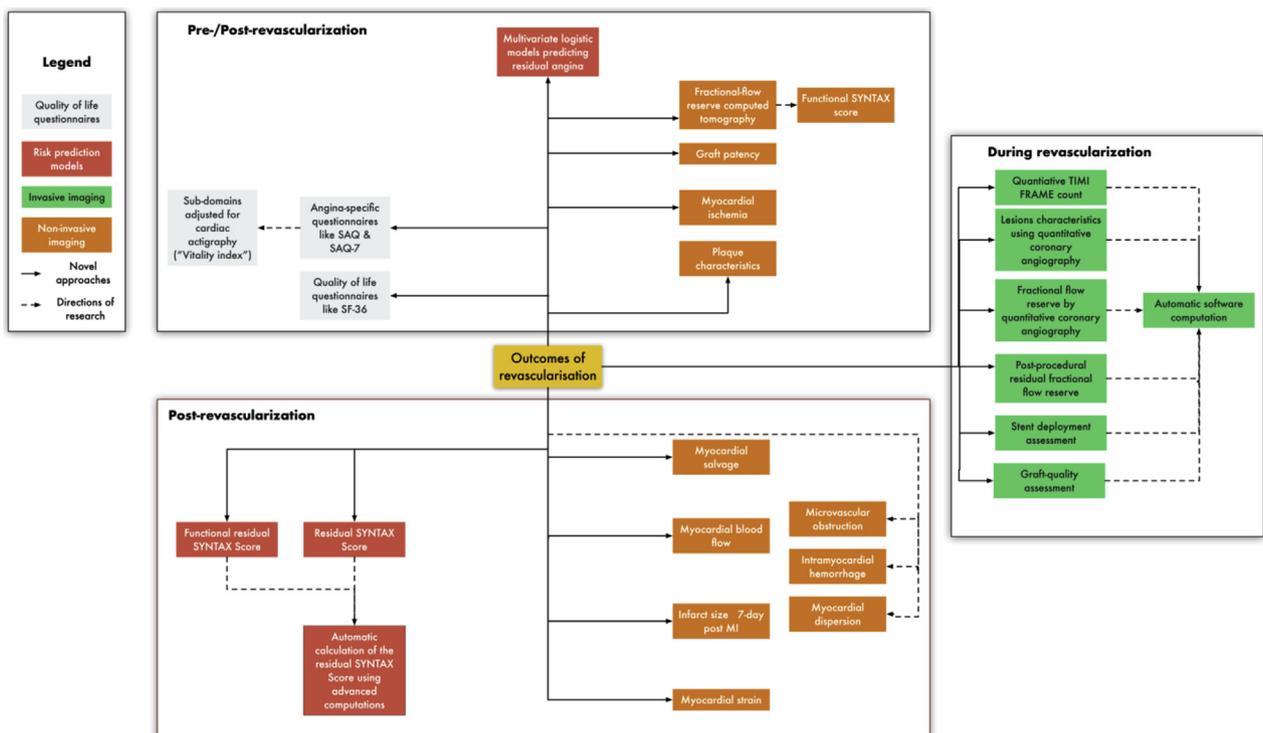


Figure 1. Novel coronary revascularization outcomes, pre-, per, and post coronary revascularization. MI, myocardial infarction; SAQ, Seattle Angina Questionnaire; SAQ-7, 7-item Seattle Angina Questionnaire; SF-36, Short Form-36; SYNTAX, **S**ynergy **B**etween **P**ercutaneous **C**oronary **I**ntervention **W**ith **T**axus and **C**ardiac **S**urgery; TIMI, **T**hrombolysis in **M**ycardial **I**nfarction.

Table 1. Quality of life outcomes

Outcomes	Novel outcome definition	When to use this outcome	Prediction of MACE	Level of evidence
SF-36 Physical Component score at baseline	Decrease of 10 points of SF-36 compared with age-adjusted mean	Undergoing CABG	OR, 1.39 (95% CI, 1.11-1.77); $P = 0.006$ for 6-month mortality ¹⁵	3956 Patients, observational registry ¹⁵
SF-36 Physical Component score difference pre- and post procedure	Reduction of 10 points compared with baseline	Undergoing CABG	OR, 1.33 (95% CI, 1.13-1.57) for increased length of stay and OR, 1.61 (95% CI, 1.04-2.49) for mortality ⁷	1178 Patients, prospective cohort ⁷
Full Seattle Angina Questionnaire	Improvement of at least 10 points in any of the subdomains of the questionnaire: angina frequency, angina stability, physical limitation, treatment satisfaction, and disease perception	Undergoing PCI/CABG	Changes in responses over time can reflect improvement/deterioration in patient symptoms ⁸	372 Patients, with stable CAD and unstable CAD, undergoing coronary angiography ⁸
Seattle Angina Questionnaire-7	Assesses 3 subdomains: angina frequency, physical limitation, and quality of life Can obtain an average score: poor, 0-50; good, 50 to < 75; and excellent, 75-100	Angina and undergoing PCI/CABG	Changes in responses over time can predict mortality (poor, 8%; good, 5%; and excellent, 4%) and hospitalization (poor, 14%; good, 11%; and excellent, 5%) at 1 year ¹⁰	10,408 Patients ¹⁰

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; MACE, major adverse cardiovascular events; OR, odds ratio; PCI, percutaneous coronary intervention; SF-36, Short Form 36.

in Stable Angina (ORBITA) trial, in which 200 patients with stable angina were assigned to PCI or sham PCI, a similar proportion of patients experienced improvement of ≥ 1 CCS class in the sham PCI and the PCI group (24% vs 26%).¹³ To account for the ischemic threshold adaptation, the burden of symptoms of the patient relative to physical activity level has to be taken into account.¹¹ The **Novel Vitality Indices Derived From the Hexoskin** in Patients Affected With Angina Undergoing Coronary Revascularization or Medical Therapy (NOVA-SKIN) study (NCT02591758), in which 30 patients with angina who were to undergo PCI or CABG were recruited, and the patients had to wear a “biometric vest” before and after these procedures, will provide insights into this topic. Using the heart rate and activity measured using the vest, a digital “vitality index” was developed, acting as a surrogate for cardiac actigraphy, which reflects the energy expenditure of the heart.¹⁴ Then they adjusted subdomains of the SAQ for this “vitality index” to determine whether these “vitality-adjusted subdomains” were superior to the original values in detecting changes after coronary angiography. Cardiac actigraphy is used as an outcome in heart failure patients¹⁴ and could also be used after coronary revascularization in patients suffering a functional limitation because of their disease. It could correlate the symptoms described by the patient to physical activity level and provide a more accurate assessment of angina-related symptom improvement by accounting for ischemic threshold adaptation.

