ORIGINAL RESEARCH

Predictors of Mortality in Patients With Severe Ischemic Cardiomyopathy Undergoing Surgical Mitral Valve Intervention

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***Background*—**Ischemic mitral regurgitation is associated with substantial risk of death. Although surgical mitral valve intervention (MVi) may improve symptoms, it has not been shown to improve survival. The aim of this study was to identify predictors of mortality in patients with ischemic mitral regurgitation and MVi.

***Methods and Results*—**We evaluated 117 consecutive patients (age, 65±10 years) with advanced ischemic cardiomyopathy who underwent cardiac magnetic resonance and subsequent MVi between January 1, 2002 and January 1, 2012. Cardiac magnetic resonance was used to assess left ventricular remodeling and myocardial scarring. The effective regurgitant orifice area was calculated from the proximal isovelocity surface area by echocardiography. There were 43 deaths (37%) during follow-up (median, 62 months). On multivariable analysis, age ≥70 years (P=0.013), diabetes mellitus (P=0.001), dyslipidemia (P=0.012), papillary muscle scar (P=0.010), incomplete revascularization (P=0.001), and total scar %×effective regurgitant orifice area ≥0.20 cm^2 (P=0.005) were each independently associated with all-cause mortality. Although patients with effective regurgitant orifice area <0.2 cm^2 at baseline demonstrated an increased hazard ratio of 3.3 for every 10% increase in scar, the hazard ratio increased to 9 for every 10% increase in scar in those with baseline effective regurgitant orifice area ≥0.20 cm^2. Mortality also was significantly higher in patients with incomplete revascularization compared with those with vascularized viable myocardium (61% versus 28%; P<0.001).

***Conclusions*—**Increased total scar burden and the presence of incomplete revascularization are powerful predictors of mortality in patients with advanced ischemic cardiomyopathy undergoing MVi. Viability assessment with cardiac magnetic resonance imaging can identify which patients with ischemic mitral regurgitation are at highest risk for mortality after surgical MVi. **(*J Am Heart Assoc*. 2017;6:e007163. DOI: 10.1161/JAHA.117.007163.)**

Key Words: ischemic cardiomyopathy • magnetic resonance imaging • mitral valve regurgitation • myocardial delayed enhancement • revascularization

Despite significant advances in medical and surgical therapies, mortality risk associated with ischemic mitral regurgitation (IMR) after myocardial infarction remains high.[1–4] Because the current data suggest that surgical mitral valve intervention (MVi) provides no significant survival benefit,[5–7] much controversy remains about the role of surgical MVi in patients with significant IMR and severe left ventricular (LV) dysfunction. In addition, the benefit of MVi in patients undergoing surgical revascularization continues to be unclear, given conflicting evidence.[8–17] Therefore, the current guideline recommendations are based on expert opinion, which states that surgical MVi can be performed in patients who are undergoing cardiac surgery for other indications and that isolated MV surgery may be considered in symptomatic patients with severe IMR and LV dysfunction.[18] However, there are no data about which patients with IMR may derive the most benefit from MVi on the basis of the degree of underlying myocardial scar burden. Infarct size assessed by delayed hyperenhancement cardiac magnetic resonance (DHE-CMR) has been a powerful predictor of adverse

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Clinical Perspective

What Is New?

- Our novel findings suggest that viability assessment with cardiac magnetic resonance provides prognostic significance in patients with ischemic cardiomyopathy who underwent subsequent mitral valve intervention (MVi) for significant ischemic mitral regurgitation.
- Patients with total scar % <25% experienced improved survival if complete revascularization was achieved concurrently with MVi.
- However, the mortality rate was higher in patients with total scar % ≥25%, despite complete revascularization at the time of MVi.
- Furthermore, patients with more severe ischemic mitral regurgitation and increased total scar % appear to have the highest risk of mortality, despite MVi.

What Are the Clinical Implications?

- Our study suggests that patients with total scar % ≥25% and significant ischemic mitral regurgitation are unlikely to benefit from MVi.

outcomes in ischemic cardiomyopathy (ICM).[19,20] We sought to determine the impact of myocardial scar burden and incomplete revascularization on survival in patients after MVi.

