

Coronary Revascularization in Ischemic Heart Failure Patients: A Rapid Review

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Rapid Review Methodology

Clinical questions are developed by the Division of Evidence Development and Standards at Health Quality Ontario in consultation with experts, end-users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials (RCTs), and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (<http://www.gradeworkinggroup.org/index.htm>), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies included in the systematic review are retrieved and a maximum of two outcomes are graded. If no well-conducted systematic reviews are available, RCTs and/or guidelines are evaluated. Because rapid reviews are completed in very short timeframes, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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List of Abbreviations

CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CI	Confidence interval
HF	Heart failure
HR	Hazard ratio
IMT	Intensive medical therapy
ITT	Intention-to-treat
MI	Myocardial infarction
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
RCT	Randomized controlled trial
SPECT	Single photon emission computed tomography
SVR	Surgical ventricular reconstruction

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to evaluate the effectiveness of coronary revascularization in ischemic heart failure (HF) patients.

Clinical Need and Target Population

Coronary artery disease (CAD), particularly the occurrence of myocardial infarction (MI), is a major risk factor for HF. (1) The development of HF has been shown to occur commonly after an index MI event, and the risk increases substantially with age. (2;3) For example, in a large Canadian prospective cohort study of MI patients over age 65 with no history of HF, three-quarters developed HF within 5 years. (2)

A national survey on acute HF patients treated in cardiology wards in Italy reported on diagnostic and therapeutic approaches in hospital. (4) The etiology of patients presenting with symptoms of either de novo (44%) or worsening (56%) HF was commonly reported to be ischemic (46%). In addition, a third of patients with acute HF of nonischemic origin had increased blood levels of troponin, an indication of some degree of myocardial injury. Prior MI was also common (36.5%), and rates were significantly higher in chronic (24.1%) than in de novo (12.8%) cases. Previous revascularization was also more common in cases with worsening symptoms (24.1%) than in de novo (12.8%) cases. During hospitalization, 5.5% had coronary revascularization, either with percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). De novo cases underwent revascularization at a higher rate than worsening cases (7.4% vs. 3.9%).

The ADHERE study is a large multicentre registry tracking clinical characteristics, physician practices, treatment patterns, and outcomes of over 100,000 patients hospitalized for either new-onset or decompensating chronic HF in 282 participating United States hospitals. (5) The registry population included patients with a mean age of 72 years, and 52% were female. Participants also commonly had a history of CAD (57%), hypertension (73%), prior MI (31%), and/or diabetes mellitus (44%). Cardiac catheterization was performed in 10% of hospitalized patients and in 20% of patients admitted to intensive/critical care. Revascularization with PCI was performed in 81% of those undergoing angiography and in 78% of those in intensive/critical care.

Revascularization has been shown to have benefits and improve prognosis in the treatment of CAD. At present, several large national prospective clinical registries are tracking and reporting PCI and CABG revascularizations. (6-8) However, the benefits of coronary revascularization for patients with HF and CAD—either to relieve symptoms, improve function, slow or reverse disease progression, or improve prognosis—are less certain. Evidence has been limited to mainly observational cohorts, (9) and large clinical trials comparing CABG revascularization with medical therapy have typically excluded patients with any significant left ventricular dysfunction. (10)

Technology/Technique

Coronary revascularization includes 2 main invasive treatments: PCI or CABG, with or without stents.

Rapid Review

Research Question

What is the effectiveness of coronary revascularization in ischemic heart failure patients?

Research Methods

Literature Search

A literature search was performed on November 5, 2012, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until November 5, 2012. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-reports
- published between January 1, 2008, and November 5, 2012
- systematic reviews, meta-analyses, health technology assessment reports, and randomized controlled trials (RCTs)
- studies evaluating coronary revascularization (CABG or PCI) in HF patients

Exclusion Criteria

- abstracts
- expert reviews, commentaries, editorials
- interventions not involving revascularization (CABG or PCI)

Outcomes of Interest

- perioperative mortality
- hospital length of stay
- readmissions
- mortality
- morbidity
- quality of life

Statistical Analysis

The RCTs that were identified evaluated different methods of coronary revascularization, different ancillary surgical procedures, and different outcome measures, precluding meta-analysis.

Expert Panel

In August 2012, an Expert Advisory Panel on Episode of Care for Congestive Heart Failure was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representation from the community laboratories.