Risk Scores Predicting Improvement After Revascularization and the Completeness of Revascularization

Despite the angina relief goal of revascularization, 1 in 5 patients continue to have residual angina after PCI.¹⁶ Arnold et al. created a multivariate logistic regression model with 8 variables predicting associated residual angina after PCI: younger age, poor economic status, SAQ quality of life score,

SAQ angina frequency score, presence of depression, and greater number of antianginal medications at the time of PCI.¹⁷ This model can be used to predict risk of residual angina and gauge patients’ expectations before coronary revascularization with PCI (c-index = 0.75).¹⁷ Depending on the score’s results, the physician can choose to pursue further investigations, medical treatment, or a more extensive revascularization.

The **Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX)** score is a tool used during coronary angiography to quantify the extent of CAD before revascularization and guide treatment. It is on the basis of the extent of disease as seen on the angiographic images.¹⁸ The residual SYNTAX score (rSS) was developed to quantify the adverse effects of incomplete coronary revascularization and is obtained after revascularization. In a series of 10,344 consecutive patients who underwent PCI, the authors showed that an rSS of 0 (full revascularization) was associated with significantly lower rates of major adverse cardiovascular events (MACE) than a higher SYNTAX score (6.9% if rSS = 0 vs 9.2% if rSS > 0-2 vs 13.6% if rSS = 2-8 vs 11.8% if rSS > 8).^{19,20} Therefore, the rSS is an important prognosis indicator after PCI as well as a marker of the extent of revascularization. However, it suffers from poor inter- and intraobserver variability.¹⁸ Recently, machine learning algorithms such as convolution neural networks, have revolutionized the field of computer vision and have achieved image recognition superior to that of humans.²¹ These algorithms could be used to analyze the coronary angiography images²² and derive an automatic, computer-generated SYNTAX score, which takes the element of human variability out of the equation, while making this score more easily accessible.²³

Coronary revascularization is often planned according to the measurement of the degree of stenosis according to visual assessment during angiography, leading to a measurement bias toward falsely diagnosing obstructive CAD.²⁴ Fractional flow reserve (FFR) is an index of the functional severity of coronary stenoses²⁵ and is obtained using a pressure wire, by calculating

the ratio of coronary pressure distal and proximal to the lesion, during maximum hyperemia.²⁵⁻²⁷ A coronary stenosis is considered physiologically significant if the FFR is ≤ 0.80 .²⁵ FFR-guided complete revascularization is the concept of treatment of all physiologically significant lesions and treating medically lesions that are not. Two recent studies^{26,27} did a post hoc analysis of a total of 974 patients who had undergone complete FFR-guided percutaneous revascularization^{12,28-30} and reviewed the post-PCI angiograms to calculate the rSS. They reported that when an rSS-based revascularization strategy was used, the rSS did not hold prognostic value. In these patients, a different indicator of complete revascularization has been suggested: the residual functional SYNTAX score (rFSS). The rFSS is the rSS measured only in vessels with FFR ≤ 0.80 . In a study of 385 patients who underwent triple-vessel FFR after stent implantation, functionally complete revascularization was achieved in 73.5% of cases.³¹ The authors reported that patients who had functionally incomplete revascularization (rFSS > 1) showed markedly higher MACE at 2 years (14.6% vs 4.2% for complete revascularization; hazard ratio [HR], 4.09; 95% CI, 1.82-9.21; $P < 0.001$), and that rFSS had the highest discrimination improvement for MACE over rSS and the SYNTAX score. The rFSS could also, theoretically, be used as a tool to further optimize stent deployment and lesion treatment, although it has not been investigated for that purpose (Table 2).³¹

Noninvasive Imaging to Define Novel Outcomes for Coronary Revascularization

In patients with obstructive CAD, noninvasive diagnostic imaging has traditionally been used to select patients who would benefit from revascularization on the basis of the location and extent of the stenosis.² Coronary revascularization success can also be measured using a variety of novel metrics derived from noninvasive imaging modalities such as single photon

emission computed tomography (SPECT), positron emission tomography (PET), and cardiac magnetic resonance (CMR) imaging, echocardiography, and coronary computed tomography angiography (CCTA) (Table 3). Viability is also an important topic that is beyond the scope of this article.

Qualitative Assessment of Myocardial Ischemia

Myocardial ischemia burden is assessed using PET imaging and graded as a percentage of ischemic involvement of the myocardium. Mild ischemic burden represents $< 10\%$ involvement, moderate burden represents 10%-20%, whereas severe burden represents an involvement of $> 20\%$ of the myocardium. Patients with $> 10\%$ involvement are at increased risk of adverse cardiac events.³³ In the nuclear substudy of Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE), which compared medical therapy with and without revascularization in patients with stable CAD, 314 patients underwent serial stress perfusion imaging. Although the study was underpowered, a $\geq 5\%$ reduction in myocardial ischemia in either group was associated with reduced rate of death or MI, especially if there was moderate to severe ischemia at baseline.³⁴ Furthermore, patients with stable CAD and incomplete revascularization on SPECT imaging, defined as ≥ 2 ischemic segments present at stress, had higher rates of all-cause mortality (HR, 1.21; 95% CI, 1.02-1.45; $P < 0.01$).³⁵

The International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) is an ongoing trial with an aim to determine the best management strategy in stable CAD patients with moderate or severe ischemia, with an invasive revascularization strategy (PCI and CABG) used with optimal medical therapy compared with optimal medical therapy alone.³⁶ Until we have the definitive results of ISCHEMIA, preintervention ischemic burden on SPECT and PET are important