Methods

Study Population

This was an observational cohort study of patients diagnosed as having ICM (≥70% stenosis in ≥1 epicardial coronary vessel on angiography and/or history of MI or coronary revascularization)[21] who were referred for clinically indicated myocardial viability assessment with CMR between January 1, 2002 and January 1, 2012. Patients with LV ejection fraction >40% were excluded. Patients with standard CMR contraindications were also not included. We identified 117 consecutive patients who underwent MVi within 1 month after initial CMR for inclusion in the study. Clinical variables were gathered prospectively through medical record review. Medical treatment, coronary revascularization (either percutaneous or surgical), and implantable cardioverter defibrillator/cardiac resynchronization therapy implantation were recorded. Assessment of the completeness of revascularization was determined on the basis of the integration of coronary angiography anatomical features, degree of myocardial scarring within these vascular territories on CMR, and subsequent revascularization in these corresponding vascular territories. Viable vascular territories were defined as areas with ≤50% transmural scarring based on DHE-CMR assessment, according to the standard American Heart Association 16-segment model, with corresponding major epicardial coronary artery stenosis ≥70%. Vascular territories with >50% transmural scarring were considered nonviable. Viable vascular territories that were not subsequently revascularized were considered incompletely revascularized.[19] The institutional review board approved supplemental review of medical records and waived patient consent for our study.

Clinical Outcomes

An end point of all-cause mortality was considered to be the primary end point. Death notification was confirmed by observation of death certificate or verified with a family member. The duration of follow-up ranged between the time of the CMR and August 2014.

Echocardiographic Assessment

All patients underwent comprehensive echocardiography with commercially available instruments as part of a standard clinical diagnostic evaluation at baseline and follow-up. Measurements and recordings were obtained according to the American Society of Echocardiography recommendations.[22] Severity of mitral regurgitation was assessed using the effective regurgitant orifice area (EROA), which was calculated from the proximal isovelocity surface area. The regurgitant volume was calculated as the product of time-velocity integral of the regurgitant flow and regurgitant orifice area. Severe IMR was defined as ≥0.2 cm^2 EROA.[18]

CMR Assessment

CMR studies were obtained on commercially available CMR scanners (Sonata/Avanto 1.5 T or Achieva 1.5-T XR/Ingenia 3.0-T), as previously described.[20] For assessment of global cardiac function, steady-state free precession cine images were acquired (slice thickness, 8–10 mm in contiguous short-axis images). LV end-systolic and end-diastolic volumes and LV ejection fraction were calculated on short-axis cine images. DHE-CMR images were obtained in long- and short-axis orientations, ≈15 to 20 minutes after injection of 0.2 mmol/kg of gadolinium dimeglumine. DHE-CMR images were analyzed using commercially available software (cvi42.[23] Endocardial and epicardial myocardial edges were manually delineated on DHE-CMR images. Scar was defined by intensity >2 SDs higher than user-defined viable myocardium.[24] The scar percentage was automatically determined as the percentage of total myocardium (infarct mass/total LV mass). Relative infarct burden within designated anterior, inferior,

and lateral territories was calculated as the proportion of segmental scores contained within each territory, multiplied by global LV infarct size, as previously described with the standard American Heart Association 16-segment model. The percentage of scarring in these vascular territories was determined by dividing the infarcted mass/total ventricular mass in the specified territory. Viable territories were defined as areas with ≤50% transmural scarring with corresponding major epicardial coronary artery stenosis ≥70%. Vascular territories with >50% transmural scarring were considered nonviable. Papillary muscle infarction was deemed present if any papillary hyperenhancement was evident on DHE-CMR short-axis images, in accordance with established criteria.[25] Mitral geometric variables were measured in 3-chamber orientation during ventricular end systole. Tenting area encompassed the area enclosed between the annulus and the MV leaflets.