The role of the Expert Advisory Panel on Episode of Care for Congestive Heart Failure was to contextualize the evidence produced by Health Quality Ontario and provide advice on the components of a high-quality episode of care for HF patients presenting to an acute care hospital. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The quality of the body of evidence for each outcome was examined according to the GRADE Working Group criteria. (11) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that RCTs are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas result in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (11) For more detailed information, please refer to the latest series of GRADE articles. (11)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	Very confident that the true effect lies close to that of the estimate of the effect
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Literature Search

The systematic literature search yielded 1,728 citations published between January 1, 2008, and November 5, 2012 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Three RCTs (12-14) involving 5 reports (12;13;15-17) on coronary revascularization focusing on patients with CAD and left ventricular dysfunction met the inclusion criteria. The reference lists of the included studies were hand searched to identify any additional potentially relevant studies, and 1 additional citation (RCT) (18) was included, for a total of 6 included citations.

The included studies are described in Table 1. The trials generally excluded HF patients with significant left main coronary artery stenosis, severe disabling angina unresponsive to nonsurgical interventions, or recent acute coronary syndrome events. These are conditions involving acute ischemic presentations in hospitalized HF patients without clinical uncertainty and for whom professional guidelines generally recommend angiographic diagnostic work-ups and revascularization of refractory angina or acute coronary syndromes in those with suitable anatomy.

Table 1: RCTs Evaluating Coronary Revascularization in Heart Failure Patients

Author, Year, Country	Trial Name, Type, Recruitment Period	Patients, N	Target Group	Study Objective
Beanlands et al., 2007, (18) Canada	PARR-2 Multicentre RCT (9 sites) 2000–2004	430	Patients with severe ventricular dysfunction (LVEF \leq 35%) and suspected CAD	To determine whether a strategy of PET imaging influenced treatment decision-making and clinical outcomes (compared to decisions without PET imaging) for patients with severe left ventricular dysfunction being considered for revascularization
D'Egidio et al., 2009, (13) Canada	PARR-2 2000–2004	182	Patients with severe LVEF and CAD being considered for revascularization work-up and randomized to PET	Substudy to identify high-risk patients benefiting from revascularization, a cut-off point for benefit, and imaging predictors of outcome
Cleland et al., 2011, (12) United Kingdom	HEART Multicentre RCT (9 sites) 2003–2004	138	Patients with HF, CAD, severe LVEF, and viable myocardium with contractile dysfunction	To determine whether coronary revascularization and optimal medical therapy improves the survival of patients with HF who have evidence of dysfunctional but viable myocardium and who are receiving optimal medical therapy
Velazquez et al., 2011, (17) United States	STICH Multicentre RCT (127 sites, 26 countries) 2002–2007	2,136 (1,212 in hypothesis 1)	Patients with CAD and LVEF \leq 35% who were eligible for IMT with or without CABG	To explore the first study hypothesis: that CABG revascularization and IMT in patients with HF improves 3-year all-cause mortality compared to IMT alone
Bonow et al., 2011, (15) United States	STICH 2002–2007	601	Subset of patients with CAD and LVEF \leq 35% who were eligible for IMT with or without CABG and who underwent assessment of myocardial viability	To evaluate whether the presence of substantial myocardial viability influenced the survival benefit of CABG revascularization and IMT compared to IMT alone
Jones et al., 2009, (16) United States	STICH 2002–2006	2,136 (1,000 in hypothesis 2)	Patients with CAD and LVEF \leq 35% and amenable to CABG and SVR	To explore the second study hypothesis: that SVR added to CABG would decrease the rate of death or hospitalization for a cardiac event compared to CABG alone

Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; HF, heart failure; LVEF, left ventricular ejection fraction; IMT, intensive medical therapy; PET, positron emission tomography; RCT, randomized controlled trial; SVR, surgical ventricular reconstruction.

PARR-2

Beanlands et al (18) reported on the beneficial role of nuclear imaging for determining myocardial viability and guiding coronary revascularization (CABG or PCI) decision-making for patients with CAD and severe left ventricular dysfunction. Participants had also undergone angiography within 6 months (53%), had had an MI (81%), and had undergone prior revascularization with CABG (21%).

