The impact of viability assessment using myocardial perfusion imaging on patient management and outcome

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Background. **Prior studies show that ischemic cardiomyopathy (ICM) patients with substantial viable myocardium have better survival with coronary revascularization (CR) than medical therapy (MT). When myocardial perfusion imaging (MPI) is used, the analysis is often based on visual scoring. We sought to determine the value of automated quantitative viability analysis in guiding management and predicting outcome.**

Methods. **We identified 246 consecutive ICM patients who had rest-redistribution gated SPECT thallium-201 MPI. Size and severity of perfusion defects were assessed by automated method. Regions with <50% activity vs normal were considered nonviable. Mortality was verified against the social security death index database.**

Results. **Of the 246 patients, 37% underwent CR within 3 months of MPI. The initial images showed a total perfusion defect size of 32 ± 17%, redistribution of 3.5 ± 4.6% and nonviable myocardium of 13 ± 14%LV. Using multivariate logistic regression analysis, independent predictors of CR included chest pains (OR 2.74) and rest-delayed transient ischemic dilatation (OR 4.49), while a prior history of CR or ventricular arrhythmias favored MT. The cohort was followed-up for 41 ± 30 m during which 111 patients (45%) died. Survival was better with CR than MT ($P < .0001$). For CR, survival was better for those with a smaller area of nonviable myocardium (risk of death increased by 5%/1% increase in size of nonviable myocardium, $P = .009$) but this was not seen in MT. CR had a mortality advantage over MT when the area of nonviable myocardium was ≤20%LV but not larger.**

Conclusions. **Automated quantitative analysis of MPI is useful in predicting survival in ICM, but the decision for or against CR is a complex one as it depends on multiple other factors and ''viability testing'' is just one variable that needs to be incorporated in the decision-making process. (J Nucl Cardiol 2010;17:378–89.)**

Key Words: Viability • coronary revascularization • myocardial perfusion imaging • mortality

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The number of patients presenting with heart failure (HF) is increasing exponentially each year. Estimates indicate that 550,000 new patients are diagnosed annually, adding to >5 million patients currently living with chronic HF in the United States.[1] Despite considerable medical advances in therapy, the prognosis of these patients remains quite poor.[2] Since coronary artery disease (CAD) is an important etiology in the majority of patients with HF due to depressed left ventricular (LV) ejection fraction (EF), coronary revascularization (CR) can complement medical therapy (MT) in the treatment of a subset of these patients. Considering the

increased morbidity and mortality associated with CR in those with depressed LVEF, careful selection of candidates for CR becomes imperative.[3]

Multiple imaging modalities have been used to identify the presence of viable but dysfunctional myocardium that is likely to benefit from CR.[4] Rest-redistribution thallium-201 myocardial perfusion imaging (MPI) has a long-standing track record, based on its favorable pharmacokinetics of redistribution, in the prediction of functional recovery and long-term survival with CR.[1] Previous thallium-201 studies have largely relied upon visual qualitative or semi-quantitative analyses using a scoring system of regional tracer activity.[5] We tested the hypothesis that an automated analysis could impact the management strategy and help predict survival in patients with LV dysfunction.

METHODS

Study Patients

The study population consisted of 246 consecutive patients with LV dysfunction (LVEF $\leq$ 40%) who underwent a rest-redistribution single photon emission computed tomography (SPECT) thallium-201 MPI for guiding CR at the Hospital of the University of Alabama at Birmingham between January 2000 and October 2007. More than 90% of the patients had a transthoracic echocardiogram available for review and none had severe mitral regurgitation. The study protocol was reviewed and approved by the local institution review board. Patient characteristics were identified from the medical records. The estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease study formula.[6]

