Review

Coronary revascularization in patients with left ventricle systolic dysfunction, current challenges and clinical outcomes

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Abstract

The effects of coronary revascularization in patients with left ventricle systolic dysfunction (LVSD) are not well studied. The decision about revascularization and its timing remain challenging, not only related to procedural risk, but also linked to other several limitations including assessment of ischemia, viability, and ability to predict LV recovery. The role of viability as a prognostic marker for patients with LVSD and its use as a therapeutic target remains debatable. In this article, we will review the role of LVSD in patients undergoing coronary revascularization alongside the role of ischemia and viability assessment. We will provide a review of the literature on the outcomes of coronary revascularization, both surgically and percutaneously, in patients with LVSD.

Keywords: Left ventricle systolic dysfunction; Percutaneous coronary intervention; Coronary artery bypass graft; Viability; Ischemia

1. Introduction

The key goal of performing coronary revascularization is to reduce anginal symptom, decrease the burden of ischemic myocardium and to improve patients' clinical outcomes [1]. Over the last two decades, randomized clinical trials helped addressing those aims cementing the role of coronary revascularization particularly in patients with coronary artery disease and preserved left ventricle (LV) systolic function. Accordingly, a pre-specified secondary analysis from the Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina (ORBITA) trial, percutaneous coronary intervention (PCI) resulted in a higher proportion of patient-reported freedom of angina compared to placebo [2]. The benefits were also extended to the elderly population in the Trial of Invasive versus Medical therapy in Elderly patients (TIME) trial, whereby PCI led to a decrease in symptomatic burden and improved quality of life [3]. In the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) nuclear sub-study, coronary revascularization reduced ischemia burden on serial myocardial perfusion scans. This effect was more evident in patients with moderate to severe myocardial ischemia at outset [4]. Reduction in major cardiac events was reported following coronary revascularization in specific subsets of patients. The Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) II trial reported a borderline reduction in myocardial infarction in patients who underwent physiology-guided coronary revascularization when compared to medical therapy [5,6]. Additionally,

patients with significant left main lesions or multivessel diseases, coronary revascularization may also derive prognostic benefit [7]. Furthermore, landmark studies help better understanding the optimal mode of coronary revascularization (stents versus surgery) based on the anatomical complexity in the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX), and the Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) studies or the disease substrate such as diabetes in the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial [8–10].

Despite the benefits of coronary revascularization, patients with significant left ventricular systolic dysfunction (LVSD) remain clinically challenging. Questions remain over viability quantification, reliability of ischemia assessment methods together with the uncertainty of achieving benefits from revascularization. The International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) trial highlighted lower cardiac events in patients with at least moderate documented ischemia, on imaging tests or severe ischemia on exercise tests, and heart failure (HF) or left ventricular dysfunction (ejection fraction 35–45%) in the invasive group when compared to the conservative group [11]. On the other hand, in patients presenting with at least moderate ischemia but without heart failure symptoms or LVSD, there was no statistical difference in major cardiac events between the invasive (both coronary artery bypass graft, CABG, and PCI)

and conservative treatment [11]. The recent European Society of Cardiology guidelines for heart failure highlighted the limited data on the benefits of coronary revascularization in patients with LVSD [12]. Nonetheless, revascularization should be considered to relieve anginal symptoms in patients with LVSD and may be considered to improve the long-term outcome. Additionally, CABG should be considered as the first revascularization choice, particularly in diabetic patients or those with multivessel disease. PCI remains an alternative revascularization strategy guided by the coronary anatomy [12].

The current review provides an overview of contemporary studies looking at the role of LV systolic dysfunction and the impact of revascularization when added to optimal medical treatment in these patients.