Patients were randomized in block fashion and by recent angiography either to a positron emission tomography (PET) imaging arm or to a standard or usual care arm without PET imaging. In the PET arm, automated scoring (low, moderate, or high likelihood of recovery) based on a predictive algorithm was performed at a core laboratory to assess myocardial perfusion-metabolism mismatch. Imaging reports included information on the extent of scar, total viable myocardium, mismatch (as a percentage of left ventricle), and likelihood for recovery and were sent to a physician or surgeon making the decision to proceed with revascularization or revascularization work-up (to be booked within 8 weeks of randomization). PET imaging recommendations were adhered to in 75% of cases, and the majority (66%) undergoing revascularization had CABG. In the standard care group, 65% (138/212) had at least 1 stress or viability imaging test.

The primary composite outcome at 1 year of follow-up (cardiac death, MI, or cardiac-related hospitalization) was not significantly different between groups (hazard ratio [HR] 0.78, 95% confidence interval [CI] 0.58–1.1, $P = 0.15$). The cumulative proportion experiencing the composite score was 30% in the PET arm and 36% in the standard care arm, and the first events occurring within the composite score were cardiac hospitalization ($n = 94$), cardiac death ($n = 29$), and MI ($n = 13$). There were 19 cardiac deaths in the PET arm, compared to 26 in the standard care arm (HR 0.77, 95% CI 0.55–1.09, $P = 0.14$). The overall survival between the 2 groups was not significantly different at 1 year (HR 0.72, 95% CI 0.4–1.3, $P = 0.25$), although among those without recent angiography (i.e., de novo cases), there was a significant reduction in deaths in the PET arm (7.1%) compared to the standard care arm (16.7%) (HR 0.4, 95% CI 0.17–0.96, $P = 0.035$).

PARR-2, Post-Hoc Report

A second report (13) on the PARR-2 trial involved a post-hoc analysis examining whether nuclear imaging parameters were able to identify high-risk patients who would benefit from revascularization, and analysis was restricted to patients in the PET arm with coronary stenosis > 50% and a good-quality imaging study. Those with a myocardial perfusion-metabolism mismatch score $\geq 7\%$ had significantly reduced incidence of the primary composite outcome with revascularization compared with standard care (3 [13%] vs. 9 [56%], respectively, $P = 0.015$). As the amount of mismatch (a measure of hibernation) increased, there was a progressive increase in patient benefit from revascularization. There was no significant interaction between PET-defined scar and revascularization, suggesting that mismatch is the dominant parameter to consider when making decisions about revascularization.

HEART

Cleland et al (12) reported on coronary revascularization and survival in HF patients with CAD. The trial randomized 138 patients (out of a planned 800) to a conservative strategy involving optimal medical therapy or an invasive strategy in which the heart team (interventional cardiologist and surgeon) choose appropriate revascularization: CABG, PCI, both, or none. The government sponsor withdrew funding after 1 year because of poor recruitment, due in part to competing recruitment by the STICH study, another RCT evaluating revascularization in HF patients (see below).

Of the 69 patients assigned to the invasive strategy, 5 died awaiting angiography, 1 patient refused, 16 were denied revascularization after angiography, and 47 were offered revascularization. Of those offered

revascularization, 65% (45/69) underwent treatment (30 by CABG and 15 by PCI); treatment was performed within 12 weeks in 78% of patients. Two patients refused treatment. Of those in the conservative arm, 9% (6/69) underwent revascularization.

The primary outcome (all-cause mortality using intention-to-treat analysis) was not significantly different between the study groups at 4 years of follow-up ($P = 0.63$). During follow-up, there were 51 (37%) deaths: 25 in the conservative arm and 26 in the invasive arm. Of the 26 deaths in the invasive arm, 5 occurred while awaiting angiography; 5 occurred after being judged unsuitable for revascularization; 2 occurred from angiography-related complications; and 1 occurred after being judged suitable but refused intervention. Fifteen patients underwent PCI, of which 4 (17%) died; 30 patients underwent CABG, of which 9 (30%) died. Quality-of-life scores were not significantly different between the study arms at 6 months' follow-up, as evaluated by the EuroQoL EQ-5D (-0.023 , 95% CI -0.144 to 0.097) and Minnesota Living with Heart Failure (-3.9 , 95% CI -11.4 to 3.5) instruments.