Myocardial Perfusion Imaging

All images were acquired and processed according to the American Society of Nuclear Cardiology guidelines.[1] Gated SPECT imaging was started 10 min after thallium injection at rest followed by a second imaging study done 4 h later. All raw data (2 sets/patient) were reconstructed using standard filtered back projection (Butterworth filter with a critical frequency of .4, order 5). Image analysis was performed using a previously validated automated program (4DM-SPECT, Ann Arbor, MI) which determines the extent and severity of LV perfusion defect size and the extent of reversible (ischemia) or fixed (scar) resting hypoperfusion.[7] The database used is specific for thallium-201 MPI and is based on 60 normal studies (30 male and 30 female). No attenuation correction was used in this analysis. Regions with <50% activity compared to normal were considered as nonviable. In addition, using the 17-segment model, the initial summed score, delayed summed score and summed difference score were also determined. The program assigned a score of 0-4 to each segment based on activity level, 0 = normal and 4 absent.[8] Although the program is automated, the reader routinely checked the accuracy of the assignment of regions of interest such as determination of the apex and base of the LV. The computer program had trouble locating the heart (because of extracardiac activity and/or because of the presence of a large perfusion defect) and the operator had to manually direct the computer program to the position of the heart in around 25% of the cases but the analysis remained completely automated. In addition to perfusion data, the LVEF, end-diastolic volume, end-systolic volume, and LV mass were measured from the gated SPECT as previously described.[7] A rest-delayed transient ischemic dilation (rTID) was considered present when the LV volume from the summed images on the initial scan was $\geq$10% higher than that at the delayed scan. All data reported here are based on automated analyses using the polar maps or summed scores as described above.

Outcome and Management Strategy

The management strategy was determined by reviewing the patients' records. The decision for or against CR was based on the opinion of the treating physician, which most likely incorporated the results of the viability testing. It must be mentioned, however, that reporting of the data has evolved over time and direct communication between reader and physician did not occur in all cases.

The outcome of the patients was defined as all-cause mortality assessed using mortality status on the US Social Security Death Master File on September 25, 2008. Survival time was calculated from the date of MPI to death or to the end of follow-up on September 25, 2008. Patients who underwent coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) within a 3-month period of their MPI were considered in the CR group. All other patients were considered in the medical management group for the purposes of this study.

Statistical Analysis

All statistical analyses were carried out using SPSS version 11.5 for Windows (SPSS Inc., Chicago, IL). Continuous variables are presented as mean ± SD and discrete variables as frequencies and percentages. The Chi-square test was used for the comparison of categorical variables between the two groups. Continuous variables were compared between the two groups by the unpaired t test or Mann-Whitney U test, as appropriate. All tests were two-tailed, and a P value of $\leq$.05 was considered statistically significant.

In order to determine the independent predictors of the management strategy (CR vs medical), a multivariate binary logistic analysis was performed using all variables in Table 1 with a P value $<$ .1 for the comparison of CR vs medical groups. A best-fit model was then built using backward elimination (Likelihood Ratio) for the prediction of CR and estimated odds were reported as odds ratio (OR) with correspondent 95% confidence intervals (CI).

Event-free survival curves were constructed using the product-limit method (Kaplan-Meier) and differences among