Table 2. Risk scores as an outcome

Outcomes	Novel outcome definition	When to use this outcome	Prediction of MACE	Level of evidence
Residual angina	Logistic regression model using 8 variables: age, poor economic status, depression, number of antianginal medications, SAQ Angina Frequency, SAQ Physical Limitation	Angina and undergoing PCI/CABG	C-index = 0.75 of predicting residual angina; these patients can have further treatment or a more extensive revascularization to address their symptoms ¹⁷	2573 Patients who had PCI at 10 US hospitals for angina or NSTEMI ¹⁷
Residual SYNTAX score	The SYNTAX score after coronary revascularization with different risks according to rSS: rSS = 0; rSS > 0 to ≤ 8 ; rSS > 8	Multivessel coronary disease and undergoing PCI	Determines a reasonable level of revascularization ³² Reduction in MACE at 30 days (6.9% if rSS = 0; 9.2% if rSS > 0 to 2; 11.8% if rSS > 2 to 8; and 14.2% if rSS > 8) Reduction in MACE at 1 year (16.3% if rSS = 0; 18.0% if > 0 to 2; 20.0% if rSS > 2 to 8; and 22.4% if rSS > 8)	10,344 Patients who underwent coronary revascularization ³²
Residual functional SYNTAX score	The SYNTAX score after FFR-guided PCI of lesions with FFR ≤ 0.80 . rFSS ≥ 1 associated with worse outcomes	Multivessel coronary disease and undergoing PCI	Reduction in MACE at 2 years if rFSS = 0 vs rFSS ≥ 1 (4.2% vs 14.6%) ³¹	385 Patients who underwent FFR-guided PCI ³¹

CABG, coronary artery bypass grafting; FFR, fractional flow reserve; MACE, major adverse cardiovascular events; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; rSS, residual SYNTAX score; SAQ, Seattle Angina Questionnaire; SYNTAX, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery; US, United States.

Table 3. General noninvasive imaging metrics as an outcome

Outcomes	Novel outcome definition	When to use this outcome	Prediction of MACE	Level of evidence
Myocardial ischemia	PET imaging: Percentage of myocardium perfusion deficit: <ul style="list-style-type: none"> • < 10% = mild deficit • 10%-20% = moderate deficit • > 20% = severe deficit SPECT imaging: <ul style="list-style-type: none"> • $\geq 5\%$ reduction in myocardial ischemia post medical therapy or revascularization Summed stress score (sum of 20 segments with a grading of 0-4 with 0 being normal and 4 indicating absence of radiotracer uptake): <ul style="list-style-type: none"> • < 4 normal • 4-8 mildly abnormal • > 8 severely abnormal Summed difference score between resting and exercise/pharmacological testing: <ul style="list-style-type: none"> • ≥ 2 	CAD undergoing revascularization or post medical therapy Partially revascularized patients	If we reach $\geq 5\%$ reduction in MI ischemia 13.4% MACE (vs 24.7% otherwise) ^{34,35,76}	322 patients with incomplete revascularization ³⁵ 170 patients with CAD and attempted revascularization ⁷⁶ 134 patients with serial rest/stress SPECT imaging at 6 and 18 months after randomization ³⁴
MBF reserve	PET imaging: <ul style="list-style-type: none"> • Ratio MBF during maximal coronary vasodilatation to resting MBF: • < 1.5 associated with diminished flow reserve and lower FFR • > 2.3 indicates a favourable prognosis 	Established CAD Suspected CAD CABG	MACE ⁵⁴ Revascularization linked with increased myocardial flow reserve and increases in FFR (0.61 ± 0.17 to 0.89 ± 0.08). No reported clinical outcomes in this population ⁵⁵ Improvement in MBF if perfusion deficit was present before PCI or CABG. No clinical outcomes reported ⁷⁷	Review of myocardial flow reserve and PET imaging ⁵⁴ 53 patients with suspected CAD ⁵⁵ 19 patients and 76 myocardial quadrants ⁷⁷
Infarct size	CMR (LGE) and SPECT: <ul style="list-style-type: none"> • $\geq 25\%$ confers increased risk of MACE at 2 years • Each increase of 5% of infarct size increases risk of adverse events by 20% 	Post STEMI	Seems to predict occurrence of MACE at 2 years ⁷⁸ Predicts all-cause mortality, reinfarction, and hospitalization for heart failure at 1 year ⁴¹	Meta-analysis of 1025 STEMI patients ⁷⁸ Meta-analysis of 10 randomized trials and > 2632 patients ⁴¹
Myocardial salvage	SPECT: Difference between the area at risk and the final infarct size < 0.5 for LVEF recovery, > 0.5 for mortality	Post MI	If ratio < 0.5: > 5% LVEF improvement ⁴⁹ If ratio > 0.5: mortality OR, 5.1 (95% CI, 1.9-13.3); $P < 0.01$ ⁵³	120 Patients post MI ⁴⁹ Myocardial salvage SPECT guidelines ⁵³
Strain imaging	CMR: <ul style="list-style-type: none"> • Longitudinal strain $\geq 11\%$ • Circumferential strain $\geq 17\%$ Echocardiography: <ul style="list-style-type: none"> • Cutoff: > 13.7% Longitudinal strain > 14% was associated with a threefold increase in risk for the combined end points Longitudinal strain > 9.9% and global circumferential strain > 12.0%	Post acute STEMI Post acute MI Post NSTEMI STEMI patients and patients with LVEF $\leq 40\%$ (only for longitudinal strain)	MACE (cardiac death, readmission for heart failure, MI) ⁷⁹ Composite end point including cardiovascular death, aborted sudden cardiac death, and hospitalization for heart failure ⁶⁴ LVEF improvement of > 5% ⁵⁸ All-cause mortality and hospitalization for heart failure (threefold increase) ⁶⁰ Composite of death, hospitalization for heart failure, nonfatal MI, and ventricular arrhythmia ⁸⁰	323 STEMI patients with CMR strain imaging ⁷⁹ 180 Patients post STEMI ⁶⁴ 147 Patients post MI ⁵⁸ 849 Patients post acute MI ⁶⁰ 691 Patients after STEMI ⁸⁰
Coronary computed tomography angiography	Description of graft failure and graft patency Functional assessment of coronary lesions Noninvasive SYNTAX score	Early and late postoperative in CABG patients Acute chest pain syndrome assessment	No outcomes described, beyond graft patency ⁶⁶ Cancels invasive coronary angiography in 61% of cases ⁷³	107 Consecutive patients ⁶⁶ 584 Patients with chest pain ⁷³

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; CMR, cardiovascular magnetic resonance; FFR, fractional flow reserve; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MBF, myocardial blood flow; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; PET, positron emission tomography; SPECT, single photon emission computed tomography; STEMI, ST-elevation myocardial infarction; SYNTAX, **S**ynergy Between Percutaneous Coronary Intervention With **T**axus and Cardiac Surgery.

prognostic factors to consider when deciding whom to revascularize and how to measure the success of revascularization.

