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POSITION PAPER

Revascularization of coronary artery disease in heart failure: a European Journal of Heart Failure expert consensus statement

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Abstract

The role of myocardial revascularization in heart failure (HF) patients with coronary artery disease by either percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) is controversial. For patients with HFrEF, prior to the advances in pharmacological heart failure therapy over the last 10 years, evidence suggests a modest, long-term benefit of CABG over guideline-recommended medical therapy. In the era of modern medical therapy, revascularization had no benefit in HFrEF. Whether a patient with HF and CAD should be advised to have revascularization and, if so, which procedure remains unclear and should be discussed by the heart team given the limited and conflicting evidence. Evidence for viability or ischaemia-guided selection strategies is controversial. In all cases with HF, establishing and optimizing guideline-directed medical therapy (GDMT) and device therapy is required. When HF symptoms dominate despite GDMT, additional invasive procedures are not indicated. When angina persists despite GDMT and device therapy, revascularization should be considered. The choice of revascularization procedure should be discussed in the heart team, considering symptoms and ischaemic burden, surgical risk, coronary complexity, and the applicable HF treatment.

Keywords Revascularization • Heart failure • Coronary artery bypass graft • Percutaneous coronary intervention

Introduction

Coronary artery disease (CAD) is a common cause of heart failure (HF).[1–5] The mechanisms underlying the development of HF in patients with CAD are either the occurrence of acute coronary syndromes or the progressive decline in cardiac function explained by a combination of scar tissue and areas of dysfunctional but still viable myocardium (stunning or hibernating myocardium).[6]

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CAD adds to the poor prognosis of HF.[7,8] The rationale for revascularization has been based on the hypothesis of reducing chronic ischaemia and restoring the function of hibernating myocardium.[9] However, while in non-HF patients the prognostic and symptomatic benefits of myocardial revascularization critically depend on the completeness of revascularization, little is known on the role of revascularization in patients with HF.[9] By ensuring normal coronary blood flow, the underlying hypothesis is to restore and save ischaemic, but still vital, myocardial tissue from irreversible damage (reversal of myocardial hibernation or stunning). This has been thought to possibly lead to an improvement in contractile cardiac function and in prognosis.

According to current HF guidelines from the European Society of Cardiology (ESC), coronary revascularization may be considered to improve outcomes in patients with HFrEF, chronic coronary syndrome, and coronary anatomy suitable for revascularization, after careful evaluation of the individual risk-to-benefit ratio, including coronary anatomy (i.e. proximal stenosis >90% of large vessels, stenosis of left main or proximal LAD), comorbidities, life expectancy, and patient's perspectives.[10] CABG should be considered as first-choice revascularization due to the lack of benefit of PCI in HFrEF.[10] There have been no trials of CABG or PCI in HFpEF or in hospitalized HF.

This expert consensus statement will present the available evidence on revascularization strategies in HFrEF, HFpEF, and hospitalized HF and propose an opinion-based management algorithm to inform clinicians on how to manage patients with HF and multivessel coronary disease.

Revascularization strategies in HFrEF

Guidelines on HF and those on chronic CAD both recognize a potential role of myocardial revascularization to manage patients with HFrEF and CAD, but they differ in the strength of recommendations.[10–12] According to the guidelines on HF, 'revascularization' may be considered (class of recommendation II-b; level of evidence C) in patients with HFrEF and severe CAD. It should be considered to relieve persistent symptoms of angina (or an angina-equivalent) in patients with HFrEF, Canadian Cardiovascular Society angina class III or IV, and coronary anatomy suitable for revascularization, despite optimal medical treatment including anti-anginal drugs (class of recommendation II-a; level of evidence C).[10] Guidelines on chronic CAD are similar to those on HF but provide a higher strength of recommendation and increased level of evidence (class of recommendation I; level of evidence B).[12]

Evidence on the role of coronary revascularization in patients with HFrEF stems largely from surgical trials predating the pharmacological advances in the treatment of HF. Evidence on the role of revascularization in patients with HFrEF and CAD derives from a limited number of randomized controlled trials (RCT), i.e. STICH, and its prolonged follow-up STICHES, PARR-2, HEART, and REVIVED-BCIS2 and from a small subset of patients enrolled in the COURAGE, FAME and ISCHEMIA trials.[13–21] (*Table 1*)

PARR-2 trial

The PARR-2 (Positron Emission Tomography and Recovery Following Revascularization) trial included 430 patients with CAD and HFrEF (LVEF ≤35%) between 2000 and 2004, randomized to either an imaging-guided management or standard care.[18] Patients randomized to the imaging strategy underwent cardiac positron emission tomography (PET) for the evaluation of myocardial viability and the prediction of the likelihood of LV function recovery, following revascularization. Invasive management was mandated for patients with a moderate-to-high likelihood of recovery after coronary revascularization and discouraged in those with a low probability of recovery. The primary outcome was defined as the composite of cardiac death, myocardial infarction or recurrent hospital stay for cardiac cause assessed at 1 year. Overall, the study failed to demonstrate a reduction in cardiac events in patients randomized to the PET-guided management vs standard care [relative risk: 0.82 (95% CI: 0.59–1.14)].[17] However, approximately 25% of patients with PET-guided revascularization did not perform any intervention, mainly due to lack of adherence to the study protocol. Hence, the study results were substantially influenced by the arbitrary decisions of physicians, introducing a substantial bias in the interpretation of the findings.