Table 1. Baseline characteristics

Variable	Entire cohort (n = 246)	Medical therapy (n = 154)	Coronary revascularization (n = 92)	*P* value
Age (years)	59 ± 12	60 ± 12	58 ± 11	.3
Female gender	56 (23%)	34 (22%)	22 (24%)	.8
Race				
Caucasian	188 (76%)	113 (73%)	75 (82%)	.3
African American	43 (18%)	30 (20%)	13 (14%)	
Other	15 (6%)	11 (7%)	4 (4%)	
Diabetes Mellitus	92 (38%)	59 (39%)	33 (36%)	.7
Hypertension	191 (79%)	121 (80%)	70 (78%)	.7
Dyslipidemia	179 (74%)	111 (74%)	68 (76%)	.8
Cerebrovascular event	26 (11%)	19 (13%)	7 (8%)	.3
Peripheral vascular disease	40 (17%)	29 (19%)	11 (12%)	.2
End-stage renal disease	12 (5%)	9 (6%)	3 (3%)	.5
Myocardial infarction	177 (74%)	110 (74%)	67 (74%)	1.0
Percutaneous coronary intervention	91 (38%)	64 (43%)	27 (29%)	.04
Coronary artery bypass graft	79 (32%)	63 (41%)	16 (17%)	<.0001
Ventricular arrhythmia	39 (16%)	33 (22%)	6 (7%)	.002
Biventricular pacemaker	13 (5%)	10 (7%)	3 (3%)	.4
Implantable cardiac defibrillator	45 (19%)	37 (25%)	8 (9%)	.002
Symptoms				
Chest pain	130 (54%)	64 (42%)	66 (73%)	<.0001
Shortness of breath	200 (81%)	129 (87%)	71 (79%)	.2
Medications				
Aspirin	203 (86%)	122 (83%)	81 (92%)	.05
Clopidogrel	95 (42%)	43 (30%)	52 (61%)	<.0001
Warfarin	65 (29%)	49 (34%)	16 (19%)	.01
Beta-blocker	180 (77%)	115 (78%)	65 (74%)	.5
ACE-I/ARB	200 (85%)	128 (87%)	78 (82%)	.3
Calcium channel blocker	21 (9%)	17 (12%)	4 (5%)	.1
Diuretic	174 (74%)	119 (81%)	55 (63%)	.002
Spironolactone	89 (38%)	65 (45%)	24 (27%)	.009
Digoxin	125 (53%)	89 (61%)	36 (41%)	.004
Nitrates	60 (26%)	40 (27%)	20 (23%)	.5
Statin	154 (66%)	90 (61%)	64 (73%)	.09
Amiodarone	40 (17%)	33 (22%)	7 (8%)	.004
Insulin	28 (12%)	16 (11%)	12 (14%)	.5
Laboratory data				
Serum sodium (mmol/L)	137 ± 6	136 ± 7	138 ± 4	.02
Glucose (mg/dL)	126 ± 49	126 ± 48	125 ± 51	.2
eGFR (ml/min/1.73 m^2)	61 ± 25	58 ± 24	66 ± 24	.01
Myocardial perfusion imaging				
LV ejection fraction (%)	22 ± 8	22 ± 8	23 ± 9	.2
LV end-diastolic volume (mL)	240 ± 108	256 ± 113	213 ± 95	.001

Table 1. continued

Variable	Entire cohort (n = 246)	Medical therapy (n = 154)	Coronary revascularization (n = 92)	*P* value
LV mass (g)	242 ± 66	252 ± 68	225 ± 60	.001
Rest-delayed transient ischemic defect	34 (14%)	13 (9%)	21 (23%)	.004
Lung-heart ratio	.55 ± .14	.56 ± .14	.55 ± .16	.5
Perfusion defect size (% LV)	32 ± 17	33 ± 18	30 ± 14	.1
Reversible defect size (% LV)	3.5 ± 4.6	3.2 ± 4.1	4.0 ± 5.1	.3
Nonviable defect size (% LV)	13 ± 14	15 ± 14	10 ± 12	.02

ACE-I, Angiotensin converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *eGFR*, estimated glomerular filtration rate; *LV*, left ventricle.

survival curves were estimated by the log-rank test. Cox regression modeling was used to estimate crude (univariate) and adjusted (multivariate) risks, using variables found to have $P < .2$ in the univariate analyses. Age and gender were forced into all models because they were considered of biological significance. Estimated risks were reported as hazard ratios (HR) with correspondent 95% CI. Variables initially introduced in the Cox regression models are shown at the bottom of Table 3. Best-fit models were then built using backward elimination (Likelihood Ratio) starting from these variables. The final models for the entire cohort, the medical group and the CR group had Chi-square of 63, 39, and 46 respectively. All models had a P value $< .0001$.