STICH

The STICH trial (14) evaluated revascularization in patients with left ventricular dysfunction and CAD; it was a complex multicentre trial involving 2 main hypotheses (see below). Subjects were initially segregated into 3 strata depending on investigator-determined suitability for continued intensive medical therapy (IMT) alone and eligibility for surgical ventricular reconstruction (SVR). Eligibility for IMT alone generally excluded patients with left main coronary artery stenosis of 50% or greater or those with severe disabling angina unresponsive to nonsurgical interventions, and eligibility for SVR was defined as dominant left ventricular akinesia or dyskinesia amenable to SVR. After being assigned to strata and providing informed consent, patients were randomized within the strata as follows: stratum A included patients eligible for IMT alone, randomized to IMT vs. CABG; stratum B included patients eligible for IMT and SVR, randomized to IMT vs. CABG vs. CABG plus SVR; stratum C included patients eligible for SVR, randomized to CABG vs. CABG plus SVR.

All patients in the trial were managed by a medical therapy committee, which was mandated to regularly review and refine optimal medical therapy for the study. The use of pacemakers and implantable defibrillators was also encouraged according to guidelines as part of IMT. The surgical study protocol included several general principles: surgery completion within 14 days of randomization; CABG performed using at least 1 internal thoracic conduit; discretionary cardiopulmonary bypass; mitral valve repair or replacement if judged necessary; PCI if more appropriate; SVR to occur after CABG and by any acceptable reconstruction method. Minimum qualification standards were set by a surgical therapy committee.

STICH Hypothesis 1: CABG Plus IMT vs. IMT Alone

Velazquez et al (17) reported on the first study hypothesis, comparing CABG revascularization and IMT to IMT alone.

Of those assigned to CABG, 91% underwent the procedure, with a median time to surgery of 10 days; surgery was electively performed in 95% of patients. The majority (91%) received at least 1 arterial conduit; 86% received 1 or more venous conduits; and 87% had 2 or more distal anastomoses. Mitral regurgitation was not uncommon: 18% of the entire study population (220/1,212) had a moderate or severe degree of regurgitation, and a concurrent mitral valve operation was performed in 11% of patients (63/610) in the CABG arm.

Of those assigned to IMT, 100 (17%) underwent CABG during follow-up, at a median time of 142 days (interquartile range 19–576 days). Common indications for crossover were progressive symptoms (40%), acute decompensation (27%), patient or family decision (28%), and physician decision (5%).

Adherence to medication was high throughout study follow-up for both study arms. During follow-up, PCI was performed (6% in IMT and 4% in CABG); pacemakers were implanted for resynchronization (4% in IMT and 5% in CABG) and heart rate (2% in IMT and 7% in CABG); and implantable cardioverter-defibrillators were also implanted (19% in IMT and in 15% in CABG). End-stage devices such as left ventricular assist devices were rarely placed (2 patients in each study arm), and heart transplantation was performed in 3 patients in the IMT group (none in the CABG group).

The primary outcome of all-cause mortality at 56 months of follow-up occurred in 41% (244/602) of patients assigned to IMT and in 36% (218/610) of patients assigned to CABG, resulting in a reduced but nonsignificant HR for CABG (Table 2). In order to account for crossovers, 2 other prespecified analyses were performed (as-treated and per-protocol): in both analyses, HR was significantly reduced with CABG vs. IMT.

Table 2: Prespecified Statistical Analyses of Coronary Revascularization vs. IMT

Analysis	Study Groups	All-Cause Mortality HR (95% CI)	P Value
ITT	602 patients assigned to IMT vs. 610 patients assigned to CABG	0.86 (0.72–1.04)	0.12
As-treated	592 treated with IMT in year 1 after randomization vs. 620 undergoing CABG (initially randomized to CABG or crossed over to CABG during year 1 of follow-up)	0.70 (0.58–0.84)	< 0.001
Per-protocol	537 patients randomized to IMT who did not cross over during year 1 of follow-up vs. 555 patients who underwent CABG	0.76 (0.62–0.92)	0.005

Abbreviations: CABG, coronary artery bypass graft; CI, confidence interval; HR, hazard ratio; IMT, intensive medical therapy; ITT, intention-to-treat.

Comparisons between the study groups on the other prespecified secondary composite outcome measures are listed in Table 3. Except for 30-day all-cause mortality—where mortality risk was higher in the CABG group compared to the IMT group—revascularization with CABG was associated with a significant reduction in all secondary composite outcomes. During follow-up (median 56 months), cardiovascular-related mortality was significantly reduced in the CABG arm (HR 0.81, 95% CI 0.66–1.00). Of total deaths in the IMT arm, 82% (201/244) were judged to be cardiovascular-related, compared to 77% (168/218) in the CABG arm.