2. Significance of left ventricular systolic dysfunction in patients with CAD

Coronary artery disease (CAD) remains the main etiology for left ventricular systolic dysfunction (LVSD) and heart failure in developed countries. The prevalence of patients with heart failure is about 2.5% of the population with more than half having reduced ejection fraction [13]. Importantly, the incidence of LVSD in patients with CAD has significantly increased over the last two decades due to the improved survival. A multicentre observational study showed a persistently impaired LVSD (ejection fraction less than 50%) in approximately 75% of patients who had LVSD after acute myocardial infarction [14]. Furthermore, LVSD secondary to CAD is associated with poor mortality and morbidity with a stepwise increase in the risk of malignant arrhythmia and heart failure proportionate to the reduction in ejection fraction [15,16]. Similar observations were evident in the ISCHEMIA trial and the primary endpoint of cardiovascular death, nonfatal MI, hospitalization or cardiac arrest over 4 years was higher in patients with heart failure or LVSD ($\leq$35%) in comparison to patients without heart failure symptoms or LVSD (22.7% versus 12.3%, respectively) [11].

The pathophysiology of ischemic myocardium in patients with LVSD is multifactorial. Whilst epicardial coronary disease remains the main culprit, other mechanisms are evident and contribute to symptoms burden and worse outcomes. Several studies showed that coronary flow reserve is significantly reduced in patients with cardiomyopathy [17]. Microvascular dysfunction, impaired coronary blood flow reserve, and raised filling pressure result in myocardial hypoperfusion and coronary ischemia [18]. Additionally, mitochondrial dysfunction is also present in impaired LV systolic function and plays a crucial role in the pathophysiology of myocardial ischemia. The switch from aerobic to anaerobic metabolism and preferential utilization of carbohydrates coupled with decreased fatty acid metabolism contribute to ischemic etiology in LVSD [19]. Lastly, any reason for impaired oxygen delivery process such as anaemia

would exacerbate the ischemic component in patients with LVSD (Fig. 1) [20].

The main treatment of heart failure with reduced ejection fraction is medical therapy and cardiac resynchronization therapy. However, other non-pharmacology therapies such as coronary bypass graft surgery, surgical ventricular reconstruction, less invasive ventricular reconstruction, and PCI, have a role as adjunctive treatment for improving symptoms or prognosis [21]. Importantly, coronary revascularization in the setting of LVSD increases procedural risk and thereby contributes to the clinical challenge of selecting patients in whom coronary revascularization will provide symptomatic and/or prognostic benefits.

In a multicentre study of 184 patients who underwent high risk PCI and severe LVSD (EF less than 35%), 51% of patients showed a significant increase in their EF (absolute increase was 13.2%) alongside significant reduction in end diastolic volume from 137.7 to 106.6 mL. Additionally, this reverse LV remodelling was associated with significant reduction in major cardiac events and reduction of New York Heart Association class [22]. A more recent study linked ischemia assessment in patients with newly diagnosed LVSD and improved clinical outcomes [23]. This study highlighted two important points. Firstly, the underuse of ischemia assessment in this group, only 40% (3859 of 9625) patients with newly diagnosed LVSD have undergone ischemia assessment. Secondly, investigations for ischemia in newly diagnosed heart failure patients could improve the long- term clinical outcome given the significant reduction in all-cause mortality in the investigated group compared to those without ischemia evaluation (adjusted hazard ratio, HR, 0.54; 95% CI, 0.47 to 0.61) [23].

3. Ischemia assessment in LVSD

Although ischemia-guided revascularization provides prognostic benefits in stable coronary syndrome, the reliability and quantification of ischemia in patients with LVSD is less well established. Clinical assessment of anginal symptoms could be masked by patients' poor functional capacity due to heart failure. Consequently, exercise-based investigations such as ECG, and exercise-based echocardiography will likely be false negative and underestimate the burden of ischemia.