RESULTS

Of the 246 patients, 92 (37%) underwent CR (52 with CABG and 40 with PCI) within 3 months, while the remaining 154 (63%) were managed medically. The baseline characteristics are reported in Table 1. In general, the 2 groups had comparable age, gender and co-morbidities, but patients in the CR group were less likely to have a prior history of CR or of ventricular arrhythmias and more likely to have chest pains and better renal function.

The LVEF was severely depressed (based on selection criteria) but comparable between the two groups. Although the LV was dilated in both groups, this was less marked in the CR group. On average, almost one third of the LV myocardium had perfusion defects and the extent of resting ''ischemia'' (reversible resting perfusion abnormality) was similar in both groups. Nevertheless, the extent of the nonviable myocardium was larger in patients in the medical group (15 ± 14% vs 10 ± 12% LV, $P = .02$).

MT VS CR

Using multivariate binary logistic regression analysis, several important predictors of the management strategy were identified (Table 2). Individuals who previously underwent CR were much more likely to be managed medically while those who were complaining of chest pain were more likely (OR = 2.74, $P = .01$) to undergo CR. The strongest predictor of CR was the presence of rTID (OR = 4.5, $P = .003$ after full adjustment for other variables). Importantly, age and gender did not influence the decision for CR. The best-fit regression model (which included a history of CABG, PCI, ventricular arrhythmia, and chest pains, intake of clopidogrel and warfarin, and the presence of rTID) had a Chi-square of 67 ($P < .0001$) for the selection of CR.

OUTCOME

The cohort was followed-up for a mean of 41 ± 30 months during which 111 patients (45%) died. These deaths occurred at a mean of 23 ± 22 months from the MPI. Patients who underwent CR within the 3-months period had a much better survival on follow-up than those managed medically (log-rank $P < .0001$). The best survival was in patients who had CABG (with long-term mortality <20%), followed by those who had PCI (4-year mortality <30%), while more than half of those treated medically died by 4 years (Figure 1; log-rank $P < .0001$). Out of the 246 patients, 20 (8%) were dead within 30 days of their MPI. There was no difference in mortality at 30 days between patients who underwent CR vs MT (4% vs 10%, $P = .1$). At 3 months after the MPI, 28 (11%) of the patients were

Table 2. Multivariate predictors of coronary revascularization

Variable	Initial model		Best-fit model	
	OR [95% CI]	*P* value	OR [95% CI]	*P* value
Age (years)*	.97 [.94-1.01]	.1	NA	NA
Female gender	1.35 [.21-1.76]	.4	NA	NA
Percutaneous coronary intervention	.26 [.11-.64]	.003	.30 [.13-.66]	.003
Coronary artery bypass graft	.24 [.09-.64]	.004	.23 [.10-.55]	.001
Ventricular arrhythmias	.37 [.08-1.66]	.2	.37 [.12-1.17]	.09
Implantable cardiac defibrillator	.91 [.21-3.94]	.9	NA	NA
Chest pain	2.53 [1.05-6.10]	.04	2.74 [1.27-5.92]	.01
Aspirin	2.11 [.49-9.08]	.3	NA	NA
Clopidogrel	4.02 [1.70-9.50]	.3	3.75 [1.74-8.06]	.001
Warfarin	.57 [.20-1.60]	.3	.41 [.17-.99]	.05
Diuretic	.60 [.23-1.55]	.3	NA	NA
Digoxin	.63 [.27-1.46]	.3	NA	NA
Spironolactone	1.01 [.39-2.63]	1.0	NA	NA
Statin	.76 [.30-1.95]	.6	NA	NA
Amiodarone	1.12 [.29-4.35]	.9	NA	NA
Serum sodium (mmol/L)*	1.05 [.93-1.17]	.5	NA	NA
eGFR (mL/min/1.73 m^2)*	1.00 [.98-1.02]	1.0	NA	NA
LV end-diastolic volume (mL)*	1.00 [.99-1.01]	.7	NA	NA
LV mass (g)*	.99 [.98-1.01]	.3	NA	NA
Rest-delayed transient ischemic defect	4.43 [1.43-13.78]	.01	4.49 [1.65-12.26]	.003
Nonviable defect size (%LV)*	.98 [.94-1.01]	.2	NA	NA

eGFR, Estimated glomerular filtration rate; *LV*, left ventricle; *NA*, not applicable.
*Continuous variable.

dead with less deaths occurring in those who underwent CR (5% vs 15%, $P = .02$).