HEART trial

The HEART (Heart Failure Revascularization Trial) trial was originally designed to enrol 800 patients with a diagnosis of HFrEF (defined as LVEF≤35%), CAD and evidence of a significant burden of residual myocardial viability on pre-enrolment imaging stress tests.[13] Patients were subsequently randomized to either an invasive or conservative strategy. The study was stopped prematurely, due to slow recruitment, and only 138 patients were finally randomized. The study was underpowered and no significant difference was detected between the two arms for the rate of all-cause mortality. However, mortality was identical in each arm. Also, in a CMR sub-study, despite a significantly greater improvement in myocardial blood flow, LV function improved similarly with and without revascularization.[22]

STICH and STICHES trial

Between 2002 and 2007 the STICH (Surgical Treatment for Ischaemic Heart Failure) trial randomized 1212 patients with extensive CAD and HFrEF (LVEF ≤35%) to either surgical revascularization (CABG) plus GDMT vs GDMT alone. After a median follow-up of 56 months, no difference was found between the 2 arms in the primary end point of all-cause mortality, even though CABG was associated with lower rates of death from cardiovascular causes and of the composite of all-cause mortality or cardiovascular admission.[15] Patients in the CABG arm had higher rates of mortality than in the medical therapy arm for the first 2 years.[15] In fact, in the Surgical Treatment for Ischaemic Heart Failure Extension Study (STICHES), which reported the long-term results of the STICH trial, after a median follow-up duration of 9.8 years, there was a 16% relative risk reduction in the rate of all-cause mortality for the CABG group, compared with the conservative strategy arm; moreover, patients with three-vessel coronary disease or with a severely remodelled LV architecture (end-systolic volume index >78 ml/m^2 or LVEF ≤27%) were the most likely to receive a clinical benefit from revascularization.[16] The presence or absence of myocardial viability did not identify those who had more or less to gain from CABG.[23] The presence or absence of diabetes did not identify those with more or less to gain from CABG.[24] Younger patients (aged < 60) appeared to benefit more than older patients.[25] Since myocardial infarction is a minor cause of death in HFrEF (and was not systematically evaluated as part of STICH), the effect of CABG in the STICH study is currently difficult to explain.

REVIVED-BCIS2 trial

From 2013 through 2020, in the REVIVED-BCIS2 (Revascularization for Ischaemic Ventricular Dysfunction) trial 700 patients with HFrEF (LVEF ≤ 35%) and CAD were enrolled to assess the potential benefit of revascularization by PCI on top of GDMT.[14] PCI had no effect on the composite of all-cause mortality and HF hospitalizations (HR 0.99; 95% CI: 0.78–1.27) over a median observation period of approximately 3.5 years. PCI had no impact on all-cause mortality or HF hospitalizations. PCI did not increase LVEF, did not reduce MI but was associated with an increase in health status at 6 months (unblinded trial) but not beyond.[26] On the other hand, it is noteworthy to mention that no increased rate of periprocedural mortality was detected in the

Table 1 Landmark randomized trials that included patients with HFrEF and coronary artery disease

TRIAL (year of publication)	PARR-2 (2007)	HEART (2011)	STICH (2011) and STICHES (2016)	REVIVED -BCIS2 (2022)	COURAGE (2007)[a]	ISCHEMIA (2020)[b]	FAME 3 (2022)[d]
Type of study	Dedicated RCT	Dedicated RCT	Dedicated RCT	Dedicated RCT	Subgroup analysis	Subgroup analysis[g]	Subgroup analysis
Revascularization	PCI	PCI or CABG	CABG	PCI	PCI	PCI or CABG	FFR-guided PCI vs CABG
Country	USA	UK	Multinational	UK	USA and Canada	Multinational	Multinational
N. of patients with HFrEF	430	138	1212	700	394[b]	398	1496
Follow-up (months)	12	59	56[e]	41	55	38	12
Age	63	67	60	70[b]	61[b]	66	65
Men	363 (84)	129 (93)	1064 (88)	614 (88)	1947 (85)	315 (79)	1235 (82)
Hypertension		69 (50)	728 (60)	391 (56)	1521 (66)	322 (81)	1094 (73)
DM	167 (39)	51 (37)	478 (39)	289 (41)	766 (33)	184 (46)	428 (28)
Previous AMI	346 (80)	101 (73)	934 (77)	372 (53)	876 (38)	146 (37)	500 (33)
Previous PCI		11 (8)	156 (13)	142 (20)	359 (16)	137 (34)	202 (13)
Previous CABG	80 (19)	11 (8)	36 (3)	34 (5)	248 (11)	31 (8)	Exclusion criteria
NYHA I-II		88 (64)	765 (63)	513 (74)		286 (72)	
NYHA III-IV		50 (36)	447 (37)	182 (26)			
LVEF	27	≤ 35%[f]	27	27		44[g]	267 (18) LVEF ≤ 50%
LM CAD			32 (3)	95 (14)		3 (1)	Exclusion criteria
Three vessel CAD			733 (60)	281 (40)	696 (30)	38/175 (22)	Inclusion criteria
BB		128 (93)	1036 (85)	634 (91)	1983 (87)	351 (88)	1051 (70)
ACE-I/ARB		128 (93)	1111 (92)	587 (84)	1451 (63)	328 (82)	740 (49)
MRA		49 (35)	556 (46)	346/697 (49)		36 (9)	
Loop diuretics		130 (94)	791 (65)	460/697 (66)[c]		146 (37)[c]	
ICD only			203 (17)	82 (12)			
CRT				67 (10)			