Moreover, a study evaluating 20 coronary arteries in 17 patients with 528 analysed cardiac cycles showed that functional flow reserve (FFR) was positively correlated to end diastolic pressure and this relationship was more significant in obstructed lesions [24]. This study finding suggests that physiological assessment in patients with LVSD, who are likely to have higher end diastolic pressure, could be less accurate and may underestimate lesion functional severity [24]. Furthermore, a post hoc analysis from the FAME trial showed that the FFR value was relatively higher in LVSD patients who had coronary artery stenosis more than 90% (0.55 vs. 0.50, p = 0.02). This finding was not
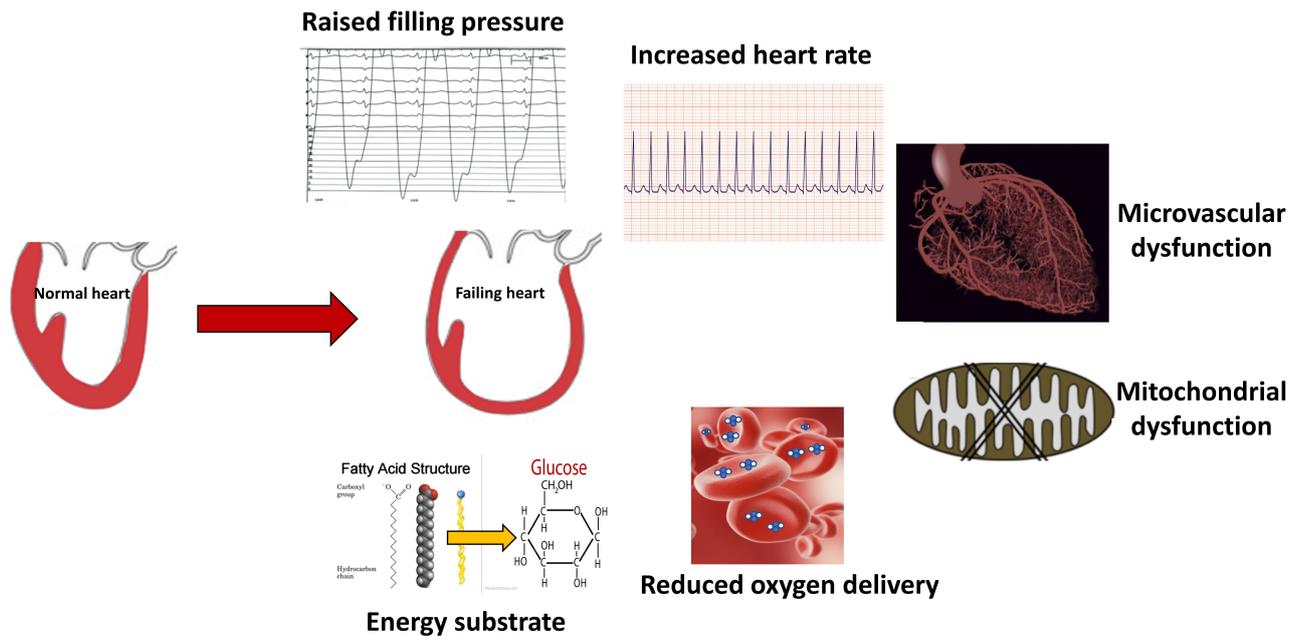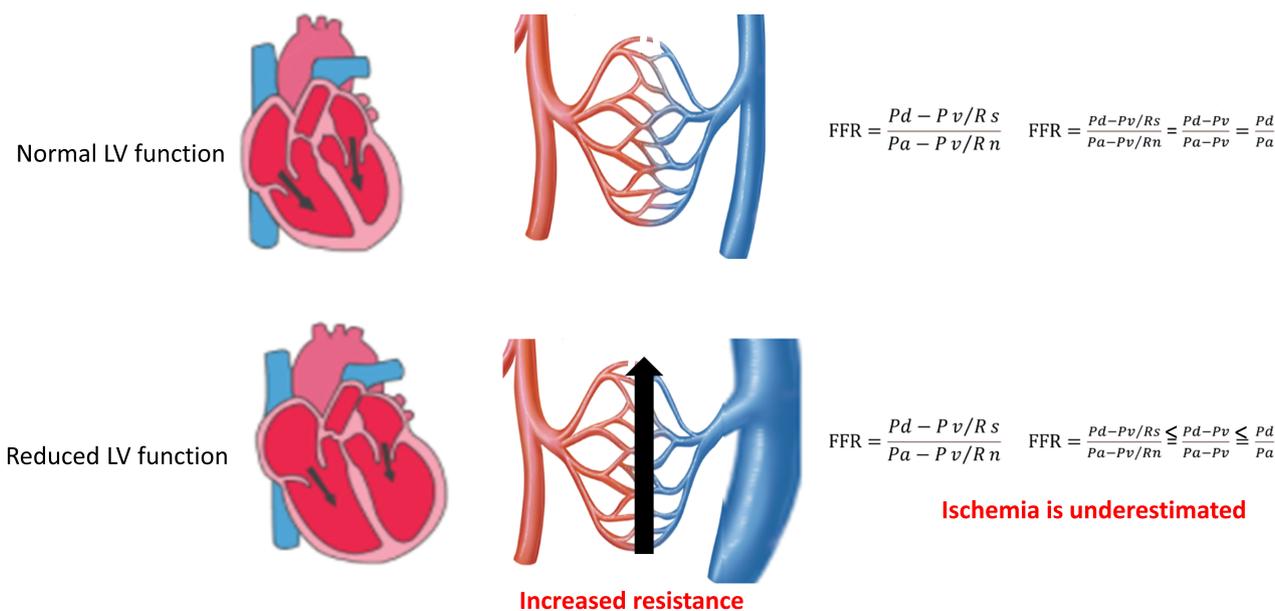
Fig. 1. Pathophysiology of myocardial ischemia in patients with LVSD. Additional mechanisms of myocardial ischemia, on top of coronary artery disease, include raised filling pressure, microvascular dysfunction, mitochondrial dysfunction, energy substrate metabolism, and reduction in oxygen delivery.