Multivariate Cox proportional hazard analysis for survival showed that age, CR, end-stage renal disease and LV end-diastolic volume were independent predictors of mortality (Table 3). Although patients with end-stage renal disease constituted a small fraction of the entire cohort (5%), they had an almost fivefold increased risk of death. Additionally, each 10 mL increase in LV volume accounted for a 3% increased mortality (HR 1.003, $P = .006$).

We then constructed separate Cox proportional hazard models for the medical and the CR groups (Table 3). In the medical group, age, gender, end-stage renal disease, treatment with ACE-I/ARB, and LVEF were independent predictors of survival. For each 1% decrease in the LVEF, the risk of death increased by 3%. In the CR group, diabetes mellitus, end-stage renal disease, prior history of CABG, shortness of breath, and the size of nonviable myocardium were independent predictors of survival. After full adjustment for the other variables, for every 1% LV increase in the size of nonviable myocardium, the risk of death increased by 5% over the follow-up period (HR 1.05, $P = .009$). The presence of end-stage renal disease increased the mortality risk by 44-folds. The size of the perfusion defect and the presence of resting ischemia were not important determinants of mortality in either group (log-rank $P = .2$-.9). Patients with small (≤15% LV), moderate (16-30% LV) and large (>30% LV) area of nonviable myocardium had identical survival when managed medically, but there was a stepwise increase in mortality in patients managed with CR (Figure 2, log-rank $P = .001$). Patients with moderate-large size nonviable myocardium did not derive any survival advantage with CR (Figure 3a, log-rank $P = .4$) unlike those with small-sized abnormality (Figure 3b, log-rank $P < .0001$). Furthermore, when we examined for the benefit of CR at each extent of nonviable myocardium, CR had a mortality advantage over MT when the area of nonviable myocardium was ≤20%LV but not larger (Figure 4).

For the subset of patients with no prior history of CR (n = 109), survival was better in those who underwent CR (log-rank $P = .002$). The stepwise association of the size of nonviable myocardium with mortality persisted in patients who underwent CR (log-rank $P = .002$), and the survival advantage of CR was maintained in those with a small area of nonviable myocardium (log-rank