Follow-up length is encounted by months; age is expressed in years; LVEF is defined as percentage; All the other variables are reported in number and (percentage of the total population enrolled).
ACE-I/ARBs, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AMI, acute myocardial infarction; BB, beta blockers; CABG, coronary artery by-pass graft; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; DM, diabetes mellitus; FFR, fractional flow reserve; ICD, implantable cardioverter-defibrillator; LVD, left ventricular dysfunction; LVEF, left ventricular ejection fraction; LM, left main; NYHA, New York heart association functional class; PCI, percutaneous coronary intervention.
[a]Data reported here refer to the overall population since numbers from the subgroup of patients with HF were not provided.
[b]Information reported refer to the subset of patients with HF/LVD.
[c]This result includes both loop diuretics and thiazide diuretics.
[d]This information refer to the whole population recruited as data on the HF subset not available.
[e]This refers to follow-up of STICH, whereas 118 months is the duration of follow-up in STICHES.
[f]All patients have a LVEF ≤ 35%.
[g]This combined participants with LVEF 35%–45%.

REVIVED-BCIS2 trial, comparing the invasive vs the conservative arm. The results from the REVIVED-BCIS2 trial differ from the short-term follow-up findings from the STICH trial, in which the CABG procedure was associated with an increased risk of all-cause mortality within 30 days after randomization.[15]

The REVIVED-BCIS2 study raised relevant methodological questions. Importantly, the extension of CAD and the size of the ischaemic myocardial area were not adequately accounted for prior to the revascularization procedures. Besides, the concordance between the coronary arteries revascularized by PCI and the viable myocardial segments was not examined. About 50% of patients had only a two-vessel CAD which suggests that less severely affected individuals were enrolled compared with those recruited in the STICH trial Functional assessment and coronary imaging were not mandated. Patients in REVIVED-BCIS2 had more severe HF symptoms than in contemporary trials of HF pharmacotherapy.[26] REVIVED-BCIS2 was mainly composed of patients with a New York Heart Association (NYHA) functional class of I-II and of recruits with little-to-no angina whereas participants in the STICH trial were more likely to report symptoms of HF as dyspnoea (86% and 85% of patients in the invasive and conservative arm, respectively, reported a NYHA functional class of II-III) and angina (43% of the overall population suffered from class II angina, according to the classification of the Canadian Cardiovascular Society). The extent of ischaemia or viability did not identify a population who benefited from PCI compared with medical therapy.[27]

Additional key differences between REVIVED-BCIS2 and STICH were found in the patients' population enrolled and in the underlying medical treatments. In a recent individual patient data analysis, patients in REVIVED-BCIS2 (in both treatment arms) had substantially better outcomes than those who received either surgery or medical therapy alone in STICH.[28] The REVIVED-BCIS2 trial consisted of an older patients' population with a mean age of 70 and 69 years in the PCI and GDMT groups, respectively; whilst the median age in the STICH trial was 60 and 59 years in the invasive and conservative strategy arms, respectively.[14,15] Finally, the STICH trial was conducted earlier, when different guidelines were in place and when devices, including cardiac resynchronization therapy (CRT) and intracardiac defibrillators (ICD), now considered a critical part in the management of HF, were less frequently adopted.[14,15]

Subgroup analyses of other randomized controlled trials

Large CAD trials such as COURAGE, ISCHEMIA, and the FAME programme were not specifically designed to enrol patients with HF, yet their post-hoc analyses in subgroups with left-ventricular dysfunction offer insights of clinical relevance. These observations, however, must be interpreted with considerable caution given their exploratory nature and the inherent limitations of subgroup analyses.

FAME trials

Coronary pressure-derived fractional flow reserve (FFR) is the current standard of care for the functional assessment of lesion severity in patients with intermediate-grade stenosis (typically around 40%– 90% of all stenosis) without evidence of ischaemia in the non-invasive assessments, or in those with a multivessel disease.[9] In patients with reduced LVEF and CAD, FFR-guided revascularization has been shown to be associated with lower rates of death and MACE at 5 years as compared with the angiography-guided strategy.[29,30] This beneficial impact was observed in parallel with less CABG and more patients deferred to PCI or medical therapy.

The FAME trial (Fractional Flow Reserve vs Angiography for Multivessel Evaluation) demonstrated that, in patients suffering from a multivessel coronary disease and randomized to a FFR-guided PCI strategy (using a cut-off ≤0.80 to indicate requirement for PCI), there was a benefit in the long-term outcomes of death for any cause or non-fatal myocardial infarction, compared with angiography-guided PCI.[31–33] The FAME-2 trial randomized 888 patients with stable CAD (approximately 17% had an LVEF <50%) in whom at least one coronary stenosis was functionally significant (FFR, ≤0.80) to FFR-guided PCI plus the best available medical therapy or the best available medical therapy alone.[34] The primary end point was a composite of death, myocardial infarction, or urgent revascularization. FFR-guided PCI plus the best available medical therapy, as compared with the best available medical therapy alone, decreased the need for urgent revascularization. However, in patients without ischaemia, the outcome appeared to be favourable with the best available medical therapy alone. The FAME-3 trial randomized 1500 patients with 3-vessel coronary disease (not involving the left main coronary artery) and amenable to revascularization to undergo CABG or FFR-guided PCI with current-generation drug-eluting stents.[35,36] The primary end point was the occurrence within 1 year of a major adverse cardiac or cerebrovascular event, defined as death from any cause, myocardial infarction, stroke, or repeat revascularization. Individuals with an LVEF <30% were excluded, but 267 participants had an LVEF between 30% and 50% (137 in the PCI vs 130 in the CABG group). The overall results of the FAME-3 trial indicate that FFR-guided PCI does not meet the criteria for noninferiority compared with CABG. The 1-year incidence of the composite primary end point was 10.6% among patients randomly assigned to PCI and 6.9% among those assigned to CABG (HR, 1.5; 95% CI: 1.1–2.2). Further subgroup analysis among individuals with a reduced LVEF did not show any statistical difference in the primary end point between revascularization strategies.[36] At 3 years, no difference was noted between the two arms but myocardial infarction and repeat revascularization were both higher with PCI.[37]