evident in patients with lesser degrees of stenosis. Importantly, this discrepancy does not have significant clinical impact, particularly since patients with very severe coronary stenoses had positive FFR, irrespective of the degree of LVSD. Moreover, FFR guided angioplasty remains a superior strategy in comparison to angiographic based PCI in patients with LVSD in the FAME trial [25]. In a retrospective study on 1299 patients with LVSD (EF ≤50%), FFR guided revascularization in 433 patients showed lower 5-year all causes mortality (22% vs. 31%. HR 0.64, 95% CI (0.51 to 0.81); $p < 0.001$) and fewer major cardiac event rates (40% vs. 46%, HR 0.81, 95% CI (0.67 to 0.97); $p = 0.019$) when compared to matched 866 patients managed with angiographically guided angioplasty [19]. The role of resting physiological indices has been less studied in the setting of LVSD. In a single centre non-randomized study conducted on 65 patients with intermediate coronary lesions, patients were divided based on left ventricular end diastolic pressure (LVEDP) cut-off of 15 mmHg [26]. A discordant result of FFR and instantaneous free wave ratio was more frequently recorded among patients with elevated compared to normal LVEDP (42.8% vs. 6.7%, $p = 0.001$) [20]. Whilst FFR is defined as the ratio of distal over proximal hyperemic flow in relation to the coronary lesion, in clinical practice mean proximal and distal arterial pressure is used as a surrogate of flow. To allow for this replacement, two assumption are made. Firstly, coronary resistance would be minimised in response to adenosine and, secondly, venous pressure is close to zero and would not contribute to the pressure difference when using Ohm's law (Fig. 2) [27]. In patients

with LVSD, elevated end diastolic pressure could alter myocardial bed resistance even during maximal hyperaemia. Additionally, the backward pressure from the left ventricular pressure to right atrium would increase venous pressure and can no longer be considered negligible as originally assumed when measuring FFR (Fig. 2). To the best of our knowledge, there are no randomized clinical trial to assess the outcome of physiology guided coronary revascularization in patients with LVSD and elevated LVEDP.

4. The role of viability in revascularization in LVSD

Viability assessment is part of the clinical work up prior to revascularization in patients with LVSD as the presence of viable myocardium is more likely to lead to symptomatic and prognostic benefits following successful revascularization. It is important to note that viable myocardium in the presence of impaired left ventricular dysfunction may still exist despite contractile dysfunction either due to hibernating or stunned myocardium. Hibernating myocardium is defined as hypo-contractile myocardium due to persistently low blood supply while stunned myocardium is a hypo-contractile myocardium due to transient ischemia followed by reperfusion and that usually exists for hours or days before recovery [28,29]. The most widely used tests for myocardial viability assessment are single photon emission computed tomography (SPECT), positron emission tomography (PET), cardiac magnetic resonance imaging (CMRI) and dobutamine stress echocardiography [29]. Viability assessment using SPECT and PET relies on the cellular and