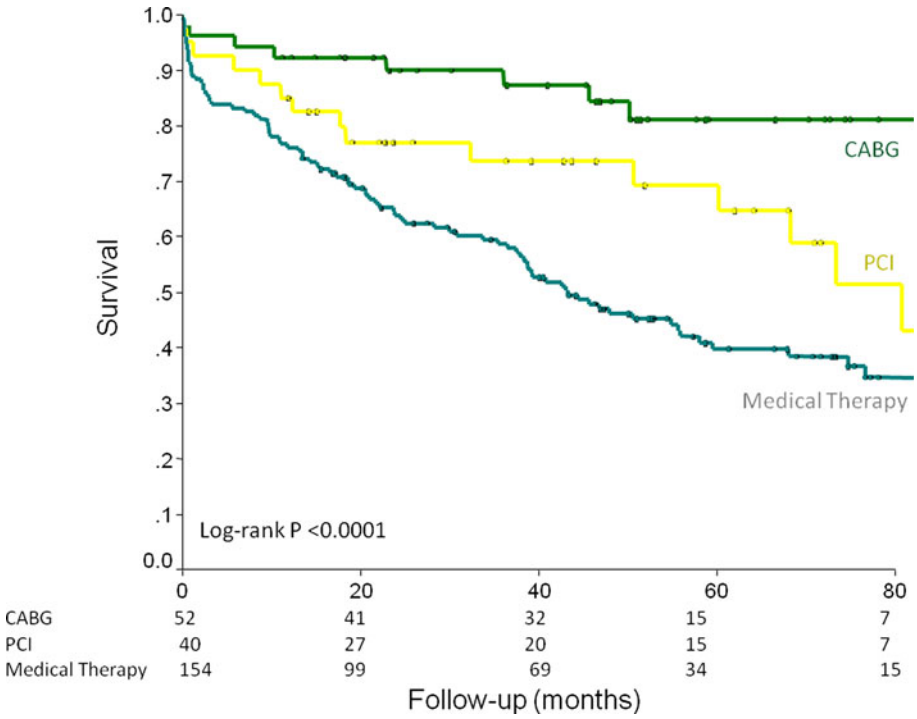

Figure 1. Kaplan-Meier analysis for survival according to treatment strategy. Patients who underwent coronary revascularization (CR) had better survival than those that did not. Patients who underwent coronary artery bypass grafting (CABG) had the best prognosis, but those who underwent percutaneous coronary intervention (PCI) had better prognosis than those who did undergo any form of CR. The number of patients available at each time-point is indicated below the graph.

$P = .0001$) but not in those with a moderate-large sized area of abnormality (log-rank $P = .7$).

We compared our quantitative data to those derived from the more widely used semi-quantitative 17-segment model. The area of resting hypoperfusion by polar maps correlated with the initial summed score ($r = .84$, $P \leq .0001$) and similarly, the extent of resting ischemia by polar maps correlated with the automated summed difference score ($r = .82$, $P \leq .0001$). Patients with smaller abnormality on the initial scan (initial summed score ≤ 18) had better survival with CR (log-rank $P \leq .0001$) unlike those with larger abnormalities (initial summed score ≥ 18, log-rank $P = .07$).

DISCUSSION

The main conclusions of this study, which was based on automated quantitative analysis of rest-redistribution gated SPECT thallium-201 MPI in patients with ischemic cardiomyopathy (ICM, CAD and depressed LVEF) in the modern era of contemporary treatment are: (1) Patients with dilated LV and those with end-stage renal disease have worse prognoses; (2) in this nonrandomized study, patients who underwent CR had better survival than those managed medically; (3) there are several imaging and nonimaging variables that impact on the management strategy utilized (CR vs MT). For example, patients with a prior CR or ventricular arrhythmias were more likely to be managed medically while those who had chest pains or rTID were more likely to be managed with CR; (4) in patients treated medically, age, gender, end-stage renal disease, and LVEF were independent predictors of mortality while the use of ACE-I/ARB was a predictor of better survival. In the CR group, the important predictors of mortality included diabetes mellitus, end-stage renal disease and the extent of nonviable myocardium (perfusion defect with <50% activity compared to normal area); (5) the mortality benefit of CR is limited to patients with a small area of nonviable myocardium while those with moderate or large sized nonviable myocardium had similar outcome with either CR or MT with a trend toward harm in those with large size.

MYOCARDIAL VIABILITY

The definition, characterization, pathophysiological mechanisms, and imaging methods to define viable

Table 3. Cox proportional hazard analysis best-fit models for survival

Variable	HR [95% CI]	*P* value
Entire cohort[$]		
Age (years)*	1.06 [1.04–1.08]	<.0001
Coronary revascularization	.36 [.20–.65]	.001
End-stage renal disease	4.93 [2.39–1.18]	<.0001
LV end-diastolic volume (mL)*	1.00 [1.00–1.01]	.006
Medical therapy[$]		
Age*	1.06 [1.03–1.08]	<.0001
Female gender	.59 [.32–1.08]	.09
End-stage renal disease	3.34 [1.39–8.04]	.007
Ace-I/ARB	.42 [.22–.81]	.01
Left ventricular ejection fraction (%)*	.97 [.94–1.00]	.03
Coronary revascularization[$]		
Diabetes mellitus	2.97 [1.13–7.81]	.03
End-stage renal disease	44.10 [8.80–221.06]	<.0001
Coronary artery bypass graft	4.38 [1.47–13.05]	.008
Shortness of breath	6.16 [1.44–26.37]	.01
Nonviable defect (%LV)*	1.05 [1.01–1.09]	.009