Infarct size, transmural infarct extent, and extracellular volume fraction

Infarct size is defined as the volume of necrotic myocardium over the whole myocardium, as observed on CMR, PET, or SPECT imaging modalities.³⁷⁻⁴⁰ CMR using late gadolinium enhancement (LGE) is currently the gold standard to delimit myocardial infarct size. A meta-analysis of 2632 patients showed a strong graded response between infarct size, measured within 1 month after ST-elevation MI (STEMI), and MACE (mortality and rehospitalization for heart failure)⁴¹; for each increase in infarct size of 5%, relative risk of MACE was increased by 20%.⁴¹

LGE-derived transmural infarct extent can also be used to measure functional myocardial recovery after an acute MI and offers the most accurate information when the transmural extent is either 0% or 100%. Similarly, extracellular volume fraction represents a quantitative assessment of myocardial disruption within the infarct zone and can be derived from T1 mapping imaging before and after contrast injection. A ratio ≤ 0.5 seems to have additive value compared with transmural extent alone in predicting improved wall motion during follow-up, especially in patients with transmural extent $> 50\%$ (Table 4).³⁷

Recent studies have shown that higher rate of fludeoxyglucose uptake using PET measured 5 days after acute MI correlated with lower left ventricular ejection fraction (LVEF) at 6 months, independent of initial infarct size measured using CMR imaging.³⁹ The area of fludeoxyglucose uptake appears to correlate with the areas of LGE in the acute and follow-up scans.⁴² Hybrid PET/CMR imaging might be useful in practice after MI to determine the infarct size and can be used to predict 6-month LVEF recovery.³⁹ The optimal timing of infarct size measurement is important to consider. Indeed, Mather et al. showed that in patients with acute MI, infarct size showed variation during the first week.⁴³ After 7 days, infarct size was similar to the infarct size at 3 months.⁴³ In addition, LVEF recovery tends to be underestimated if infarct size is measured acutely.⁴³⁻⁴⁵ Thus, to obtain accurate information on myocardial damage and potential recovery after acute MI, it might be preferable to defer the measurement of infarct size for at least a week and this outcome can predict 6-month LVEF recovery.

Myocardial salvage

Myocardial salvage, defined as the difference between the actual (final infarct size) and potential infarct size (initial area at risk during acute coronary occlusion), represents the area that can potentially improve after a myocardial infarct.⁴⁶⁻⁴⁸ Because studies have shown that MACE are related to the size of infarction, the concept of myocardial salvage is appealing and could be used to determine strategies to optimize management of myocardial infarct and therefore minimize final infarct size.⁴⁹

In recent years, CMR has emerged as the optimal way of measuring myocardial salvage.⁴⁷ Myocardial salvage is measured using T2 weighted imaging. It provides prognostic

information according to the measurement of myocardial salvage index, which represents the ratio between area at risk and the infarct area (measured using LGE). The myocardial salvage index was proven to predict functional improvement (cutoff value of $\geq 40\%$) and LVEF normalization (cutoff value of $\geq 48\%$) (Table 4).⁵⁰ These findings were corroborated by O'Regan et al., who concluded that segments with myocardial salvage index $< 50\%$ had worse functional recovery.⁵¹ Patients who might benefit from myocardial salvage quantification are those who present with late infarction, usually > 12 hours after onset of symptoms, for whom primary coronary angioplasty might not be the best initial treatment.⁵² Patients having intermittent coronary occlusions due to partial lysis of the thrombus had a higher myocardial salvage index and coronary revascularization might improve LVEF in this subset of patients.⁵² We can also use myocardial salvage as an outcome of coronary revascularization. Calabretta et al. measured myocardial salvage post-PCI using SPECT imaging and were able to predict $> 5\%$ LVEF improvement at 6 months in patients after acute MI.⁴⁹ The cutoff value that predicted a lower mortality rate at 6 months was a ratio < 0.5 of myocardial salvage on SPECT imaging.⁵³

Myocardial blood flow and myocardial flow reserve

Myocardial blood flow (MBF) is defined as the absolute amount of blood flow that the myocardium receives per minute per gram of tissue under baseline conditions.⁵⁴ Using PET, myocardial flow reserve (MFR; or coronary flow reserve) can then be determined (ratio of MBF during maximal coronary vasodilation to resting MBF)⁵⁴ and has been shown to correlate well with FFR findings within the same individuals.⁵⁵ Furthermore, successful revascularization was linked to increased MBF measured with PET imaging and correlated to increased FFR (0.61 ± 0.17 to 0.89 ± 0.08).⁵⁵ MFR is not only a more sensitive tool to detect multivessel CAD than traditional myocardial perfusion imaging but can also help in risk stratification. However, no clinical outcomes were correlated to MFR and we can only extrapolate possible benefits by considering its positive correlations with FFR.

Strain evaluation

Left ventricular strain evaluation using speckle-tracking echocardiography or tissue tracking CMR imaging is a newer modality that represents deformation of a segment of myocardium in response to an applied force or stress.⁵⁶ It has the potential to detect early myocardial damage-induced ischemia before wall motion abnormalities become apparent.⁵⁶

Abnormal left ventricular global longitudinal strain (GLS) using echocardiography predicts mortality risk with higher accuracy than LVEF alone in patients with STEMI and heart failure.⁵⁷ It has been used in post-MI patients to predict LVEF recovery and detect myocardial viability. An absolute GLS cutoff value of $> 13.7\%$ (absolute value) predicted accurately $> 5\%$ LVEF improvement at 1 year.⁵⁸ In a recent study 110 STEMI patients with preserved LVEF were evaluated and GLS predicted MACE at 30 days.⁵⁹ Similar results were shown in patients admitted for coronary angiography and LVEF $\geq 40\%$ whereas a GLS $< 14\%$ was associated with a threefold increase in risk of combined end point MACE.⁶⁰

