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BCS Editorial

Coronary Revascularisation in Severe Ischaemic Cardiomyopathy - To Stent or Not to Stent?

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Take Home Messages

- Heart failure with reduced ejection fraction carries significant mortality and morbidity despite optimal medical and device therapy.
- Coronary artery disease is the most common cause of left ventricular dysfunction in Europe.
- To date, there is no evidence to suggest that revascularisation with percutaneous coronary intervention improves mortality, reduces heart failure hospitalisation or improves LV function in patients with severe left ventricular dysfunction and coronary artery disease.
- Even in patients with viable myocardium on stress testing, randomised controlled trials have not yet shown any prognostic benefit in percutaneous coronary intervention.

Introduction

Heart failure with reduced ejection fraction (HFrEF) still has significant morbidity and mortality despite the advancements in medical and device therapy (1). In the West, the most common cause of left ventricular dysfunction is coronary artery disease (CAD) (1). The management of patients with severe left ventricular systolic dysfunction (LVSD) and significant CAD without a clear indication for revascularisation, such as acute coronary syndrome (ACS) or angina, has divided cardiology opinion.

Current Guidance

Both national and international guidance differ due to the paucity in evidence for revascularisation for patients with HFrEF. This is summarised in **Table 1** below (1-3).

About the author

Avraj Virdi is a Cardiology Registrar working in South Wales and recently started his out of programme research at the University Hospital of Wales. He has a great interest in interventional cardiology and medical education which he aims to continue to pursue in the future. He is originally from Kenya and moved to the UK after completing his A levels to graduate from Cardiff University. Outside medicine, he has a great passion for global health and extreme poverty and he continues to carry out voluntary projects in Kenya.

Table 1: Current scientific recommendations for management of patients with heart failure and coronary artery disease

GUIDANCE	PCI	CABG
ESC (2021) (1)	PCI may be considered as alternative to CABG, based on Heart Team evaluation, considering coronary anatomy, comorbidities, and surgical risk (Class IIb)	CABG should be considered as the first-choice revascularisation strategy, in patients suitable for surgery, especially if they have diabetes and for those with multi-vessel disease (Class IIa)
ACC/AHA (2021) (2)	There is insufficient data to make recommendations for using PCI in this patient population	In patients with stable ischaemic heart disease and severe LVSD, CABG is recommended to improve survival (Class 1)
NICE (2018) (3)	Do not routinely offer coronary revascularisation to people who have heart failure with reduced ejection fraction and coronary artery disease (Class 3)	Do not routinely offer coronary revascularisation to people who have heart failure with reduced ejection fraction and coronary artery disease (Class 3)

ACC/AHA = American College of Cardiology/American Heart Association; CABG = coronary artery bypass graft; ESC = European Society of Cardiology; LVSD = left ventricular systolic dysfunction; NICE = National Institute for Health and Care Excellence; PCI = percutaneous coronary intervention.

Randomised Controlled Trials

Randomised controlled trials (RCTs) have investigated the benefit of revascularisation in patients with severe LVSD and CAD. These are summarised in **Table 2** (4-9). Limited data exists as previous studies looking at CABG versus PCI versus medical therapy for stable CAD have excluded patients with severe LVSD and left main disease.

The Surgical Treatment for Ischemic Heart Failure (STICH) trial investigated the role of CABG in the treatment of patients with CAD and severe LVSD (4). Patients were randomly assigned to medical therapy or medical therapy and CABG, with a median follow up of 56 months. The study showed no significant difference between the two groups in the primary outcome of the rate of death from any cause. The secondary outcomes which included death from any cause or hospitalisation from cardiovascular causes favoured CABG although CABG was associated with an early risk of death at 30 days (4). Furthermore, there was a significant improvement in quality of life with CABG compared to medical therapy over 36 months (10). Importantly, the STICH-Extended study at 10 years follow up favoured CABG in the primary outcome for all-cause mortality and the secondary outcomes for cardiovascular death and a composite of all-cause mortality or cardiovascular hospitalisations (5). Younger patients (≤54 years) compared to older patients (>67 years) had a greater benefit with CABG, as well as those patients with triple vessel disease (5). It is important to note however, that the STICH trial included younger patients (60 years) compared to 78 years as per the UK National Heart Failure Audit, therefore not representative of real-world populations. Also, sites were selected on surgical expertise hence had to demonstrate a 30-day mortality of ≤ 5% for patients similar to the STICH cohort (4).

The International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial investigated the effects of PCI compared to medical therapy in patients with stable CAD and moderate to severe ischaemia. However patients with severe LVSD (≤35%) were excluded. There was no significant difference between the two groups in the primary outcome of death from cardiovascular cause, myocardial infarction, or hospitalisation for unstable angina, heart failure or cardiac arrest. However, there was a reduction in power for the study as the sample size reduced from 8,000 to 5,179 (11).

A sub-group analysis of the ISCHEMIA trial compared patients with and without heart failure (defined as heart failure with reduced ejection fraction LVEF 35% to 45%, HF with preserved ejection fraction LVEF >45%) with at least moderate ischaemia.

Table 2: Randomised controlled trials assessing the outcome of revascularisation in left ventricular systolic dysfunction.