Table 3: Secondary Composite Outcomes of Coronary Revascularization vs. IMT

Secondary Composite Outcome	IMT, N (%)	CABG, N (%)	HR With CABG (95% CI)	P Value
30-day all-cause mortality	7 (1)	22 (4)	3.12 (1.35–7.31)	0.006
Cardiovascular-related mortality	201 (33)	168 (28)	0.81 (0.66–1.00)	0.05
All-cause mortality or HF hospitalization	324 (54)	290 (48)	0.84 (0.71–0.98)	0.03
All-cause mortality or cardiovascular-related hospitalization	411 (68)	351 (58)	0.74 (0.64–0.85)	< 0.001
All-cause death or all-cause hospitalization	442 (73)	399 (65)	0.81 (0.71–0.93)	0.003
All-cause death or revascularization with CABG or PCI	333 (55)	237 (39)	0.60 (0.51–0.71)	< 0.001

Abbreviations: CABG, coronary artery bypass graft; CI, confidence interval; HF, heart failure; HR, hazard ratio; IMT, intensive medical therapy; PCI, percutaneous coronary intervention.

STICH: Impact of Myocardial Viability on CABG vs. IMT

Bonow et al (15) reported on the ability of myocardial viability imaging to identify patients with CAD and severe LV dysfunction for whom CABG would confer a survival benefit. The requirement for single-photon-emission computed tomography (SPECT) imaging in the original study protocol was an impediment to recruitment, so the protocol was amended to allow for the use of either SPECT, dobutamine echocardiography (DE), or both, as determined by investigators. This report involved a subgroup of 601 patients who had SPECT (n = 471), DE (n = 280), or both (n = 150).

The patients who underwent imaging investigations were significantly different from those who did not (n = 611) in terms of disease severity, medical management, and prior interventions. Among those who underwent imaging, 81% (487/601) were judged to have viable myocardium; those with and without myocardial viability were then randomized roughly equally to the treatment arms. Patients with viable myocardium tended to have significantly fewer prior MIs (76.6% vs. 94.7%, $P < 0.001$) and PCI revascularizations (15.8% vs. 23.7%, $P = 0.045$), but more hypertension (64.1% vs. 44.7%, $P < 0.001$) and diabetes (40.7% vs. 22.8%, $P < 0.001$) compared to those without a viable myocardium. Those with myocardial viability also tended to have lower angina scores (41.5% vs. 29.8% with no angina) and better New York Heart Association (NYHA) functional scores (42.3% vs. 28.9% with NYHA class I/II).

During follow-up (median 5.1 years), there were 236 deaths, including 51% (58/114) in those without myocardial viability and 37% (178/487) in those with myocardial viability. Primary all-cause mortality was significantly lower among those with myocardial viability (HR 0.64, 95% CI 0.48–0.86, $P = 0.003$). However, after multivariate correction for significant prediction covariates, viability status was no longer significantly associated with mortality ($P = 0.21$).

Patients with myocardial viability also had significantly lower rates of secondary endpoints, such as cardiovascular-related mortality (HR 0.61, 95% CI 0.44–0.84, $P = 0.003$) and the composite endpoint of mortality or cardiovascular-related hospitalization (HR 0.59, 95% CI, 0.47–0.74, $P < 0.001$). After multivariate adjustment, only the composite endpoint of mortality and cardiovascular-related hospitalization remained significant ($P = 0.003$).

STICH Hypothesis 2: CABG and SVR vs. CABG Alone

Jones et al (16) reported on the second main hypothesis—that revascularization with CABG and simultaneous SVR conferred a survival advantage over CABG alone in patients with significant akinesia or dyskinesia of anterior wall LV segments.