Normal LV function

$$\text{FFR} = \frac{Pd - Pv/Rs}{Pa - Pv/Rn}$$

$$\text{FFR} = \frac{Pd - Pv/Rs}{Pa - Pv/Rn} = \frac{Pd - Pv}{Pa - Pv} = \frac{Pd}{Pa}$$

Reduced LV function

$$\text{FFR} = \frac{Pd - Pv/Rs}{Pa - Pv/Rn}$$

$$\text{FFR} = \frac{Pd - Pv/Rs}{Pa - Pv/Rn} \lesssim \frac{Pd - Pv}{Pa - Pv} \lesssim \frac{Pd}{Pa}$$

Ischemia is underestimated

Increased resistance

Fig. 2. Fractional Flow Reserve measurement in LVSD. Top panel, derivation of FFR from mean pressure using Ohm's law. Bottom panel, venous congestion in the setting of LVSD leads to increase resistance and underestimation of ischemia. The ratio of distal over proximal mean pressure would likely be higher than true FFR. Pa, aortic pressure; Pd, pressure distally to the stenotic lesion; R, resistance through myocardial vascular bed; Pv, venous pressure. Rs, resistance of myocardial vascular bed in stenotic vessel and Rn; resistance of myocardial vascular bed in theoretically normal vessel.

metabolic functions of the cardiac myocytes, respectively [29]. Mismatch pattern in PET scan (preserved uptake with reduced perfusion) is related to higher probability of myocardial functional recovery [30]. Stress echocardiography indicates viable myocardium when the baseline hypokinetic segments improve with dobutamine infusion followed by subsequent hypokinesia at the end - the so called biphasic response [29]. The biphasic response in dobutamine stress echo is a very good predictor of myocardial recovery in LVSD after revascularization [31]. The main advantage of CMRI in viability assessment is demonstrating both anatomical contractile recovery akin to stress echocardiography and tissue characterization with delayed contrast enhancement. CMRI assessment has also great resolution in comparison to other techniques, however, the presence of late gadolinium enhancement (LGE) does not necessitate non-viable myocardium, particularly in the early days after myocardial infarction [32,33]. Emerging technique such as T1 mapping would have advantages over LGE in predicting infarct characteristics and establishing viability in the early stages following MI without the need for contrast agents [32,34].

In a study to compare imaging modalities, 41 patients underwent myocardial contrast echocardiography, low dose dobutamine stress and nuclear imaging (SPECT and PET scans) [35]. The accuracy of each test to predict improvement in myocardial function was demonstrated as 86% sensitivity and 43% specificity, 90% sensitivity and 44% speci-

ficity, 83% sensitivity and 76% specificity respectively [35]. In a study comparing CMRI and nuclear imaging in 29 patients with ischemic cardiomyopathy, CMRI was found to be superior to nuclear imaging in identifying non-viable segments which were less likely to recover after revascularization [36].

It is evident that viability assessment, regardless of the used tool, is a clinically useful strategy to assess the possibility of myocardial recovery after revascularization. However, the more pertinent question is whether myocardial recovery after coronary revascularization adds incremental benefits to patients' long-term outcomes. In a meta-analysis by Allman *et al*. [37] of 3088 CAD patients with LVSD (ejection fraction <40%), there was a significant reduction in mortality only in patients with viable myocardium who underwent revascularization.

The annual mortality rate was 3.2% in the revascularized patients compared with 16% in the medically managed group ($p < 0.0001$). However, the mortality rates in the revascularized and the medically managed groups were comparable in patients with non-viable myocardium (7.7% and 6.2%, respectively) [37]. This meta-analysis highlighted the importance of viability assessment when selecting patients for revascularization in the presence of LVSD [37].

In contrast, in the viability sub-study of the Surgical Treatment for Ischemic Heart failure (STICH) trial, 601 of 1212 randomised patients had their viability assessment

Table 1. 10 year all-causes mortality in viability sub-study of the STICH trial [32].