It is important to emphasize that the FAME trials did not require viability assessment for inclusion. The FAME trials focused exclusively on identifying physiologically significant lesions (functional ischaemia) using FFR to guide revascularization.

COURAGE trial

The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial enrolled 2287 patients with evidence of myocardial ischaemia and obstructive CAD between 1999 and 2004.[20] This was not a dedicated HF trial. It tested whether an initial management strategy of PCI with optimal medical therapy was superior to optimal medical therapy alone in reducing the risk of death or MI. Medical treatment consisted of lifestyle and pharmacologic therapy with aspirin, statins, ACE-I/ARBs, beta-blockers, calcium channel blockers, and nitrates. After a median follow-up of 4.6 years, revascularization with PCI in addition to optimal medical therapy did not reduce the risk of death, myocardial infarction, or other major cardiovascular events compared with medical therapy alone (HR for the PCI group, 1.05; 95% CI: 0.87–1.27; $P = .62$). In a small subgroup analysis, the effects of a depressed LVEF and burden of CAD, defined as an LVEF ≤50% and number of diseased coronary vessels, was further examined.[38] The risk of death was higher with low LVEF (HR, 1.86, 95% CI: 1.34–2.59; $P < .001$) and number of diseased coronary disease vessels (HR,1.45; 95% CI: 1.20–1.75; $P < .001$), but that risk was not decreased by PCI.

ISCHEMIA trial

Between 2012 and 2018 the ISCHEMIA trial enrolled 5179 patients with moderate or severe ischaemia to an initial invasive strategy (angiography and revascularization when feasible) and GDMT or to an initial conservative strategy of GDMT alone and angiography if medical therapy failed.[19] Patients with NYHA class III or IV heart failure or a LVEF less than 35% were excluded. The primary outcome was a composite

of death from cardiovascular causes, myocardial infarction, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest. In addition to LVEF <35%, key exclusion criteria included a recent acute coronary syndrome and unprotected left main stenosis of at least 50%. Patients were followed until June 2019 with a median duration of follow-up of 3.2 years. The trial did not find evidence that invasive management added to GDMT reduced the risk of the primary outcome (HR, 0.93; 95% CI: 0.80–1.08; $P = .34$). A small sub-analysis of the ISCHEMIA trial analysed 221 participants with left ventricular dysfunction, defined as LVEF ≥35% but <45% of whom 28 also had a history of HF prior to randomization.[39] These 'HF patients' were not carefully phenotyped at baseline with cardiac imaging or cardiac biomarkers. There was a lower rate of the primary outcome for participants with left ventricular dysfunction and history of HF randomized to the initial invasive strategy vs conservative strategy (17.2% vs 29.3%, difference in 4-year event rate −12.1%; 95% CI: −22.6, −1.6%), but no difference between strategies in patients without HF (13.0% vs 14.6%, difference in 4-year event rate −1.6%; 95% CI: −3.8%, 0.7%; *P*-interaction = .055). Surprisingly, there were more hospitalizations for heart failure with the invasive strategy as compared with the conservative strategy.

Critical appraisal of current trial evidence on revascularization in HFrEF

Over the past ten years, medical therapy has substantially improved the prognosis for HFrEF patients. Modelling analyses suggest that comprehensive implementation of these treatments can extend life expectancy by several years, underscoring the transformative impact of modern multidimensional HF and CAD care.

The selection of an optimal revascularization strategy in HFrEF requires clear recognition that CABG and PCI are fundamentally different therapeutic modalities rather than interchangeable alternatives. Each carries distinct mechanisms of benefit, risk determinants and prognostic implications that must be weighed within the context of advanced CAD and impaired ventricular function. Moreover, beyond specific cardiac and coronary condition, the success of revascularization is related to comorbidity burden, frailty and neurological status.

The incremental value of CABG in the context of contemporary medical therapy is unknown. Recent evidence could show that patients with HFrEF receiving medical therapy in the REVIVED-BCIS2 trial had better outcomes compared with those in STICHES (with or without CABG surgery).[28] Data from the Swedish Coronary Angiography and Angioplasty Registry indicate that PCI has become the revascularization strategy[40] of choice in CAD with almost three times more procedures than CABG.[41] Currently, no head-to-head comparison between CABG and PCI exists. The international STICH 3 initiative (NCT05761067) combines four separate international trials randomizing to CABG vs PCI in patients with ischaemic left ventricular dysfunction (including chronic HFrEF and NSTEMI with LVEF≤40%) with comparable inclusion criteria into a large international programme to demonstrate potential differences in mortality.[42,43]