The assigned surgical intervention was performed in 93% of patients in the CABG arm and 91% in the CABG plus SVR arm. Of the patients assigned to CABG alone, 9 did not undergo any surgery and 27 underwent CABG plus SVR. Of those assigned to CABG plus SVR, 12 did not undergo any surgery and 35 underwent CABG alone. Surgery was electively performed in 84% of patients (819/979) and was more likely to be off-pump bypass in the CABG-only arm (10% vs. 1% $P < 0.001$). Other surgical interventions, notably for mitral valve, were performed at similar rates (17% vs. 19%) in the 2 study groups, but the valve was more commonly repaired (rather than replaced) in the CABG-plus-SVR group (98% vs. 89%). Most technical outcome measures were significantly longer with CABG plus SVR: bypass pump time ($P < 0.001$), total operating room time ($P < 0.001$), total intubation time ($P = 0.002$), total intensive/critical care time ($P < 0.001$), and length of hospital stay ($P < 0.001$).

At 4 months of follow-up, the pre/post end-systolic volume index available for a subset of patients (43% in the CABG group and 32% in the CABG-plus-SVR group), was reduced significantly greater in the CABG-plus-SVR group than in the CABG only group (19% vs. 6%; $P < 0.001$).

About three-quarters of patients in each treatment group performed the 6-minute walk test for functional assessment, and the increase over baseline in median distance walked was similar in the 2 groups: 13.7% in the CABG group and 14.5% in the CABG-plus-SVR group.

Canadian Cardiovascular Society–defined angina class was significantly improved, but not differently over baseline in both surgery groups: angina symptoms in both groups improved by an average of 1.7 classes ($P = 0.84$), with no angina symptoms reported at follow-up by 339 patients (vs. 121 at baseline) in the CABG group and by 339 patients (vs. 128 at baseline) in the CABG-plus-SVR group. NYHA class also improved by an average of 1 class in the 2 surgery groups: the number of patients with class III/IV symptoms was similarly reduced ($P = 0.70$) at follow-up over baseline, from 241 to 80 patients in the CABG group and from 244 to 62 patients in the CABG-plus-SVR group.

During follow-up (median 48 months), the primary composite outcome of all-cause mortality or cardiac-related hospitalization occurred in 499 patients (59%) in the CABG group and 289 (58%) in the CABG-plus-SVR group and was not significantly different between groups (HR 0.99, 95% CI 0.84–1.17, $P = 0.90$). All-cause mortality was also not significantly different between groups (141 [28%] vs. 138 [(28%)]; HR 1.00, 95% CI 0.79–1.26). Hospitalizations between the 2 groups were not significantly different for cardiac-related (42% vs. 41%) or all-cause (55% vs. 53%) indications ($P = 0.73$). Perioperative death within 30 days was also not significantly different between groups, in either the intent-to-treat (5% vs. 5%) or the as-treated (5% vs. 6%) analyses.

Procedures performed subsequent to surgery were not significantly different between groups and included pacemakers (15% vs. 15%) and implantable cardioverter-defibrillators (20% vs. 17%). Further revascularization with PCI was performed in 6% of the CABG group and 3% of the CABG-plus-SVR group. Interventions for advanced stages of HF, such as left ventricular assist devices (4 patients) or heart transplantation (9 patients—2 in the CABG group, 7 in the CABG-plus-SVR group) were rarely performed.

Discussion

The PARR-2 trial was the first prospective RCT to evaluate whether imaging for myocardial viability could help detect areas of hibernation and chronically dysfunctional myocardium in order to more appropriately evaluate the benefit of coronary revascularization. Physicians generally adhered to PET recommendations for revascularization, and overall survival at 1 year and the composite outcome of cardiac hospitalization or cardiac death were lower (but not significantly) in the PET arm. Limiting the interpretation of this study was the fact that the majority of physicians managing patients in the standard care group also had access to other stress or viability imaging investigations.

The HEART trial was the first to evaluate whether coronary revascularization using either PCI or CABG in addition to optimal medical therapy improved the survival of HF patients with CAD. Unfortunately, the trial was stopped early because of low recruitment; it remains the only trial to evaluate both PCI and CABG in HF patients. Overall survival between study groups was not significantly different at 5 years' follow-up, but deaths occurring in those assigned to and awaiting the intervention diluted the study power; of the 25 deaths occurring in the revascularization arm, 13 died before receiving the intervention. Quality of life, as measured by both generic and disease-specific HRQOL instruments, was also not significantly different between the study groups at 6 months' follow-up, although confidence intervals were wide.