Whole cohort of patients who underwent viability assessment	CABG and medical treatment group	Medical treatment only group	HR (95% CI)
	(n = 298)	(n = 303)	
All-cause mortality	182 (61%)	209 (69%)	0.73 (0.60–0.90)
Patients with viable myocardium	CABG and Medical treatment group	Medical treatment only group	
	(n = 244)	(n = 243)	
All-cause mortality	144 (59.6%)	169 (69.8%)	0.70 (0.56–0.88)
Patients with non-viable myocardium	CABG and Medical treatment group	Medical treatment only group	
	(n = 54)	(n = 60)	
All-cause mortality	38 (72.3%)	40 (67.2%)	0.81 (0.50–1.31)
p value (for interaction)	0.34		

with either SPECT or dobutamine stress echocardiography before revascularization. An interaction between long term outcomes and viability was evaluated in patients who underwent CABG plus medical therapy or medical therapy alone (Table 1, Ref. [32]) [38]. Regardless of the treatment strategy, patients with viable myocardium had significantly lower mortality rate compared to patients without viable myocardium (37% versus 51%; HR 0.64, 95% CI 0.48 to 0.86) [38] (Table 1).

At 10-year follow up, there was a significant reduction in mortality in patients who underwent CABG compared to medical treatment in the whole cohort [61% (182 of 298) versus 69% (209 of 303), HR 0.73, 95% CI 0.6 to 0.9]. Importantly, there was no significant interaction between the presence or absence of viability and effect of CABG plus medical therapy over medical therapy alone on long term survival ($p = 0.34$ for interaction) (Table 1). In summary, CABG had incremental benefits when added to medical therapy in both viable and non-viable myocardium and the magnitude of benefit was comparable in those two settings. On the other hand, an increase in EF was only evident in patients with viability irrespective of the assigned treatment, CABG plus medical or medical therapy only. However, this LV systolic function improvement did not translate into significant reduction in mortality risk [39] (Table 1). Although there are not enough data in the literature to support viability as a predictor of better outcome in patients undergoing coronary revascularization, viability assessment is helpful in clinical decision making and prognosis assessment. The STICH trial did not randomize patients stratified by viability, additionally, viability was assessed using two different methods. This highlights the need for more randomized clinical trials to answer the question of whether patients with viable myocardium would benefit from coronary revascularization, when added to medical therapy.

5. Benefits from revascularization over medical therapy alone in LV systolic dysfunction

Accumulating data support the role of coronary revascularization in patients with LVSD, with a strong signal suggesting incremental benefits from coronary revasculariza-

tion in patients with LVSD (Table 2, Ref [38–52]). In a randomised clinical trial of 138 patients with LVSD and viable myocardium, there were no difference in the primary composite clinical outcomes but re-hospitalization with heart failure following CABG was significantly lower when compared to conservative treatment [53]. A meta-analysis of 21 studies including 16191 patients highlighted mortality reduction in the group treated with revascularization, either surgically (HR, 0.66; 95% CI, 0.61 to 0.72; $p < 0.001$) or percutaneously (HR, 0.73; 95% CI, 0.62 to 0.85; $p < 0.001$), when compared to medical treatment alone. CABG showed lower mortality rate when compared to PCI (HR 0.82, 95% CI 0.75 to 0.9) [40].

In the STICH trial, patients randomized to CABG plus medical treatment had a significant reduction in all-cause mortality compared to medical treatment alone [359 of 610 (59%) versus 398 of 602 (66%), $p = 0.004$]. Similarly, CABG was associated with a reduction in cardiovascular mortality (247 of 610 (40%) versus 297 of 602 (49%), $p = 0.002$). A significant reduction in all-cause mortality and re-hospitalization was also observed in patients who underwent CABG compared to medical treatment alone, 77% and 87%, respectively [41]. The benefits from surgical revascularization was consistent across age in reducing cardiovascular mortality ($P_{interaction} = 0.307$) while that beneficial effect on all-cause mortality decreased with older age ($P_{interaction} = 0.062$) [41].

Furthermore, data from the ISCHEMIA trial showed that invasive management incurred lower rate of cardiac events in patients who had previous history of heart failure or moderate to severe LVSD (35–45%) when compared to conservative treatment (17.2% versus 29.3%) [11]. Similar results were seen for other endpoints, including cardiovascular death, or myocardial infarction and readmission with heart failure [11]. These benefits were more evident in the subgroup of patients with LVSD. Nonetheless, this was a subgroup analysis and included only 398 patients representing 7.7% of the whole ISCHEMIA trial cohort [11].