Revascularization strategies in HFpEF

Very limited evidence is currently available from RCTs on the role of revascularization in HFpEF.[44] Importantly, no randomized trial has evaluated PCI or CABG specifically in HFpEF, and major CAD trials have included insufficient numbers of HFpEF patients to permit meaningful inference. Most information stems from small subsets of RCTs, not originally targeted to assess the HFpEF cohort, as well as from observational data which suffer from inherent methodological limitations and predate the novel pharmacological therapeutic options.[19,45–49] (Supplementary Table S1). In addition, the heterogeneous clinical presentation of HFpEF and the substantial overlap between symptoms of HF and myocardial ischaemia may complicate the identification of clinically relevant CAD in this population.[50] Compared with HFrEF, the presence, extent and functional significance of CAD are often less systematically investigated in HFpEF, while ischaemic symptoms may be underrecognized or attributed to HF itself. Furthermore, both epicardial CAD and coronary microvascular dysfunction may contribute to symptoms and adverse outcomes in HFpEF, further complicating patient phenotyping and selection for revascularization strategies.[51,52] Most RCT data on revascularization in HFpEF stem from subgroup analysis of the ISCHEMIA trial.[39] There appeared to be a possible benefit in favour of revascularization plus GDMT over GDMT alone in a small number of patients who presented a diagnosis of HF with a mid-range LVEF (HFmrEF); conversely, no benefit was found in the HFpEF cohort.[39] These patients were not carefully phenotyped by detailed cardiac imaging or cardiac biomarkers, preventing them from being properly diagnosed as having HF.

Based on the available evidence, it remains unclear whether patients with HFpEF should undergo revascularization and which revascularization procedure, PCI or CABG, should be preferred. Current ESC guidelines on HF, coronary revascularization and chronic coronary syndrome do not provide information or recommendations for HFpEF.[9–12] RCTs on the role of revascularization in HFpEF are lacking and until such evidence becomes available, multidisciplinary heart teams should be involved in decision-making. In addition, no evidence-based decisions about the role of CABG vs PCI in HFpEF can be made.

Revascularization strategies in acute HF and acute coronary syndrome

Amongst large registries of patients admitted with acute heart failure (AHF), up to 27% are reported to be complicated by acute coronary syndrome (ACS).[53–56] Conversely, large registries of patients with ACS report that 15% had pre-existing HF and 11% had new-onset HF, suggesting that the clinical course of ACS may be complicated by HF in about one in four patients.[57,58] Of the randomized trials including >1000 patients which assessed revascularization strategies for ACS, one did not report information on a prior history of HF,[59] some excluded those participants with a previous diagnosis of HF[60,61] and, in two other studies, only about 14% of patients enrolled had HF.[62,63]

Although AHF complicating ACS and ACS occurring in patients with chronic HF represent distinct clinical entities, their clinical presentation may substantially overlap in routine practice. Acute myocardial injury, troponin elevation, worsening congestion and ischaemic symptoms frequently coexist, making it challenging to distinguish acute coronary instability from acute decompensation of chronic HF in some patients.[64–66]

The presence of HF symptoms after an episode of ACS (ACS-HF) is a strong predictor of an adverse outcome.[67] ACS-HF increases the risk of worsening renal function, respiratory infection and death. The prognosis of patients with ACS-HF is worse than when either condition occurs alone.[68,69] In this setting, the extent and duration of ischaemia may contribute to progressive myocardial dysfunction, particularly in the presence of viable or hibernating myocardium that may still recover after timely revascularization.[70] For patients with new-onset HF, most ACS events are likely to be ST-segment elevation myocardial infarction (STEMI), whereas for patients with chronic HF, many ACS events will be non-ST-segment elevation myocardial infarction (NSTEMI).[71]

Many registries report lower rates of revascularization in patients with ACS-HF compared with those with ACS only.[72–77] In the GRACE (Global Registry of Acute Coronary Events) registry, only

20% of patients with ACS-HF were revascularized, vs 35% of those without ACS-HF. Patients with ACS-HF are older, have more co-morbidities and are more likely to present with NSTEMI.[58] There are no dedicated randomized controlled trials specifically designed to assess the role of revascularization for ACS-HF.[78] The 2023 ESC guidelines for the management of ACS recommend an immediate invasive strategy of angiography and revascularization when feasible and appropriate for patients with ACS-HF (level of recommendation: I; class of evidence: C).[65] In patients presenting with cardiogenic shock complicating ACS, early revascularization remains the cornerstone of management (I-C) and is associated with improved survival, although evidence specifically focused on patients with pre-existing HF remains limited.[65,79]

In six large, randomized trials enrolling patients with ACS, but not originally targeted to HF, a routine, early invasive strategy (early angiography followed by revascularization, depending on angiographic findings) was compared with a 'conservative' approach (angiography and subsequent revascularization only if medical therapy failed or substantial residual ischaemia was documented).[59–61,63,80,81] An early invasive approach was beneficial in the RITA-3,[59] TACTICS–TIMI 18,[61] and FRISC II[63] studies. However, it remains unclear whether an early invasive strategy improves HF outcomes, including mortality, for patients with ACS-HF. A reduction in mortality was only reported in the FRISC II trial and applied only to men.[63] Moreover, three of these RCTs[60,61,80] excluded patients with HF, two provided no information (both in terms of population recruited and on outcomes) on HF[59,81] and only one[63] enrolled a small (13% of the overall population) subset of participants with an LVEF <45%. Even less information is available for older patients who are under-represented in clinical trials of revascularization.[82] The SENIOR-RITA trial evaluated the efficacy of an invasive approach plus GDMT over GDMT alone in 1518 patients aged >75 years presenting with an ACS, of whom only 143 (9%) had a history of HF.[83] The invasive strategy reduced the risk of myocardial infarction but not hospitalization for HF, cardiovascular death or all-cause mortality.