Statistical Analysis

Data are presented as mean±SD. The following variables were considered as potential predictors: demographics (patient age and sex), cardiovascular disease risk factors (glomerular filtration rate, previous revascularization, hypertension, medication, diabetes mellitus, body mass index, and hyperlipidemia), and imaging factors from echocardiography and CMR. Age and glomerular filtration rate were negatively correlated ($r=-0.57$); thus, to reduce collinearity, age was dichotomized as <70 versus ≥70 years. Also, mean tenting area index and apical displacement were positively correlated ($r=0.62$); because apical displacement was a stronger predictor of mortality in the univariate analyses, it was included in the multiple-variable analysis. Total scar % was positively correlated with peri-infarct scar ($r=0.61$), anterior scar ($r=0.71$), lateral scar ($P=0.78$), and inferior scar ($r=0.50$). Because most of the scar variables were significant predictors of mortality in the univariate analysis, total scar was used as the scar variable in the primary analysis. In addition, separate models were evaluated with each of the scar variables. Cox proportional hazards regression was used to build models of survival time. Model assumptions, including proportional hazards assumption, linearity, and normality, were evaluated. Potential predictors were first assessed in univariate analyses, and risk factors at $P>0.20$ were not considered in the multiple-variable analysis. In the multiple-variable analyses, a backward variable selection process was used, in which 2-way interactions with scar were considered first; interaction terms not significant at $P=0.05$ were removed from the models. In the final models, only interaction terms and main effects not involved in the interaction terms that were significant at $P=0.05$ were included. SAS version 9.2 was used in the statistical analysis.

Results

Study Population

We analyzed 117 patients who underwent MVi (15 underwent MV replacement and 102 underwent MV repair). Baseline clinical variables are summarized in Table 1. The following concomitant procedures were also performed at the time of MVi: 101 coronary bypass grafting procedures (86%), 22 Dor procedures (19%), 20 left atrial appendage closures (17%), 19 epicardial lead placements (16%), 17 tricuspid valve repairs (15%), 9 radiofrequency/cryoablation procedures (8%), 8 aortic valve replacements (7%), and 1 patent foramen ovale closure (1%). Our study cohort was middle aged (65±10 years) and predominantly male (73.5%), with a high prevalence of cardiovascular risk factors. A total of 86.3% had concomitant coronary artery bypass grafting (CABG) at the time of MVi. Most patients received concomitant optimal medical therapies, including β blockers, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and statin. A total of 91 patients (78%) had severe IMR (EROA, ≥0.2 cm^2), and the mean EROA at baseline was 0.31±0.14 cm^2. Mean total scar % was 21.2±16.2%, and prevalence of papillary muscle infarction was 26% in our study group.

There were 31 patients (26%) who had at least 1 territory of incomplete revascularization: 20 patients (65%) could not be completely revascularized because of nongraftable epicardial coronary arteries and/or no available conduits attributable to prior CABG; 9 patients (29%) had areas that were clinically deemed nonviable on the basis of surgical inspection of the myocardium and/or decision based on the clinical MR imaging report, but met our study's predefined criteria for viability (viable territories were defined as areas with ≤50% transmural scarring with corresponding major epicardial coronary artery stenosis ≥70%); and 2 patients (6%) underwent concomitant positron emission tomography studies, and the clinical decision to not revascularize was based on the positron emission tomography results.

Effect of Clinical Variables on Survival

There were 43 patients with events (all-cause death) during follow-up (median, 62 months). The unadjusted hazard ratios (HRs) obtained by Cox proportional hazards regression are shown in Table 2. The following variables were significant univariate predictors of mortality: age (HR, 1.03; $P=0.035$), hyperlipidemia (HR, 2.89; $P=0.002$), diabetes mellitus (HR, 2.65; $P=0.003$), incomplete revascularization (HR, 2.70; $P=0.001$), peri-infarct scar (HR, 1.22; $P<0.001$), total scar % (HR, 1.03; $P=0.003$), anterior scar % (HR, 1.03; $P=0.050$), and lateral scar % (HR, 1.02; $P=0.015$).