Trial	Cohort	Participants	Treatment	Primary Outcome	Median Follow Up	Results
STICH (2011) (4)	EF ≤35%, CAD amenable to CABG	1212	Medical therapy vs Medical therapy + CABG	Rate of death from any cause	56 months	No difference (P=0.12)
STICH-Extended (2016) (5)	EF ≤35%, CAD amenable to CABG	1212	Medical therapy vs Medical therapy + CABG	Rate of death from any cause	9.8 years	CABG superior in all-cause death (P=0.02 and NNT=14)
HEART (2014) (6) *	EF <35%, CAD, viable myocardium	138 (target 800)	Conservative vs Invasive (PCI or CABG)	All-cause mortality	59 months	No difference (p=0.63)
ISCHEMIA Substudy Analysis (2020) (7)	EF 35%-45% vs EF>45%, CAD, at least moderate ischemia	5174	Medical therapy vs Invasive	Death from CV causes; MI; hospitalisation	3.2 years	LVSD group had lower primary outcome with invasive strategy (P=0.055)
ISCHEMIA-Extended (2022) (8)	EF >35%, CAD, moderate or severe ischemia	5179	Medical therapy vs Invasive	Death from CV causes; MI; hospitalisation	5.7 years	No difference
REVIVED BCIS2 (2022) (9)	EF ≤35%, CAD amenable to PCI, myocardial viability	700	Medical therapy vs PCI + Medical therapy	Death from any cause or hospitalisation for heart failure	41 months	No difference (p=0.96)

STICH = Surgical Treatment for Ischaemic Heart Failure; HEART = The Heart Failure Revascularisation Trial; ISCHEMIA = International Study of Comparative Health Effectiveness with Medical and Invasive Approaches; REVIVED-BCIS2 = Revascularisation for Ischaemic Ventricular Dysfunction - British Cardiovascular Intervention Society.
** the study was discontinued prematurely due to slow recruitment.*

Patients with history of heart failure/LVSD assigned to the invasive strategy had a numerically lower rate of the primary outcome when compared to the conservative strategy (p=0.055), however it did not reach statistical significance and furthermore there was no effect for patients who did not have symptoms (7). While this analysis suggested a signal for benefit of coronary revascularisation in patients with heart failure and at least moderate ischaemia, further randomised controlled trials are needed to confirm these findings.

The Revascularisation for Ischaemic Ventricular Dysfunction - British Cardiovascular Intervention Society (REVIVED-BCIS 2) trial is the most recent trial published assessing whether revascularisation with PCI can improve event-free survival and left ventricular function in patients with severe ischaemic LVSD as compared to optimal medical therapy. This trial showed no significant difference between the two groups in the primary outcome of death from any cause or hospitalisation from heart failure. The secondary outcomes of LVEF, quality of life scores and NYHA class also showed no significant difference (9).

Discussion

Evidence for PCI

There is no evidence that PCI has any prognostic benefit for patients with severe LVSD and stable CAD. This is illustrated by the recently published REVIVED-BCIS2, the HEART trial and the sub-group analysis of the ISCHEMIA study (6,7,9). This questions the concept of myocardial hibernation which was coined in the 1980s (12). REVIVED-BCIS2 was a well-designed and adequately powered study and importantly included older patients (aged over 70 years) and those with left main disease, therefore a more representative patient population. However it showed no benefit with PCI on mortality, hospitalisation and LVEF. There was improvement in quality of life at 6 and 12 months, but not at 24 months (9).

The REVIVED-BCIS2 trial used a BCIS Jeopardy Score ≥6 to define extensive CAD (9). Importantly, this has a sensitivity of 76% for diagnosing ischaemic cardiomyopathy, hence highlighting the challenges in differentiating between ischaemic cardiomyopathy and bystander CAD (13). Further data analysis is needed to clarify the PCI territory and whether this myocardium was viable. Finally, the 10% cross-over of patients from the medical therapy arm to PCI may have affected the results. The sub-analyses are eagerly awaited.

Evidence for CABG

The STICH-extended trial suggested that CABG is beneficial although for only a highly specific patient group: younger patients (≤54 years) and those with triple vessel disease (5). However it took 10 years to show benefit largely because of the early mortality in the CABG arm. Furthermore, medical therapy did not include more recent therapies such as sodium glucose cotransporter-2 inhibitors and Sacubitril/Valsartan, which have shown to improve cardiovascular outcomes (1).

Evidence for viability testing

There is no role for viability studies in managing this patient group as per the STICH and REVIVED-BCIS2 studies (4,9). The STICH viability sub-study assessed 601 patients, and showed no difference in mortality in either the medical therapy group with viability or the CABG group with viability (p=0.21) (14). This is also shown in the PARR-2 trial, where 430 patients with severe LVSD and suspected CAD were randomised to either FDG-PET assisted management or standard care. Again, there was no difference in the primary outcome of cardiac death, myocardial infarction or hospitalisation (p=0.16) (15).

Conclusions

There is no current evidence supporting revascularisation with PCI in patients with severe LVSD and CAD without angina or ACS. These patients should be managed with guideline directed medical therapy which is supported by the available evidence. On the other hand, CABG may be beneficial at 10 year follow up for younger patients and those with triple vessel disease.

Declarations

None

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