Only modest evidence is currently available on the role of coronary revascularization, either by PCI or CABG, in patients with ACS-HF. Current recommendations rely only on experts' opinion, based on observational studies which provided very limited data on patients with HF, particularly for those with HFpEF.[65] Further randomized trials are warranted to determine the optimal management of ACS-HF, particularly for those with pulmonary congestion that can make invasive procedures challenging to deliver.

Medical therapy for ischaemic heart disease and heart failure

General advice about risk factors, prevention and treatment of HF with ischaemic heart disease has been outlined elsewhere.[10] Medical therapy for ischaemic heart disease with the aim of angina symptom control should be tailored to each patient's haemodynamic profile (blood pressure, heart rate), presence of HFpEF or HFrEF, potential drug interactions, preferences, and take into account the pathophysiological basis of myocardial ischaemia in each patient, as well as local availability of different drugs.[12,84,85] Currently, the empirical paradigm for the selection of anti-ischaemic medical therapy consists of a hierarchical, stepwise approach including first-line (beta-blockers, calcium-channel blockers) and second-line drugs (long-acting nitrates, nicorandil, ranolazine, ivabradine, trimetazidine).[12,86,87]

The decision to treat patients with HF with antiplatelet therapy remains largely influenced by the presence or absence of concomitant arterial disease and arterial intervention. The utility of oral anticoagulant and/or antiplatelet therapy has never been evaluated in an adequately powered dedicated clinical trial of HF patients in sinus rhythm. Two large RCTs, including mainly patients with HFrEF, as well as a meta-analysis of 24 RCTs, showed no benefit of statin treatment on CV mortality or stroke in patients with HFrEF.[88–91] Current ESC HF guidelines do not recommend the routine use of statins in patients with HF without other indications for their use (e.g. CAD).[10] Consistent evidence on the use of colchicine in HF with coronary multivessel disease is missing.

Regarding medical therapy for heart failure, remarkable advances have been made in treatment of HFrEF and HFpEF over the past few years, such as the introduction of angiotensin receptor–neprilysin inhibitor and sodium–glucose cotransporter 2 inhibitors, resulting in a substantial improvement of prognosis (Supplementary Figure S1 and Supplementary Figure S2).[10,92–94] Additionally, CRT, in combination with an ICD, decreased the risk of death and HF-related events in patients with HFrEF exhibiting a wide QRS complex in the ECG.[95,96] The COAPT and RESHAPE-HF2 trial showed that in symptomatic patients with HF and severe mitral regurgitation, transcatheter mitral edge-to-edge repair on top of GDMT led to a lower rates of HF hospitalization or cardiovascular death better health status than medical therapy alone.[97–99] Other measures, which might be considered, are pulmonary vein isolation ablation in case of concurrent atrial fibrillation, intravenous iron repletion for patients with iron deficiency, percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure and implantation of a left ventricular assist device in case of terminal HF.[100–105] Physical activity has been associated with significant reductions for both all-cause mortality or hospitalization in patients with HFrEF.[106] Among patients with clinically stable HFpEF and obesity, caloric restriction or aerobic exercise training has increased exercise capacity, and the effects may be additive.[107] More recently, glucagon-like peptide-1 receptor agonists, namely semaglutide and tirzepatide, have significantly improved quality of life, exercise capacity and markers of inflammation and cardiac function, vs placebo in randomized controlled trials in patients with HFpEF and obesity.[108,109]

Role of viability and ischaemia testing

Several imaging modalities have historically been deemed appropriate for ischaemia and viability assessment.[110] Myocardial contrast echocardiography, single-photon emission CT (SPECT) and late gadolinium enhancement cardiac magnetic resonance (CMR) all assess cellular integrity. PET assesses cellular metabolism, whereas dobutamine techniques assess contractile reserve. Current ESC guidelines on revascularization state that non-invasive stress imaging (CMR, echocardiography, SPECT or PET) may be considered for the evaluation of myocardial ischaemia and viability in patients with HF and CAD (suitable for coronary revascularization), before the decision on revascularization.[9] To this date, there are no data available to support regular assessment of myocardial viability or inducible ischaemia to guide revascularization decisions in HFrEF.[40] In the REVIVED-BCIS2 cohort the ischaemic burden as assessed by stress CMR was not associated with clinical outcomes.[111] Furthermore, no association between ischaemic burden, clinical outcomes, and randomized treatment assignment was seen. Other findings from the REVIVED-BCIS2 cohort suggest that the extent of dysfunctional yet viable myocardium was not associated with revascularization outcomes.[112]

Assessment of surgical risk and coronary complexity

An evaluation of surgical risk and coronary complexity in the context of local expertise is always mandatory for final decision-making regarding the revascularization modality. The Society of Thoracic Surgeons (STS)