Regardless of the underlying mechanism (stunning versus hibernating), successful revascularization has the potential to improve LV systolic dysfunction and subsequently clinical outcomes. Importantly, change in systolic

Table 2. Result of studies comparing PCI, CABG, and medical treatment on CAD with LVSD.

Name of trial	Year of publication	Design	Number of patients	Comparison	End points	Outcome
STICH [38]	2011	RCT	601	Viable versus Non-viable	Mortality	HR 0.64, 95% CI (0.48–0.86)
						CABG versus Medical
						In whole sample
						HR 0.73, 95% CI (0.6–0.9)
STICH [39]	2019	RCT	601	CABG versus medical	Mortality	In viable myocardial
						HR 0.7, 95% CI (0.56–0.88)
						Non-viable myocardium
						HR 0.81 (0.5–0.1.31), p value (for interaction = 0.34)
STICH [41]	2016	RCT	1212	CABG versus Medical	All-cause mortality	59% versus 66%, p value = 0.004
					Cardiovasc mortality	40% versus 49%, p value = 0.002
Meta-analysis Wolff *et al.* [40]	2017	21 studies	16,191	CABG versus PCI (13 registries + 2 RCT)	Mortality	HR 0.82, 95% CI (0.75 to 0.9), p value < 0.001
				CABG versus MT (6 studies + 2 RCT)		HR, 0.66; 95% CI (0.61 to 0.72); $p < 0.001$
				PCI versus MT 2 registries		HR, 0.73; 95% CI (0.62 to 0.85); $p < 0.001$
Meta-analysis Pei *et al.* [42]				CABG versus PCI	All-causes mortality	HR 0.7, 95% CI (0.61–0.8), <0.01
				16 registries	Cardiovascular mortality	HR 0.6, 95% CI (0.43–0.85), <0.01
	2020	18 studies	11,686	2 RCT	MI	HR 0.51, 95% CI (0.36–0.72), <0.01
					Repeated revascularization	HR 0.32, 95% CI (0.23–047), <0.01
					30-day stroke	HR 2.88, 95% CI (1.07–7.77), 0.04
CREDO-Kyoto PCI/CABG Registry Cohort-2 [43]	2014	Registry	908	PCI versus CABG In EF <50%	All-cause mortality	HR 1.49 (1.04–2.14), 0.03
Meta-analysis Cui *et al.* [44]	2018	8 Registries	10,268	PCI versus CABG	All-cause mortality	HR 1.36, 95% CI (1.16–1.6)
					Repeated RV	HR 4.95, 95% CI (3.28–7.46)
Meta-analysis Xiao *et al.* [45]	2018	11 registries + 1 small RCT	9248	CABG versus PCI	All-cause mortality	HR 0.83, 95% CI (0.76–0.9), <0.001
Meta-analysis Kang *et al.* [46]	2017	3 Registries	911	CABG versus PCI	All cause Mortality	HR 0.43, 95% CI (0.31–0.61), <0.001
Meta-analysis Kunadian *et al.* [47]	2012	19 Studies	4766	PCI versus CABG	All-cause Mortality	Relative risk 0.98, 95% CI (0.8–1.2), 0.83
Meta-analysis Bangalore *et al.* [48]	2016	Registry	4616	PCI versus CABG	All cause Mortality	HR 1.01, 95% CI (0.81–1.28), 0.91
APPOO *et al.* [49]	2004	Registry	2169	CABG versus medical	Mortality	HR 0.56 (0.409–0.774), <0.001
Hannan *et al.* [50]	2008	Registry	2673	CABG versus PCI	Mortality	HR 0.77 (0.59–1.002), 0.052
LaBarbera *et al.* [51]	2012	Registry		CABG versus medical	Mortality	HR 0.49 (0.4–0.59), <0.001
LaBarbera *et al.* [51]	2012	Registry	1345	CABG versus PCI	Mortality	HR 0.68 (0.56–0.83), <0.001
LaBarbera *et al.* [51]	2012	Registry		PCI versus medical	Mortality	HR 0.73 (0.62–0.85), <0.001
Nagendran *et al.* [52]	2013	Registry	1436	CABG versus PCI	Mortality	HR 0.91 (0.78–1.05), 0.194

function, in response to surgical revascularization, was not always associated with reduction in mortality suggesting additional mechanisms for improved outcomes following surgical revascularization. One plausible mechanism is the protective role of bypass graft against future fatal MI. The presence of non-viable myocardium as a binary classification on non-invasive testing does not eliminate areas of viable myocardium. Surgical revascularization may prevent those areas from future ischemic insults and further deterioration leading to subsequent events including ventricular arrhythmias, progressive heart failure, and cardiac death.