ACE-I, Angiotensin converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *LV*, left ventricle.
[$]In addition to shown variables, age and gender, the Cox regression models initially included the following; for the entire cohort: race diabetes mellitus, hypertension, CABG, chest pain, intake of warfarin, ACE-I/ARB, amiodarone, insulin, serum sodium, eGFR, LVEF, LV mass and size of nonviable myocardium. For the medical group: diabetes mellitus, hypertension, CABG, beta-blocker, amiodarone, serum sodium, and eGFR. For the CR group: intake of insulin, eGFR, and the perfusion defect size.
*Continuous variable.

dysfunctional myocardium have been reviewed elsewhere.[9] Suffice it to say several imaging methods have been used and these continue to be refined. Of the SPECT methods, rest-redistribution thallium-201 is the oldest and is based on unique kinetics of this tracer in which the initial distribution is proportional to regional myocardial blood flow while the delayed images (redistribution images) reflect cell membrane integrity.[10-18] In stable patients, stress-redistribution-re-injection imaging is used while in sicker and less stable patients or in patients with known coronary anatomy (such as severe proximal disease in one or more vessels), rest-redistribution imaging might be sufficient. It should be noted that although we label myocardium as viable or nonviable, viability is a continuum and the probability of recovery of regional function is also a continuum and that is also true for any cutoff point for the extent of viable or nonviable myocardium. These cutoff points have statistical relevance but limited clinical relevance as recently pointed out by Beller and Budge.[19] Traditionally, regional tracer concentration <50% of normal zone (or 60% in some reports) indicates a *low probability* of recovery. It has been argued that the end-point of ''viability assessment'' itself is not well defined, since an improvement in outcome could occur without improvement in regional function and an improvement in quality of life could be observed without improvement in survival.[1] These issues notwithstanding, our report addresses two important aspects: decision-making in managing ICM patients and the prediction of outcome as defined by survival.

PRIOR STUDIES

Obviously, the clinical decision to proceed with CR vs MT in patients with ICM is complex and depends on multiple factors, only one of which is myocardial viability. In the study by Beanlands et al,[20] there was no difference in outcome between patients randomized to receive viability assessment (using F-18 fluorodeoxyglucose positron emission tomography) vs not. Impressively, in the subset of patients in whom recommendations from the viability assessment were adhered to, there was a significant benefit. Post hoc analysis of the 182 patients who underwent viability assessment revealed that in the presence of significant myocardial viability (≥7% LV perfusion-metabolism mismatch in this study) CR reduced the composite outcome of cardiac death, myocardial infarction, or cardiac hospitalization at 1 year but not in its absence.[21] Most of that improvement was due to reduction in rehospitalization rate, an important quality of life measure. Unlike our cohort, this