The STICH trial is the largest prospective RCT so far to evaluate the benefit of cardiac surgeries involving CABG revascularization and ventricular construction in HF patients with CAD. Although the

primary outcome of all-cause mortality at 4 years' follow-up was lower (but not significantly) in the CABG intention-to-treat analysis, mortality in the as-treated and per-protocol analyses was significantly reduced. The high proportion of patients not receiving an assigned surgical intervention (often due to unsuitable anatomy) or crossing over highlights the difficulties inherent in conducting and interpreting surgical trials. That 5 secondary composite outcome measures involving combinations of death and hospitalization were all significantly lower in the CABG group further supports the advantages of revascularization in HF patients. The 30-day mortality rate, however, which was significantly higher in the CABG group, highlights the trade-off between higher short-term and lower longer-term mortality risk.

Survival benefits were not shown with CABG plus SVR, and neither primary nor the secondary composite outcome measures were significantly improved. However, SVR surgery was not under protocol, and any acceptable method of surgical reconstruction was allowed, resulting in a number of technical variations that may have influenced outcome. CABG plus SVR did result in a significantly greater reduction in end-systolic volume than CABG surgery alone, and although 30-day perioperative mortality was not significantly different between groups, all other technical and care-related outcome measures were significantly higher in the CABG-plus-SVR group. Functional status, angina symptoms, and HF symptoms were all significantly improved at short term-follow-up but improvements were similar in the surgical groups.

Guidelines

The American College of Cardiology and the American Heart Association Task Force (19) concluded that indications in all cases for coronary angiography and revascularization should be tempered by individual patient characteristics and preference. Judgements regarding risk and benefit were said to be particularly important for patients who might not be candidates for revascularization, such as the frail elderly and those with a serious comorbidity, such as inoperable cancer or severe hepatic, pulmonary or renal failure.

The 2010 Heart Failure Society of America (20) guidelines for treating HF in the setting of ischemic HF also recommend that the diagnostic approach for CAD be individualized based on patient preference, comorbidities, eligibility, and willingness to undergo revascularization. It was also recommended that patients with HF and symptoms suggestive of angina undergo cardiac catheterization with coronary angiography to assess the potential for revascularization, and that coronary revascularization be performed in HF patients with suitable anatomy for relief of angina or acute coronary syndrome.

There is extensive literature on appropriateness criteria using the RAND/UCLA methodology for surgical procedures—particularly for coronary revascularization. (21) However, studies also show that panel membership significantly alters appropriateness ratings, particularly between those performing the procedure and those not performing the procedure. (22) Several societies (23) have therefore recommended that a heart team collaborative approach (involving a cardiac surgeon, an interventional cardiologist, and often the patient's general cardiologist) followed by discussions with the patient regarding treatment options is optimal, particularly when the revascularization strategy is not straightforward, as may be the case in patients with ischemic HF.

Conclusions

The evidence suggests that coronary revascularization improves survival compared to medical therapy in patients with CAD and significant left ventricular systolic dysfunction, and for those in whom treatable targets are identified. Decisions to perform revascularization in these patients should not be overly influenced by imaging-defined myocardial viability status, as an association with clinical outcomes was not shown. The routine use of SVR as an adjunct to CABG coronary revascularization is not supported by the evidence.

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Appendices

Appendix 1: Literature Search Strategies

Literature Search – Heart Failure Rapid Review – Revascularization

Search date: November 5, 2012

Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; CRD

Q: Cardiac catheterization and/or revascularization for ischemic heart failure CHF QBF

Limits: 2008-current; English

Filters: health technology assessments, systematic reviews, and meta-analyses, RCTs

Database: Ovid MEDLINE(R) <1946 to October Week 4 2012>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <November 02, 2012>, Embase <1980 to 2012 Week 44>

Search Strategy:

#	Searches	Results
1	exp Heart Failure/	329125
2	(((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab.	259578
3	or/1-2	419254
4	exp Myocardial Revascularization/ use mesz	76332
5	exp heart muscle revascularization/ use emez	19839
6	exp heart catheterization/	98980
7	exp coronary artery bypass graft/ use emez	48721
8	exp percutaneous coronary intervention/ use emez	51270
9	exp stent/ use emez	84699
10	exp Stents/ use mesz	47303
11	(coronary artery bypass or cabg or ptca).ti,ab.	80212
12	((coronary or heart or cardiac or myocardial) adj2 (stent* or catheter* or revasculari* or balloon* or angioplast*)).ti,ab.	105866
13	or/4-12	417307
14	3 and 13	35325
15	limit 14 to english language	30047
16	limit 15 to yr="2008 - 2012"	12710
17	Meta Analysis.pt.	37256
18	Meta Analysis/ use emez	66936