Table 1. Baseline Clinical Variables

Variables	MVi
No. of patients	117
Age, mean (SD), y	64.8 (10.4)
Male sex, %	73.5
Body mass index, mean (SD), kg/m^2	28.7 (5.6)
Hypertension, %	55.7
Diabetes mellitus, %	19.7
Hyperlipidemia, %	51.3
Statin, %	74.1
β Blocker, %	83.3
ACE inhibitor or ARB, %	77.8
Spironolactone, %	23.9
Loop diuretics, %	35.0
Aspirin, %	89.0
GFR, mean (SD), mL/min per 1.73 m^2	84.3 (37.6)
CAD characteristics, %	
With >2 vessels CAD	47.0
PCI/CABG	86.3
Incomplete revascularization	26.5
CRT*	41.9
ICD†	17.1
MRI variables	
Total scar, mean (SD), %	21.2 (16.2)
Anterior scar, mean (SD), %	24.8 (23.5)
Lateral scar, mean (SD), %	14.6 (18.7)
Inferior scar, mean (SD), %	18.5 (21.6)
Peri-infarct scar, mean (SD), %	5.4 (2.9)
Papillary muscle infarction, %	24.4
LVESVi, mean (SD), mL/m^2	114.0 (34.9)
LVEF, mean (SD), %	23.0 (8.5)
Tenting area index, mean (SD), cm^2/m^2	0.84 (0.43)
Apical displacement, mean (SD), cm	0.53 (0.21)
Echocardiographic variable	
EROA at baseline, mean (SD), cm^2	0.31 (0.14)

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; EROA, effective regurgitant orifice area; GFR, glomerular filtration rate; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; MRI, magnetic resonance imaging; MVi, mitral valve intervention; and PCI, percutaneous coronary intervention.
*n=49. The time between MRI and ICD was <6 months for 57% of patients, and ranged from 0.5 to 6 years for the remaining patients.
†n=20. The time between MRI and CRT was <6 months for 50% of patients, and ranged from 0.5 to 6 years for the remaining patients.

Table 2. Univariate Predictors of Outcomes

Predictor	HR (95% CI)	*P* Value
Age	1.03 (1.00–1.07)	0.035
Male sex	0.54 (0.29–1.01)	0.054
Body mass index	0.99 (0.94–1.05)	0.844
ACE-i	1.14 (0.53–2.45)	0.743
Lasix	0.83 (0.45–1.56)	0.573
Hyperlipidemia	2.89 (1.49–5.59)	0.002
Hypertension	1.45 (0.77–2.72)	0.247
Diabetes mellitus	2.65 (1.39–5.08)	0.003
Statin	1.00 (0.50–2.00)	0.998
Spironolactone	0.72 (0.34–1.57)	0.413
Aspirin	1.01 (0.55–1.85)	0.974
GFR	0.99 (0.98–1.00)	0.117
No. of vessels of CAD	1.16 (0.82–1.65)	0.411
Incomplete revascularization	2.70 (1.47–4.95)	0.001
CRT†	1.22 (0.60–2.47)	0.590
ICD†	0.78 (0.43–1.44)	0.426
Mean tenting area index	0.70 (0.33–1.47)	0.343
Mean apical displacement	0.31 (0.05–1.75)	0.184
LVESVi	0.99 (0.98–1.00)	0.194
LVEF	1.01 (0.97–1.05)	0.710
Total scar %	1.03 (1.01–1.05)	0.003
Anterior scar %	1.01 (1.00–1.03)	0.050
Lateral scar %	1.02 (1.00–1.03)	0.015
Inferior scar %	1.00 (0.99–1.02)	0.858
Peri-infarct scar %	1.22 (1.13–1.33)	<0.001
Papillary muscle infarction	2.13 (0.94–4.766)	0.067
EROA ≥0.20 cm^2 at baseline	0.42 (0.16–1.07)	0.068

ACE-i indicates angiotensin-converting-enzyme; CAD, coronary artery disease; CI, confidence interval; CRT, cardiac resynchronization therapy; EROA, effective regurgitant orifice area; GFR, glomerular filtration rate; HR, hazard ratio; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; and LVESVi, left ventricular end-systolic volume index.
†Time-dependent covariates.

Effect of Imaging Variables on Survival

Table 3 summarizes the final model for survival analysis. Older age (HR, 2.64; *P*=0.013), presence of diabetes mellitus (HR, 3.20; *P*=0.001), presence of hyperlipidemia (HR, 2.48; *P*=0.012), papillary muscle infarction (HR, 3.72; *P*=0.010), and incomplete revascularization (HR, 3.04; *P*=0.001) (Figure 1) were each independently associated with a higher HR for death. Patients with surgical MVi with complete revascularization demonstrated significantly improved survival compared with those with incomplete revascularization. Differential survival is seen immediately, and survival curves continue to further separate over time.