Table 4. Cardiovascular resonance magnetic specific methods

Outcomes	Novel outcome definition	When to use this outcome	Prediction of MACE	Level of evidence
Native T1 mapping remote from infarcted myocardium	Measures the relaxation time of the myocardium, which is dependent on its physiological properties: < 969 ms associated with adverse prognosis	STEMI	Independently associated with MACE ($P = 0.048$) and all-cause death or heart failure hospitalizations ($P = 0.049$) ⁸⁴	300 STEMI patients ⁸⁴
Extracellular volume fraction	Represents the percent of tissue comprised of extracellular space after the injection of contrast: ≤ 0.5 for prediction of ejection fraction recovery	Post MI	Prediction of infarct size and improvement in segmental recovery ^{37,40}	39 Patients post acute MI ³⁷ 50 patients post MI ⁴⁰
Microvascular obstruction	Measured with late gadolinium enhancement and is recognized when areas of hypoenhancement within the hyperenhanced myocardium appear	Post acute STEMI	Freedom of MACE at 2 years was 76.5% in patients with microvascular obstruction vs 93.0% in patients without ⁷⁸	Meta-analysis including 1024 patients from 10 trials ⁷⁸
Intramyocardial hemorrhage	Measure of severe microvascular obstruction (T2* imaging); the paramagnetic effects of hemoglobin breakdown products affect T2 relaxation: cutoff is T2* < 20 ms	Post acute MI	Predicts MACE ⁸² Reduced LVEF ⁸² Increased infarct size ⁸² Greater LV volumes ³⁸	Meta-analysis 1 106 patients from 9 studies ⁸² SCMR imaging consensus ³⁸
Myocardial salvage index	Ratio of area at risk divided by the infarct size (measured using T2 weighted imaging): $\geq 40\%$ predicts LVEF improvement and $\geq 48\%$ LVEF normalization	STEMI patients with delayed presentation	Improvement and recovery of the LVEF ⁵⁰	153 STEMI patients ⁵⁰
Myocardial dispersion	The regional heterogeneity of myocardial contraction throughout the cardiac cycle measured using feature tracking modalities on cine-CMR: > 9.79% seems related to a greater risk of adverse events	Post acute STEMI	Increased risk of adverse clinical outcomes ⁸³	130 Patients post MI ⁸³

CMR, cardiovascular magnetic resonance; LV, left ventricular; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; SCMR, Society for Cardiovascular Magnetic Resonance; STEMI, ST-elevation myocardial infarction.

The use of strain imaging with CMR is gaining popularity in adding prognostic information. GLS obtained using CMR imaging is a predictor of MACE in patients with preserved LVEF after revascularization.^{61,62} Furthermore, strain was noninferior to LGE in predicting patients with functional recovery at follow-up.⁶³ Conflicting results exist regarding the additional value of strain over LGE in predicting long-term adverse events, but this approach could be considered in patients post-MI with reduced LVEF to assess prognosis and LVEF recovery.^{50,64}

CCTA for coronary anatomy, graft patency, and functional assessment

CCTA is an imaging modality that uses iodine contrast material and computed tomography to examine coronary arteries and plaque characteristics.⁶⁵ Driessen et al. showed that independent from luminal stenosis severity, positive remodelling and noncalcified plaque volume derived from CCTA correlate with reduced invasive FFR measurements.⁶⁵ Pre-procedural CCTA findings can predict the need for further revascularization. For example, low attenuation plaque and positive remodelling at baseline CCTA correlated with in-stent restenosis and progression of plaque at follow-up.³¹ Additionally, catheter coronary angiography is the preferred method for graft evaluation in acute settings for immediate assessment and treatment of the disease. CCTA is becoming the gold standard to assess patency of grafts.⁶⁶⁻⁶⁸ Remote from the CABG surgery, it can determine the need for intervention on residual graft stenosis.⁶⁹ It is important to note that vein

graft failure leads to increased revascularization, but no difference in MI or death.⁷⁰ The **Patency Assessment of Grafts Performed in Coronary (PATENCY-CORONARY)** pilot study compared CABG patency in a subgroup of patients randomized to on-pump vs off-pump techniques in the Coronary Artery Bypass Grafting Surgery Off- or On-pump Revascularisation Study (CORONARY) trial.⁷¹ All consecutive CORONARY patients in the 3 highest recruiting cardiac surgery centres in Canada who reached 1-year follow-up were included in the study. From the 335 patients eligible, 157 (47%) underwent CTA for graft patency assessment to find correlations between MACE and graft failure. Of the 512 grafts (261 in the off-pump group and 251 in the on-pump group), 504 were evaluable (98.4%) using CTA. Patency index (percent of nonoccluded grafts) was 89% for the off-pump technique and 95% for the on-pump technique ($P = 0.09$). Patency was similar for arterial and vein grafts (both 92%; $P = 0.88$), as well as between target territories (89%-94%; $P = 0.53$). The occurrence of graft occlusion did not affect the CORONARY composite outcomes of adverse cardiovascular events. To our knowledge, PATENCY-CORONARY is the largest single trial to assess graft patency after on-pump and off-pump surgery with CTA, and is also the first study in which most patients were assessed with a large-array system such as a 256-slice scanner, allowing a high rate of evaluable graft segments (close to 100%). This demonstrates the efficacy of CTA for the detection of graft failure after CABG.

Recently, the FFR-computed tomography (FFR_{CT}), a computational fluid dynamics technique combined with

computer-generated 3-D renderings of CCTA has shown that it can be used to noninvasively evaluate the hemodynamic significance of a coronary lesion.⁷² Recent trials^{73,74} reported that the use of FFR_{CT} could reduce the rate of invasive coronary angiography. Collet et al. showed that in patients with multivessel disease, CCTA-derived functional SYNTAX score was feasible and yielded results similar to invasive measurements.⁷⁵ Furthermore, FFR_{CT} showed good diagnostic accuracy in patients with 3-vessel disease and yielded results similar to invasive pressure wire.⁷⁵

Other CMR Features of Poor Prognosis (Table 4)

Microvascular obstruction

Microvascular obstruction is measured with LGE and is recognized when areas of hypoenhancement within the hyperenhanced myocardium appear. It has been linked with the “no reflow” phenomenon and with increased susceptibility of the myocardium to microvascular injury.⁸¹ It is said to be present in 50%-82% of patients who present with STEMI and predicts the occurrence of MACE at 2 years.^{78,82}

Intramycocardial hemorrhage

Intramycocardial haemorrhage is a more severe form of microvascular obstruction related to important vascular endothelial damage. It predicts MACE at 24 weeks and is related to greater infarct size, ventricular volumes, and lower LVEF. It is identified through T2* weighted imaging with a cutoff of T2* < 20 ms for its distinction.