19	Systematic Review/ use emez	54406
20	exp Technology Assessment, Biomedical/ use mesz	8883
21	Biomedical Technology Assessment/ use emez	11409
	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies	
22	or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	295445
23	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	3810
24	exp Random Allocation/ use mesz	76290
25	exp Double-Blind Method/ use mesz	117930
26	exp Control Groups/ use mesz	1380
27	exp Placebos/ use mesz	31496
28	Randomized Controlled Trial/ use emez	332138
29	exp Randomization/ use emez	59934
30	exp Random Sample/ use emez	4293
31	Double Blind Procedure/ use emez	111711
32	exp Triple Blind Procedure/ use emez	35
33	exp Control Group/ use emez	39177
34	exp Placebo/ use emez	207567
35	(random* or RCT).ti,ab.	1392418
36	(placebo* or sham*).ti,ab.	450420
37	(control* adj2 clinical trial*).ti,ab.	38578
38	(controlled clinical trial or meta analysis or randomized controlled trial).pt.	458049
39	or/17-38	2282012
40	16 and 39	2022
41	remove duplicates from 40	1728

Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Heart Failure] explode all trees	4873
#2	((cardia? or heart) next (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) next (failure or insufficiency)):ti,ab,kw (Word variations have been searched)	9337

#3	#1 or #2	9342
#4	MeSH descriptor: [Myocardial Revascularization] explode all trees	7841
#5	MeSH descriptor: [Heart Catheterization] explode all trees	1950
#6	MeSH descriptor: [Stents] explode all trees	2939
#7	coronary artery bypass or cabg or ptca:ti (Word variations have been searched)	2472
#8	coronary artery bypass or cabg or ptca:ab (Word variations have been searched)	5026
#9	((coronary or heart or cardiac or myocardial) near/2 (stent* or catheter* or revasculari* or balloon* or angioplast*)):ti (Word variations have been searched)	1955
#10	((coronary or heart or cardiac or myocardial) near/2 (stent* or catheter* or revasculari* or balloon* or angioplast*)):ab (Word variations have been searched)	3363
#11	#4 or #5 or #6 or #7 or #8 or #9 or #10	14338
#12	#3 and #11 from 2008 to 2012	188

CRD

Line	Search	Hits
1	MeSH DESCRIPTOR heart failure EXPLODE ALL TREES	510
2	((cardia? OR heart) ADJ (decompensation OR failure OR incompetence OR insufficiency)) OR cardiac stand still OR ((coronary OR myocardial) ADJ (failure OR insufficiency))):TI	317
3	#1 OR #2	552
4	MeSH DESCRIPTOR myocardial revascularization EXPLODE ALL TREES	534
5	MeSH DESCRIPTOR Heart Catheterization EXPLODE ALL TREES	349
6	MeSH DESCRIPTOR Stents EXPLODE ALL TREES	678
7	(coronary artery bypass or cabg or ptca):TI	208
8	((coronary or heart or cardiac or myocardial) ADJ2 (stent* or catheter* or revasculari* or balloon* or angioplast*)):TI	172
9	#4 OR #5 OR #6 OR #7 OR #8	1479
10	#3 AND #9	6
11	(#10):TI FROM 2008 TO 2012	2

Appendix 2: GRADE Tables

Table A1: GRADE Evidence Profile for Revascularization in Ischemic Heart Failure Patients

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Revascularization Treatment Decision-Making Guided by PET Myocardial Viability Imaging							
1 (RCT)	Serious limitations (-1) ^a	No serious limitations	No serious limitations	No serious limitations	Not evaluated	None	⊕⊕⊕ Moderate
Revascularization for Ischemic Heart Failure							
2 (RCTs)	Serious limitations (-1) ^b	No serious limitations	No serious limitations	No serious limitations	Not evaluated	Other considerations (+1) ^c	⊕⊕⊕ Moderate

Abbreviations: No., number; RCT, randomized controlled trial.

^aThe control group also had access to imaging information, and interventions were performed at the discretion of the treating surgeons.

^bThe study group was initially selected on physician's opinions on suitability for different treatment arms.

^cLarge trial; well-conducted and analyzed.

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