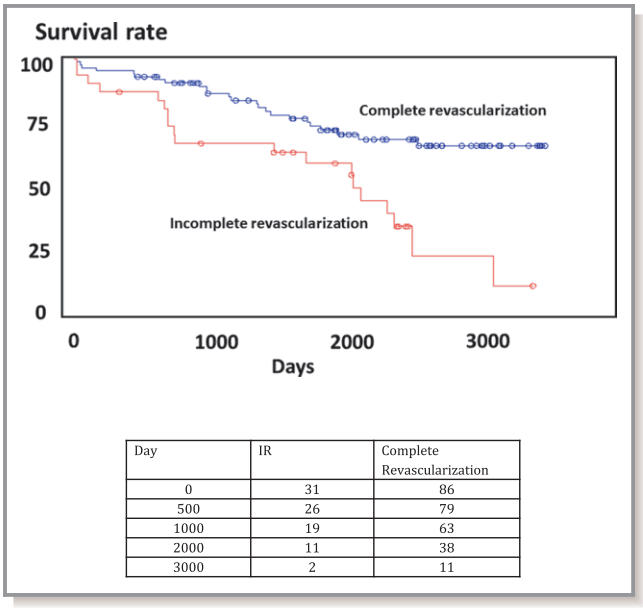
In addition, there was a significant interaction between amount of total scar % and EROA at baseline (Figure 2). In

Table 3. Final Model for Outcomes

Independent Variable	HR (95% CI)	*P* Value
Hyperlipidemia	2.48 (1.23–5.01)	0.012
Diabetes mellitus	3.20 (1.60–6.40)	0.001
EROA ≥0.20 cm^2 at baseline	6.55 (0.53–81.5)	0.144
Age ≥70 y*	2.64 (1.22–5.70)	0.013
Papillary muscle infarction	3.72 (1.37–10.12)	0.010
Total scar %	1.13 (1.06–1.20)	<0.001
Incomplete revascularization	3.04 (1.54–5.99)	0.001
Total scar × EROA ≥0.20 cm^2 at baseline	0.92 (0.86–0.97)	0.005

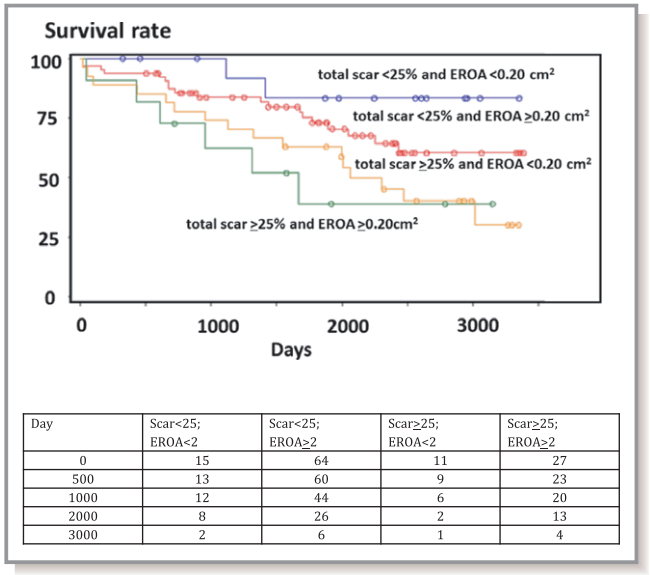
CI indicates confidence interval; EROA, effective regurgitant orifice area; and HR, hazard ratio.
*Age ≥70 years relative to age <70 years. Note that similar results were obtained when age was treated as a continuous variable in the model.

particular, among patients with ERO <0.20 at baseline, for every 10% increase in total scar, the HR for mortality was 3.3. In contrast, the HR was 9 for every 10% increase in scar among patients with ERO ≥0.20. Patients with a smaller myocardial scar burden demonstrated improved survival compared with those with greater scar burden. Patients with lower scar burden and less IMR had better survival than those with lower scar burden and more significant IMR. In addition, patients with lower scar burden and more significant IMR had better survival than patients with higher scar burden and less significant IMR. On the other hand, patients with increased scar burden had significantly worse survival, regardless of the severity of IMR before MVi.