Myocardial dispersion

Myocardial dispersion represents the regional heterogeneity of myocardial contraction throughout the cardiac cycle visualized using feature tracking analysis on CMR imaging. These contraction abnormalities are associated with left ventricular dysfunction and occurrence of heart failure. Severe myocardial dispersion (> 9.79%) was associated with an increased risk of adverse clinical outcomes including cardiac death in patients after MI.⁸³

Invasive Imaging

TIMI frame count

For the past few decades, the Thrombolysis in Myocardial Infarction (TIMI)⁸⁵ flow grade has been used to assess the coronary blood flow. Its association with clinical outcomes has been validated in multiple trials⁸⁶⁻⁹⁷ and the benefits have been attributed to re-establishment of normal blood flow in the artery, defined as TIMI 3 flow. Although TIMI flow grade is a valuable tool to compare results of revascularization, there are number of limitations, such as large inter- and intra-observer variations in interpretation of degree of luminal obstruction, observer bias, and the fact that nonculprit flow (used to gauge TIMI grade 3 flow) is abnormal. The corrected TIMI frame count (CTFC) was developed⁹⁸ to offer a quantitative and reproducible method of assessing coronary flow. It represents the number of cine frames required for dye

to reach standardized distal landmarks in the coronary vessels and is measured with a frame counter on a cine viewer, assessing dye velocity. Studies have shown that CTFC offers greater discriminative power than the TIMI flow grade and that it can identify different subgroups of risk within the same TIMI class. Gibson et al.⁹⁹ reported that in-hospital death increased with higher CTFC and that it was an independent predictor of in-hospital mortality. The CTFC identified a subgroup at particularly low mortality risk among those classified as having normal flow. In the TIMI grade 3 subgroup (defined as CTFC < 40), patients with CTFC ≤ 20 had a 7.9% risk of adverse outcomes compared with patients with CTFC > 20 to ≤ 40, who had a 15.5% risk. Hamada et al.¹⁰⁰ measured the CTFC after successful (TIMI 3) primary percutaneous transluminal coronary angioplasty (PTCA) in 104 patients with acute MI. On the basis of the CTFC, there was a significantly greater improvement of the wall motion score index in the fast group (CTFC < 23) compared with the slow group (40 > CTFC ≥ 23) and there was more clinical congestive heart failure in the slow group. To overcome the manual calculation of CTFC, ten Brinke et al. developed an algorithm that determines the TIMI frame count automatically with 3-D coronary modelling.¹⁰¹ Their results showed good correlation between the algorithm and the cardiologist measurement of the TIMI frame count ($r = 0.98$; $P < 0.001$) (Table 5).

Quantitative coronary angiography

Quantitative coronary angiography (QCA) is a software-based technique that quantifies coronary stenosis by comparing the diameter of the stenosis with a reference diameter, usually the guiding catheter.^{24,102-104} It can provide objective parameters such as lesion length and reference vessel diameter that can help choose which specific measures of the stent to use.¹⁰⁵ In a recently published study, Watanabe et al.¹⁰⁶ investigated the effect of angiography residual percent diameter stenosis using QCA after drug-eluting stent implantation on 3-year clinical outcomes. It consisted of 3679 patients divided into 3 groups according to the residual in-stent percentage diameter stenosis (optimal group: < 10%; intermediate group: 10%-20%; and suboptimal group: ≥ 20%). They showed that the cumulative 3-year incidence of target lesion revascularization was significantly higher in the suboptimal group than in the intermediate and optimal groups (9.8% vs 5.8% and 5.7%, respectively; $P < 0.01$). To overcome some limitations of 2-dimensional angiography, like foreshortening, 3-D QCA has been developed, offering 3-D assessment of the vessel.¹⁰⁷⁻¹⁰⁹ Additionally, software using 3-D QCA specifically designed to evaluate bifurcations has been developed and was superior to standard 2-dimensional QCA and visual assessment to classify a bifurcation lesion as “true bifurcation” (with 50% stenosis in main and side branch).¹¹⁰

Combining the flow evaluation with CTFC and the diameter of stenosis with 3-D QCA offers the opportunity to develop a computer model for computation of myocardial FFR using computational fluid dynamics instead of an actual pressure wire.¹¹¹ Computation of FFR quantitative coronary angiography was performed on 77 vessels in 68 patients and showed that there was a good intra- and interobserver correlation between FFR quantitative coronary angiography and wire-based FFR ($r = 0.81$; $P < 0.001$).¹¹¹ This technique