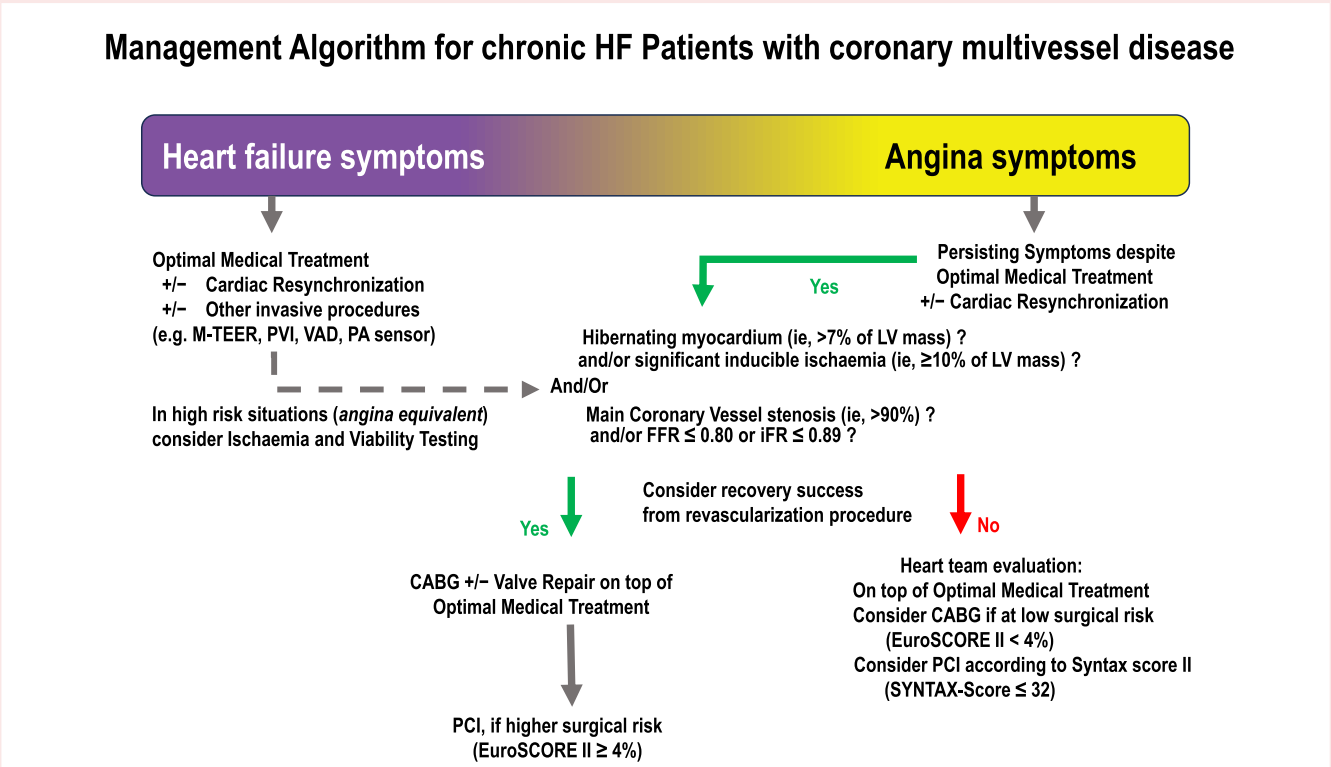

Figure 1 Suggested opinion-based management algorithm for chronic HF patients with coronary multivessel disease. CABG, coronary artery bypass graft; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; LV, left ventricular; PA, pulmonary arteries; PCI, percutaneous coronary intervention; PVI, pulmonary vein isolation; VAD, ventricular assist device. GDMT must be ensured for all HF patients. If the symptoms can be attributed to heart failure, further invasive measures should be discussed. If angina pectoris symptoms are prominent despite optimized medical therapy, revascularization using CABG including possible mitral valve repair should be considered if there is a significant ischaemia load and/or hibernating myocardium and haemodynamically effective stenosis of a main coronary vessel. PCI may be an alternative in situations with high surgical risk and for coronary lesions of lower complexity. Involving the cardiac team is important for an interdisciplinary, patient-oriented decision-making process

risk score and Euro-SCORE-2 are suitable to predict the 30-day postoperative mortality of CABG.[113] The STS and EuroSCORE II scores can be calculated using the online calculators at https://acsdriskcalc.research.sts.org/ and www.euroscore.org. A 30-day perioperative mortality <4% appears to be acceptable to prompt surgery. In patients deemed at higher risk for CABG (30-day perioperative mortality >4%), the SYNTAX score/SYNTAX score II is a useful tool for considering PCI by assessing coronary complexity.[114] The SYNTAX score is a score determined from the coronary angiogram and is calculated, among other things, from the number of affected vessel segments and adverse coronary lesion characteristics (e.g. length of the lesion, calcification). PCI is recommended in patients with lower coronary complexity (SYNTAX score ≤22) and may be considered in patients with an intermediate SYNTAX score (i.e. 23–32) after Heart Team discussion and decision.[9,12,37]

Suggested opinion-based management algorithm for chronic HF with (multivessel) coronary disease

Considering the currently available and partly conflicting evidence, clinicians face the task of reconciling inconsistent findings from RCTs. For the daily management of patients with HFpEF or HFrEF and multivessel coronary disease, we suggest the following opinion-based algorithm and synthesis of available major findings while we await new RCTs that evaluate the benefits of revascularization when added to novel therapies (*Figure 1*).[40,115,116] The primary task for clinicians is to identify if the patients' symptoms are more related to HF driven by myocardial dysfunction or related to angina:

In all patients with HF, establishing and optimizing GDMT is required. In cases where angina symptoms are present despite GDMT, involvement of the Heart Team and adhering to an interdisciplinary approach is advised. FFR-guided revascularization strategies should be pursued, however, acknowledging that the evidence on revascularization in HFrEF patients based on ischaemic burden is controversial and currently widely discussed.[29,30,111] In the presence of severe inducible ischaemia, surgical revascularization in addition to valve repair (if required) and continued GDMT is advised to improve prognosis. PCI is justifiable in high surgical risk situations or in case of coronary lesions with lower complexity even though evidence is largely lacking.[14,19] Similarly, coronary revascularization may also remain an option in presence of limited myocardial ischaemic burden but angina symptoms that are refractory to medical treatment. In this case, CABG is suggested to be the primary revascularization strategy and ischaemia-guided PCI is reserved to high-surgical risk patients in whom symptom control would become the main therapeutic target or in case of lower coronary complexity.[117,118]

When HF symptoms dominate despite GDMT, again involvement of the Heart Team and discussion of additional invasive procedures (e.g. mitral transcatheter edge-to-edge repair) seems prudent. When no typical angina symptoms are present or in selected cases of patients with HF (e.g. diabetics), an assessment of myocardial viability and ischaemia testing may be considered to further evaluate the extent of ischaemia, myocardial scar and viable hibernating myocardium for the consideration of potential revascularization strategies although evidence is controversial and an issue of on-going debate.[111,112,119]

Ongoing and future trials

The relationship between CAD and HF is complex and major knowledge gaps persist. A new generation of randomized clinical trials is now underway and will be pivotal in resolving uncertainties:

Two PCI-vs-medical-therapy trials are addressing whether percutaneous revascularization provides prognostic benefit in ischaemic LV dysfunction: RESTORE-PCI (NCT05828719) and IMPROVE-ICMP (NCT06930092). One CABG-vs-medical-therapy trial, MASS-4 HF (NCT04177190), is evaluating whether surgical revascularization retains survival benefit in the context of contemporary HF management.

The comparative strategy between CABG and PCI will be addressed by STICH3 (NCT05761067), an international consortium of nine harmonized trials enrolling patients with left ventricular dysfunction (including chronic HFrEF and NSTEMI with LVEF≤40%) and an indication for revascularization.

In HFpEF, where no randomized data currently exist, the first dedicated trial, REPRIEVED (ISRCTN12843546), will test whether PCI provides symptomatic and functional benefit in patients with demonstrable inducible ischaemia.

Finally, ongoing mechanistic and interventional trials, including CHIP-BCIS3 (NCT05436620) and PROTECT-4 (NCT05146082), will refine the role of mechanical circulatory support in high-risk PCI and may identify patient subpopulations in whom invasive strategies are safer or more effective. Overall, these studies will offer evidence that may support and inform future guideline development.

Summary and conclusion

The role of revascularization in patients with multivessel coronary disease and HF is limited.[14–16] Revascularization has not been shown to be superior to medical therapy for HF. Current efforts and resources should be directed to ensure optimal medical treatment for patients with chronic HF and CAD, as the first and most important measure to improve symptoms, wellbeing, and prognosis.[28]

Major gaps in knowledge

- Only two RCTs have investigated the role of revascularization in HFrEF—STICH (CABG vs medical therapy in HFrEF) and REVIVED-BCIS-2 (PCI vs medical therapy in HFrEF)
- No RCTs have investigated revascularization in HFpEF.
- Most available trial data (except BCIS-REVIVED-2) on revascularization in HF predate the medical advances in the treatment of HF achieved over the last 10 years.
- No RCTs comparing CABG vs PCI vs GDMT in patients with chronic HF and CAD available.
- No RCTs have investigated the role of revascularization in hospitalized or acute HF.
- Important populations (e.g. women, older individuals) are understudied.
- No trials have yet investigated the use of antiplatelet and anti-inflammatory therapies in HF and CAD.
- Symptom derived management algorithms for HF patients with multivessel coronary disease warrant further validation.

Supplementary data

Supplementary data are available at *European Journal of Heart Failure* online.

Declarations

Disclosure of Interest

A.B.-G. has participated in advisory boards and/or lectured for Abbott, AstraZeneca, Bayer, Boehringer-Ingelheim, Medtronic, Novartis, Roche Diagnostics, Vifor. B.H. has received lecture fees from Bristol Myers Squibb, Novartis, Daiichi Sankyo, Boehringer Ingelheim, Inari, and Pfizer for lectures on topics unrelated to the content of this article. D.J.M. reports grants from the National Heart, Lung, and Blood Institute, stock in Ablative Solutions, Inc., research funding to institution from Cleerly, Inc and Omada Health, and consultant fees from Regeneron, Scilex, and Johnson & Johnson. D.F.: Lecture of advisory board honoraria or grants from Abbott Laboratories, Astra-Zeneca, Bayer, Boehringer-Ingelheim, Eli-Lilly, Leo, Roche Diagnostics, outside the present work. E.B. declares speakers' fees from Abbott Vascular, Boston Scientific, Medtronic, Insight Lifetech. G.M. reports no disclosures. M.B. has received lecture fees from Abbott, Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cytokinetics, Edwards, Medtronic, Novartis, ReCor, Servier, and Vifor. M.B. is a member of the advisory boards of Amgen, Bayer, Boehringer Ingelheim, Cytokinetics, Edwards, Medtronic, Novartis, Pfizer, ReCor, Servier, and Vifor. He has received research funding from the German Research Foundation: DFG, SFB-TTR 219, S-01. M.M.: Consulting personal fees from Astra-Zeneca, Bayer, Boehringer Ingelheim, NovoNordisk and Roche Diagnostics and speaker's bureau from Boehringer Ingelheim in the last 3 years.

Data Availability

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Ethical Approval

Ethical Approval was not required.

Pre-registered Clinical Trial Number

None supplied.

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