Day	IR	Complete Revascularization
0	31	86
500	26	79
1000	19	63
2000	11	38
3000	2	11

Figure 1. Event-free survival by presence/absence of incomplete revascularization: patients with complete revascularization (blue curve, N=86, with 24 events) and patients with incomplete revascularization (red curve, N=31, with 19 events). IR indicates incomplete revascularization.



Day	Scar<25; EROA<2	Scar<25; EROA≥2	Scar≥25; EROA<2	Scar≥25; EROA≥2
0	15	64	11	27
500	13	60	9	23
1000	12	44	6	20
2000	8	26	2	13
3000	2	6	1	4

Figure 2. Event-free survival by baseline total scar and effective regurgitant orifice area (EROA): patients with baseline total scar <25% and EROA <0.20 cm^2 (blue curve, N=15), patients with baseline total scar <25% and EROA ≥0.20 cm^2 (red curve, N=64), patients with baseline total scar ≥25% and EROA <0.20 cm^2 (green curve, N=11), and patients with baseline total scar ≥25% and EROA ≥0.20 cm^2 (orange curve, N=27). At 500 days, there were 13 patients with total scar <25% and EROA <0.20 cm^2 at risk, 60 patients with total scar <25% and EROA ≥0.20 cm^2 at risk, 9 patients with total scar ≥25% and EROA <0.20 cm^2 at risk, and 23 patients with total scar ≥25% and EROA ≥0.20 cm^2 at risk. At 1000 days, there were 12 patients with total scar <25% and EROA <0.20 cm^2 at risk, 44 patients with total scar <25% and EROA ≥0.20 cm^2 at risk, 6 patients with total scar ≥25% and EROA <0.20 cm^2 at risk, and 20 patients with baseline total scar ≥25% and EROA ≥0.20 cm^2 at risk. At 2000 days, there were 8 patients with total scar <25% and EROA <0.20 cm^2 at risk, 26 patients with total scar <25% and EROA ≥0.20 cm^2 at risk, 2 patients with total scar ≥25% and EROA <0.20 cm^2 at risk, and 13 patients with total scar ≥25% and EROA ≥0.20 cm^2 at risk.

Discussion

Optimal management of patients with advanced ICM and significant IMR continues to be unclear, and much controversy remains about which therapeutic interventions will provide the best outcomes and sustainable relief of symptoms. This present study sought to determine the prognostic utility of viability assessment with CMR imaging in patients with advanced ICM and significant IMR who underwent subsequent MVi. The results of this study demonstrate the following novel findings: (1) increased total myocardial scar burden and incomplete revascularization are powerful independent predictors of mortality in patients with advanced ICM and IMR

who underwent MVI; and (2) significant interaction between baseline EROA and total scar burden independently predicts mortality. We found that the risk associated with IMR was modulated by the amount of underlying myocardial scar burden. However, patients with increased myocardial scar burden had significantly worse survival than those with less myocardial scar burden, regardless of the severity of IMR before MVi.

Effect of Viability Assessment With CMR on Survival

Although IMR has been shown to be a well-established predictor of mortality, unfortunately, several studies have suggested that surgically reducing the severity of IMR does not result in improved survival.[6,7,26–28] Furthermore, there are conflicting data in the literature about the impact of CABG alone versus CABG+MVi for the treatment of IMR and whether MVi results in improved survival,[8–17] symptoms, or LV remodeling.[26–28] The uncertain benefit of MVi for significant IMR suggests that the risk associated with increasing degrees of IMR may be more a reflection of greater adverse LV remodeling and subsequent annular dilation, impaired coaptation, and lateral displacement of the papillary muscles attributable to myocardial infarction in patients.

Despite the controversy over the benefit of MVi for IMR, patients with IMR are frequently referred for coronary revascularization+MVi. Viability assessment before CABG and CABG+MVi was not included in prior studies in the literature. Differences in outcome between CABG and CABG+MVi among the published studies may, in part, reflect differences in (1) the severity of underlying myocardial scar and (2) completeness of revascularization. Furthermore, prior studies have not included an assessment of incomplete revascularization in their survival analysis.