Table 5. Invasive imaging outcomes

Outcomes	Novel outcome definition	When to use this outcome	Prediction of MACE	Level of evidence
Anatomical Corrected TIMI frame count	Quantitative and reproducible method of assessing coronary flow CTFC < 20 Algorithm that determines the TIMI frame count automatically being developed	CAD diagnosis Elective PCI Acute coronary syndrome	Greater discrimination power than TIMI flow grade Predictor of in-hospital mortality ⁹⁹ Lower risk of death, recurrent MI, shock, congestive heart failure, or LVEF ≤ 40% ¹⁰⁰	Retrospective analysis ⁹⁹ Observational ¹⁰⁰
Quantitative coronary angiography assessment of lesions	Dedicated software that allows determination of specific measures of coronary lumen Bifurcations evaluation 3-D reconstruction < 20% Residual percent diameter stenosis post PCI	CAD diagnosis Elective PCI Acute coronary syndrome	More parsimonious selection of severe lesions (≥ 70% stenosis) according to clinical assessment ^{106,109,110,111} High reproducibility and precision in evaluating stenosis severity Accurate for quantification of stenosis in bifurcation lesions ¹⁰² 3-D QCA combined with TIMI frame count can determine FFR and associated outcomes Reduce target lesion revascularization ²⁴ Reduce MACE ^{153,154} Reduce target lesion revascularization Reduce definite or probable stent thrombosis	Observational and experimental studies ^{106,109-111} 175 Patients who underwent PCI of 228 lesions ¹⁰² 929 Patients with symptoms suggestive of CAD ²⁴
IVUS-defined good stent expansion/graft characteristics	All stent struts against vessel wall Optimal stent expansion: minimum stent area > 5 mm ² or CSA > 90% of distal reference lumen CSA Edge dissection: 5-mm margins proximal and distal to the stent Small artery (proximal cross-section diameter < 2.0 mm), diffuse atherosclerosis (plaque area > 50% of the vessel area distributed for a length of > 50 mm during the pullback) and diffuse calcifications (calcified segment length > 50 mm)	ACS Left main lesions Complex lesions: Long lesions • (≥ 28 mm) • Chronic total occlusions • Lesions involving a bifurcation • Small vessels (≤ 2.5mm) • Patients requiring ≥ 4 stents During CABG	Graft failure (no long-term outcomes)	Observational ^{153,154} Metanalyses ^{119,121-123,125,154} Randomized-controlled trial of 1400 patients with long coronary lesions (> 28 mm) ¹²⁶ 58 Patients undergoing CABG using radial grafts and IVUS ¹⁴²
OCT-defined stent expansion/graft characteristics	Minimum stent area > 90% mean reference lumen area or > 4.85 mm ² Complete apposition with a stent lumen distance < 200 μm No edge dissection No intrastent plaque or thrombus protrusion Assesses intimal trauma, residual thrombi, and the quality of the distal anastomosis	Stable angina Unstable angina NSTEMI STEMI Chronic total occlusion recanalization CABG patients During CABG	Pre-PCI OCT findings: Help plan the treatment strategy (selection of stent length and diameter) ¹³³ Post-PCI OCT findings: Help guide further procedural optimization ¹⁵⁵ Lower 1-year risk of cardiac death, cardiac death or MI, and the composite of cardiac death, MI, or repeat revascularization ¹⁵⁵ Might predict graft failure	Prospective observational studies ¹³³ Retrospective registry of 832 patients (1002 lesions) ¹⁵⁵ 35 Patients undergoing CABG with either saphenous or radial artery grafts ¹³⁸

Continued

Table 5. Continued.

Outcomes	Novel outcome definition	When to use this outcome	Prediction of MACE	Level of evidence
Functional Residual FFR	Post PCI residual FFR > 0.86-0.89	PCI	Variable but statistically significant reduction in MACE in various observational studies ¹⁴⁷⁻¹⁴⁹	Observational studies ¹⁴⁷⁻¹⁴⁹ Meta-analysis ¹⁴⁶

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CFTC, corrected TIMI frame count; CSA, cross-sectional area; FFR, fractional flow reserve; IVUS, intravascular ultrasound; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography; STEMI, ST-elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

could offer a virtual FFR using a simple coronary angiogram, deriving anatomical and functional lesion characteristics without the risk of the pressure wire. Additionally, coronary wall shear stress, computed using coronary angiography images, identifies area of plaque vulnerability and high wall shear stress was linked to incident MI in the Fractional Flow Reserve Versus Angiography for Multivessel Evaluation 2 (FAME 2) study (Table 5).¹¹² Currently, these digital technologies are rarely performed in daily clinical practice and have been principally used for clinical research.

Intravascular ultrasound and optical coherence tomography to guide coronary revascularization

Orthogonal angiography imaging does not reveal the 3-D geometry that is required to fully appreciate the CAD and the full expansion of the intracoronary stent. Intravascular ultrasound (IVUS) is the use of ultrasound to define the coronary anatomy and the morphology of the plaque. Many studies have shown that angiography-guided stent deployment leads to suboptimal results and worse outcomes.¹¹³⁻¹¹⁹ Fujii et al.¹¹³ conducted a study using IVUS to assess factors leading to acute/subacute stent thrombosis after successful stent implantation. They reported that the minimum stent cross-sectional area was smaller in the stent thrombosis group compared with the control group without stent thrombosis ($4.3 \pm 1.6 \text{ mm}^2$ vs $6.2 \pm 1.9 \text{ mm}^2$; $P < 0.01$). After multivariate logistic regression analysis, predictors of stent thrombosis were stent under expansion ($P = 0.03$), residual reference segment stenosis ($P < 0.02$), defined as the presence of a reference plaque burden $> 70\%$ and a minimum lumen area $< 4 \text{ mm}^2$. Many studies showed that IVUS guidance during stent implantation was associated with a significant reduction in MACE, stent thrombosis, and target lesion revascularization.¹¹⁹⁻¹²⁴ Recently, Shin et al.¹²⁵ published a meta-analysis of 3 randomized studies that evaluated IVUS-guided PCI vs angiography-guided PCI in patients treated with drug-eluting stents.¹²⁶⁻¹²⁸ The analysis of 2345 patients showed that 1-year MACE had occurred in 0.4% of patients who underwent IVUS-guided PCI vs 1.2% of those who underwent angiography-guided PCI (HR, 0.36; $P = 0.04$). In addition, less MI (0% vs 0.4%; $P = 0.03$) and less target lesion revascularization (3% vs 5%; $P = 0.02$) were observed in patients who underwent an IVUS-guided procedure. Although there are no criteria defining successful revascularization with IVUS in the guidelines, studies define correct stent placement as good apposition (all stent struts against the vessel wall), optimal stent expansion (minimum stent area $> 5 \text{ mm}^2$ or cross-sectional area $> 90\%$ of distal reference lumen cross-sectional area) and no edge dissection (5-mm margins proximal and distal to the stent).^{129,130}

Optical coherence tomography (OCT) is a high-resolution intracoronary imaging technology that uses near-infrared interferometry.¹¹⁴ The spatial resolution of OCT is 10-20 μm , approximately 10 times greater than IVUS and offers more detailed information on microstructural findings missed with angiography.¹¹⁴ It can be used to maximize stent deployment and reduce stent thrombosis.¹¹⁴ Optimal stent deployment is defined as follows: good stent expansion with minimum stent area $> 90\%$ of the mean reference lumen area or $> 4.85 \text{ mm}^2$, complete apposition of stent with a

stent–lumen distance < 200 μm , no edge dissection (linear rim of tissue, with a width of $\geq 200 \mu\text{m}$ and a separation from the vessel wall or underlying plaque < 5 mm to the stent edge), and no intrastent plaque or thrombus protrusion.^{131,132} Studies have compared OCT-guided PCI vs PCI alone and have shown that stents can be optimized on the basis of OCT findings in 27%¹³³ to 34.7% of cases.^{131,134} This leads to a reduction of in-hospital MACE¹³⁴ and MACE at 1 year.^{114,131} Additionally, OCT has also been used to compare features of stented segments involved in a stent thrombosis revealing important characteristics of stent deployment missed using conventional angiography (Table 5).^{115-118,135,136} Despite these encouraging results, large-scale randomized trials are needed to establish whether OCT guidance brings superior clinical outcomes compared with angiography guidance. ILUMIEN IV (NCT03507777) should grant us more insights into the use of OCT to define successful revascularization.