There is no published randomised clinical trial assessing the role of PCI over medical treatment in patients with LVSD. The REVIVED BCIS2 trial is a randomised prospective multi-center trial, enrolling patients with ischemic cardiomyopathy (ejection fraction ≤35% and extensive coronary artery disease with at least 4 viable segments). Patients are randomised into PCI or medical treatment and followed for at least 2 years. The result of this trial is still waited [54].

6. Percutaneous versus surgical revascularization in LVSD

Numerous studies compared the effect of PCI and CABG in patients with CAD and LVSD with a signal to suggest better outcomes with CABG over PCI (Table 2). A large retrospective multicentre study of 12113 patients with CAD and LVSD showed higher mortality and all major cardiac events in PCI in comparison to CABG over a 5.2-year median follow up [55]. A further meta-analysis of 18 studies including 11686 patients demonstrated CABG resulted in lower long-term mortality (HR 0.7, 95% CI 0.61 to 0.8, $p < 0.01$), lower cardiovascular death HR 0.6, 95% CI 0.43 to 0.85, $p < 0.01$, lower myocardial infarction HR 0.51, 95% CI 0.36 to 0.72, $p < 0.01$, less repeated revascularization (HR 0.32, 95% CI 0.23 to 0.47, $p < 0.01$) but higher 30 day stroke HR 2.88, 95% CI 1.07 to 7.77, $p = 0.04$, in comparison to PCI [42]. A similar conclusion of lower mortality associated with CABG (HR 0.82, 95% CI 0.75 to 0.9) in comparison to PCI was demonstrated in other meta-analysis [40]. Similarly, the survival benefit of CABG over PCI was demonstrated in a registry of patients with CAD and less impaired left ventricular systolic function, i.e., (EF ≤50%) [43]. The survival benefit with CABG over PCI was also evident in studies using drug eluting stents [44–46].

Other studies have reported conflicting findings. A meta-analysis of 19 studies reported that in-hospital and one-year outcomes with PCI were comparable to CABG in patients with LVSD [47]. In a registry of 4616 patients with multivessel CAD and severe left ventricular systolic dysfunction, both CABG and PCI showed similar long-term mortality (HR 1.01, 95% CI 0.81 to 1.28), $p = 0.91$. However, PCI had higher risk of myocardial infarction and repeated revascularization while stroke was higher in patients undergoing CABG [48]. This inconsistency and conflicting results of meta-analyses comparing outcomes of PCI versus CABG in patients with LVSD may be related to the observational nature of the included studies and the use of different generations of stents in the PCI group. That highlights the need for a large randomized clinical trial to answer the question about the recommended revascularization strategy in LVSD patients, particularly with the new generation of drug eluting stents and contemporary PCI practice with physiology-guided, imaging optimized and successful chronic total occlusion strategies to achieve complete revascularization. Interestingly, complete revascularization in patients with multivessel disease and left ventricular systolic dysfunction demonstrated lower major cardiac events in comparison to incomplete revascularization [56]. This is an important finding that could improve outcomes in patients with LVSD.

7. Conclusions

Improved medical and device therapy has led to increased survival of patients with LVSD secondary to CAD but the optimal management of these patients remains challenging. Assessing and quantifying ischemia and viability are relevant and provide prognostic markers in this high-risk group. Several studies show that in patients selected on the basis of myocardial viability, coronary revascularization, particularly with CABG, provides additional benefits over medical therapy alone. Data on the role of PCI are limited and future studies will help understand its role in this patient population.

Major strides have been made in defining this patient population and medical, device based and surgical strategies have seen a marked improvement in both quantity and quality of life. Further ongoing studies will help to address identification of parameters that can better predict those patients who can benefit from coronary artery revascularization.

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