Our study demonstrates the importance of complete revascularization of viable myocardium in patients with advanced ICM and significant IMR undergoing MVi. This finding supports a large retrospective observational study that suggested that surgical revascularization may provide significant survival benefit in this patient population.[9] Castleberry et al[9] found that patients who underwent CABG±MVi experienced improved survival compared with patients who underwent percutaneous coronary intervention and/or medical therapy alone. Although this study did not demonstrate significant survival benefit in patients who underwent CABG versus CABG+MVi, a STICH (Surgical Treament for IsChemic Heart failure) substudy suggested that CABG+MVi may provide survival benefit compared with CABG alone in patients with significant IMR. However, a viability assessment to examine the possibility of differential outcomes in patients with increased scar burden was not performed in either of these analyses. The mean ejection fractions in our study and in the STICH substudy were significantly lower compared with those of prior randomized control studies, suggesting that CABG+MVi may be more beneficial in patients with more advanced LV dysfunction and adverse remodeling, but significant viability.

The current study demonstrates the powerful prognostic ability of myocardial scar quantification with DHE–MR imaging to predict outcomes; patients who underwent MVi with smaller areas of myocardial infarction experienced more favorable outcomes after MVi compared with those with larger areas of myocardial infarction. In addition, patients with smaller areas of myocardial infarction with less significant IMR demonstrated >75% survival, whereas patients with larger areas of myocardial infarction had <50% survival over a median follow-up of 5.2 years. We have previously demonstrated increasing survival benefit with CABG in patients with increased scar burden.[20] However, most patients in our prior study did not undergo MVi, and the relationship of myocardial scarring to the location of epicardial coronary artery disease was not available. Therefore, the completeness of revascularization of viable myocardium was not included in our previous analysis.

The current study demonstrates the importance of relating the location of myocardial scarring with coronary artery anatomical features. Complete revascularization of viable myocardium in the setting of significant IMR likely improves outcomes by decreasing the ischemic burden attributable to the increased wall stress associated with adverse LV remodeling and IMR. It also provides greater potential for improved myocardial function in the viable segments, regression of hypertrophy and end-systolic volume index, and potential stabilization of increased arrhythmic substrate. Our current data demonstrate that patients undergoing MVi with large areas of myocardial infarction and more severe IMR experience the highest rate of mortality.

Much controversy remains about the utility of viability testing in patients with advanced ICM. However, there are no studies that have evaluated the impact of viability testing specifically in patients with significant IMR. Our study suggests that incompletely revascularized viable myocardium is an independent predictor of increased mortality in patients with significant IMR undergoing MVi. This finding confirms the recommendations to make every effort to completely revascularize patients with advanced ICM and significant IMR.[18,29] Most patients in our study population (86%) underwent concomitant surgical revascularization. However, complete revascularization was not possible in a minority of patients (26%) because of poor-quality epicardial vessels with diffuse disease and/or lack of adequate conduits for surgical bypass grafts. These patients with incompletely revascularized viable myocardium demonstrated a significantly higher rate of

mortality. Further studies are needed to determine if hybrid procedures, with combined CABG+percutaneous interventions to achieve complete revascularization, versus advanced therapies, such as LV assist device or heart transplant, may provide significantly improved survival in patients with advanced ICM and significant MR with poor epicardial coronary artery targets.

This study revealed a novel interaction between the amount of total scar % and EROA at baseline in patients who subsequently underwent surgical MVi. There was a 3.3-fold increase in risk for every 10% increase in total scar burden for patients with less significant IMR, with ERO <0.20. In contrast, there was a 9-fold increase in risk in mortality for every 10% increase in scar among patients with an ERO ≥0.20. Therefore, the risk associated with IMR is significantly modulated by the degree of myocardial scarring. Patients with lower scar burden and less significant degree of IMR demonstrated better survival that those with lower scar burden and more significant IMR. On the other hand, patients with increased myocardial scarring with significant IMR have significantly worse survival compared with patients with the same degree of IMR with less scarring. In addition, patients with lower scar burden and more significant IMR had better survival than patients with higher scar burden and less significant IMR. This finding suggests that patients with lower EROA may have developed adaptive abilities to abate the risk associated with increased myocardial scar burden. On the other hand, patients with increased scar burden had significantly worse survival, despite the severity of IMR before MVi. Higher mortality in the setting of more severe IMR and increased total scar % likely reflects the inability for the LV to adapt to IMR, regardless of the severity, because of increased myocardial scar burden. Higher EROA, reflecting more severe IMR, likely results in further maladaptive LV remodeling, higher wall stress attributable to higher filling pressures, and higher risk of mortality in the setting of increasing myocardial scar burden. These findings suggest that the quantification of myocardial scar burden provides incremental risk stratification in patients with significant IMR and advanced LV remodeling.