Intraoperative graft assessment

To provide complete revascularization with CABG, most patients need other vessels besides the internal thoracic artery. The saphenous vein and/or the radial artery are the most common “add-on” vessels used, but they have higher rates of intimal irregularities and graft occlusion.¹³⁷ Brown et al.¹³⁸ evaluated the utility of intraoperative screening of harvested conduits for CABG procedures using OCT. A total of 27 radial artery and 33 saphenous vein conduits were evaluated. OCT was done *in situ* before surgical manipulation to identify pre-existing intimal pathology and *ex vivo* to assess for damage incurred during harvest. In 3 saphenous vein grafts, OCT imaging was done to evaluate patency of the graft-to-coronary anastomosis. They found that OCT easily identified radial artery atherosclerosis, characterized plaques and calcium in the vessel wall, and showcased intimal trauma like medial dissection. Those are important feature to recognize because studies have shown that fibrocalcific and fibrous atheromatous plaques are at higher risk of graft failure or postoperative vessel spasm.^{139,140} Also, radial artery CABG led to lower MI and revascularization rates compared with saphenous vein CABG. Proper artery harvesting using these novel technologies could lead to superior outcomes.¹⁴¹ Regarding the saphenous vein, OCT improved diagnosis of retained clot compared with *ex vivo* examination, potentially leading to graft thrombosis and occlusion.¹³⁸ In a study by Oshima et al.,¹⁴² IVUS was used to examine the radial artery in 58 patients during a transradial procedure and identified vessel characteristics that can predict the rate of graft failure, such as small artery (proximal cross section diameter < 2.0 mm), diffuse atherosclerosis (plaque area > 50% of the vessel area distributed for > 50 mm during the pullback), and diffuse calcifications (calcified segment > 50 mm). Five of these vessels had these characteristics and 2 were considered unsuitable for CABG (one because of diffuse disease and the other because of small diameter). OCT and IVUS during/after vessel harvesting could optimize the selection of the “add-on” vessels and assess the quality of the distal anastomosis to improve long-term outcomes of revascularization.^{137,138} However, larger clinical trials are needed to confirm the relationship between OCT findings and graft patency, as well as defining criteria of nonoptimal conduits.

Invasive Coronary Physiological Measurement: FFR

Coronary artery physiological data, using FFR and instant wave-free ratio (iFR; measured without the need for pharmacologically-induced hyperemia¹⁴³) has proven to be helpful in decision-making regarding the management of intermediate-severity stenosis.^{28-30,144} However, physiological measurements are not routinely performed after revascularization although restoring normal physiology is possible¹⁴⁵ and could intuitively be a main goal of PCI.

The potential benefits of using post-PCI measurements would be to identify suboptimal revascularization, to allow the operator to optimize the revascularization procedure and further improve long-term clinical outcomes. FFR has a continuous relationship with the occurrence of MACE, and different post-PCI targets between 0.86 and 0.89 have been described as targets for “optimal stent results.”¹⁴⁶⁻¹⁴⁹ More recently, a study¹⁴⁷ prospectively following 574 patients who had pre- and post-PCI FFR measurements sought to establish a relationship between post-PCI FFR and long-term outcomes. They found that 21% of the studied lesions showed post-PCI FFR ≤ 0.81 despite satisfactory angiography appearance. After further interventions in this group, such as further post-dilatation in 42%, additional stenting in 33%, both in 18%, and intravascular imaging in 9%, the operators were able to increase the average FFR from 0.78 ± 0.08 to 0.87 ± 0.06 ($P < 0.01$). Patients with a final FFR > 0.86 had a lower incidence of MACE compared with patients with a final FFR ≤ 0.86 (17% vs 23%; $P = 0.02$). Another group published⁷⁷ a larger cohort of 1476 patients followed for 3 years. The primary outcome of target vessel failure was a composite of cardiac death, target vessel MI, and clinically driven target vessel revascularization 1 year after the index procedures. A multivariate analysis including stent diameter, stent length, location of lesion, and all other reported clinical, lesion, and procedural characteristics showed that a post-PCI FFR ≤ 0.88 was the only predictor of target vessel failure at 1 (OR, 3.71) and 3 years (OR, 2.63). The target vessel failure rate was 10.0% in the FFR ≤ 0.88 group and 4.0% in the FFR > 0.88 group ($P < 0.01$). The authors believe that achieving a post-PCI FFR > 0.86-0.89 should be the goal of modern, FFR-guided angioplasty.¹⁴⁶⁻¹⁴⁹

Although measuring post-PCI FFR is not a novel idea in itself, it has not been widely implemented as a tool to routinely evaluate coronary angioplasties. Failure to achieve an adequate post-PCI FFR should prompt the operator to immediately try to functionally optimize the revascularization through further postdilatation or using intravascular imaging to detect any problems with the stent deployment.^{150,151} One should also evaluate whether the residual flow obstruction could be caused by another lesion in the artery that has been previously underestimated. Rest indices such as iFR are especially useful in such circumstances because they can identify the specific location where the artery flow obstruction occurs when multiple lesions coexist, during pressure wire pullback.¹⁵² Data are sparse regarding iFR cutoffs in the post-PCI context as well as which stent optimization strategy would lead to better results. This remains a question to be answered by randomized trials. Other topics for which data are lacking are cost-effectiveness and revascularization outcomes determined after using an FFR pressure wire vs using additional intracoronary imaging.

Conclusion

Coronary revascularization is performed for symptom relief and/or for altering prognosis. Despite this, the current assessment, intervention, and follow-up of patients with CAD is greatly variable. Novel outcomes can refine patient selection as well as vessel selection for revascularization and assess the results of revascularization. These tools, if used meticulously, allow the clinician to more objectively plan, intervene, and follow-up patients with CAD.

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