Further studies are needed to determine if MVi should be considered at an earlier stage in patients with smaller areas of myocardial infarction, but with significant LV dysfunction. In addition, further studies are needed to determine if advanced therapies, such as LV assist device or heart transplant, may provide survival benefit in patients with large areas of myocardial infarction.

Clinical Implication

IMR is an extremely complex process, with continued controversy about optimal treatment. Our study is the first to demonstrate the prognostic significance of viability assessment with CMR in patients with advanced ICM who underwent subsequent MVi for significant IMR. Our study demonstrates that assessment of viability with CMR may provide important prognostic information, which may help to customize the optimal treatment strategy for each patient. Total myocardial scar burden, incomplete revascularization assessed by viability evaluation with CMR, and an interaction between baseline IMR severity and scar burden may identify the highest-risk patients. Patients with myocardial scar burden <25%, with adequate epicardial vessels and surgical bypass grafts, appear to experience favorable survival if complete revascularization is achieved at the time of MVi. On the other hand, patients with myocardial scar burden ≥25% appear to have poor survival, despite the ability to achieve complete revascularization at the time of MVi. In addition, patients with more severe IMR in the setting of increased myocardial scar burden appear to have the highest risk of mortality, despite MVi. Therefore, our study suggests that further studies are needed to determine if patients with myocardial scar burden ≥25% in the setting of significant IMR should be considered for advanced therapies, such as LV assist device or heart transplant, rather than MVi.

Limitations

This was an observational, single-center study that only included patients with advanced ICM, who were able to undergo DHE-CMR study. In addition, only patients who underwent MV repair or replacement at our institution after the baseline CMR were included. Furthermore, the CMR findings may have influenced the clinicians' decision to refer patients for surgical MVi. Patients with prior device implantation were excluded from this study because of contraindications for CMR, Therefore, significant selection bias may be present.

Assessment for optimal medical therapy in our patient population was complex, because medical therapy changed in a significant portion of our population during follow-up. Although additional medications were added to optimize the medical regimen during follow-up in a proportion of our patients, some medications were discontinued because of relative hypotension or development of acute renal failure/hyperkalemia/elevated liver enzymes postoperatively. In addition, it is possible that some patients may have undergone cardiac resynchronization therapy/implantable cardioverter defibrillator implantation outside of our institution. The limited follow-up data may affect the results of our study. Therefore, further studies are needed to determine how the risk of incomplete revascularization and increased scar burden is mitigated by optimal medical therapy and cardiac resynchronization therapy/implantable cardioverter defibrillator when compared with surgical revascularization and MVi.

All-cause mortality was used as the primary end point in our patient population. The most likely cause of death in our patient population is cardiac, given the known high risk nature of our patient population. Although discerning how incomplete revascularization and increased scar burden is associated with risk of sudden cardiac death, myocardial infarction, or pump failure would be of important interest, determining the definitive cause of death by death certificates can be difficult in such a high-risk population, and can pose a source of bias.

Despite the limitations, this is the largest study of patients who have undergone CMR before MVi in the literature. We believe that the findings of this study reveal important findings about the prognostic utility of viability assessment with CMR in patients with significant IMR undergoing evaluation for MVi.

Conclusions

Increased total scar burden and the presence of incomplete revascularization are powerful predictors of mortality in patients with advanced ICM undergoing MVi. Viability assessment with CMR imaging can identify which patients with IMR are at highest risk for mortality after surgical MVi.

Complete revascularization in the setting of small myocardial scar burden appears to be associated with favorable survival in patients undergoing MVi for significant IMR. Patients with large myocardial scar burden appear to have the highest risk of death, and further studies are needed to determine if these patients would derive survival benefit from more advanced therapies (ie, LV assist device or heart transplant).

Disclosures

None.

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Predictors of Mortality in Patients With Severe Ischemic Cardiomyopathy Undergoing Surgical Mitral Valve Intervention

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