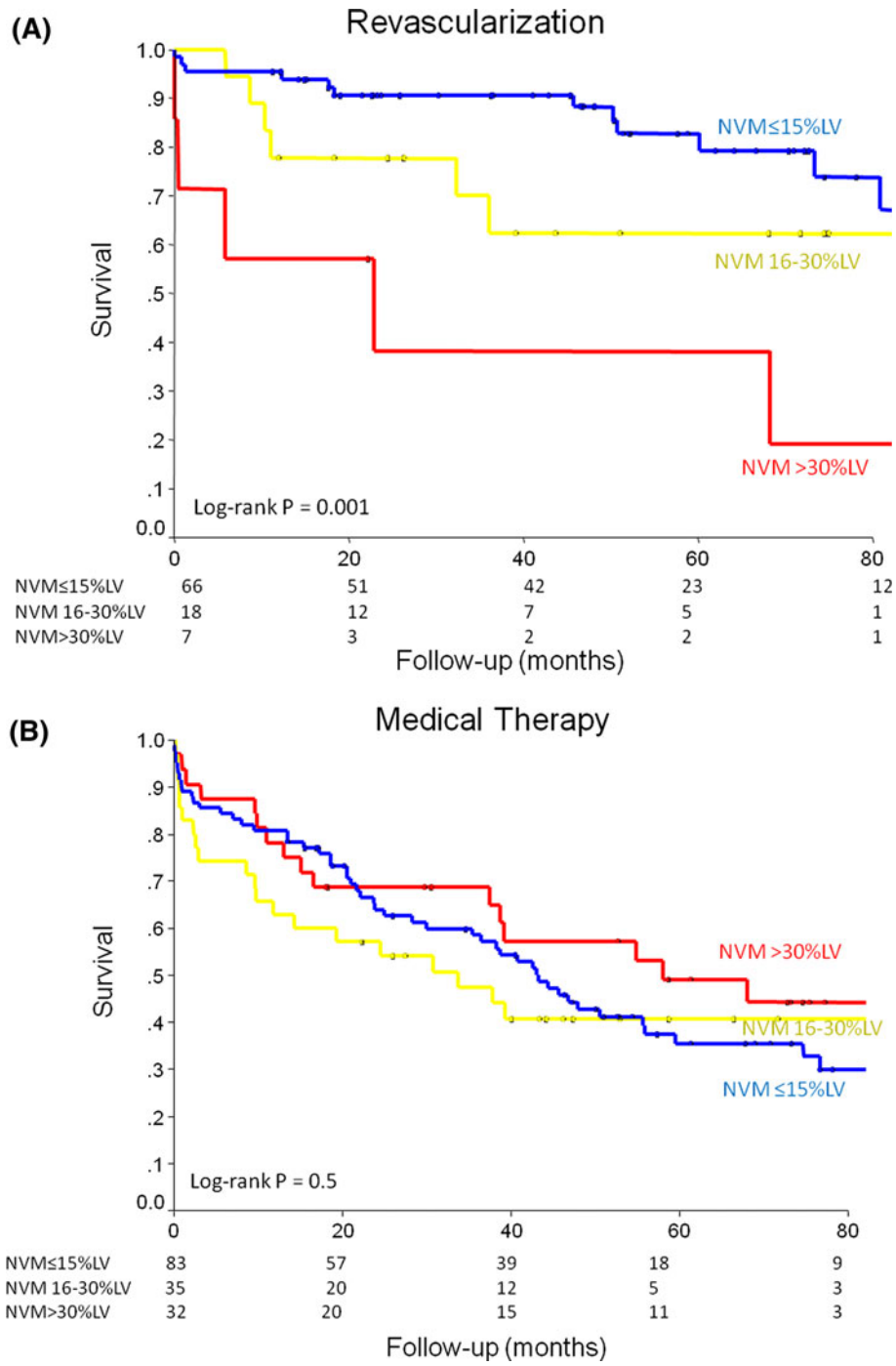

Figure 2. Kaplan-Meier analysis for survival according to the extent of nonviable myocardium (NVM) on myocardial perfusion imaging. Patients who underwent CR had higher mortality with increasing extent of NVM (**A**), but the extent of NVM did not affect survival in patients managed medically (**B**).

study was not powered to detect differences in mortality. Patients who underwent CR in our study had a better survival than patients treated medically even after adjustments for other important variables (Table 3), in agreement with earlier observations.[22] Prior reports (mostly retrospective, observational from single centers and meta-analyses of these studies) have shown that patients with viable myocardium have better prognosis when managed with CR while in the absence of viability there is no advantage of CR over MT.[1,5,23,24] In one

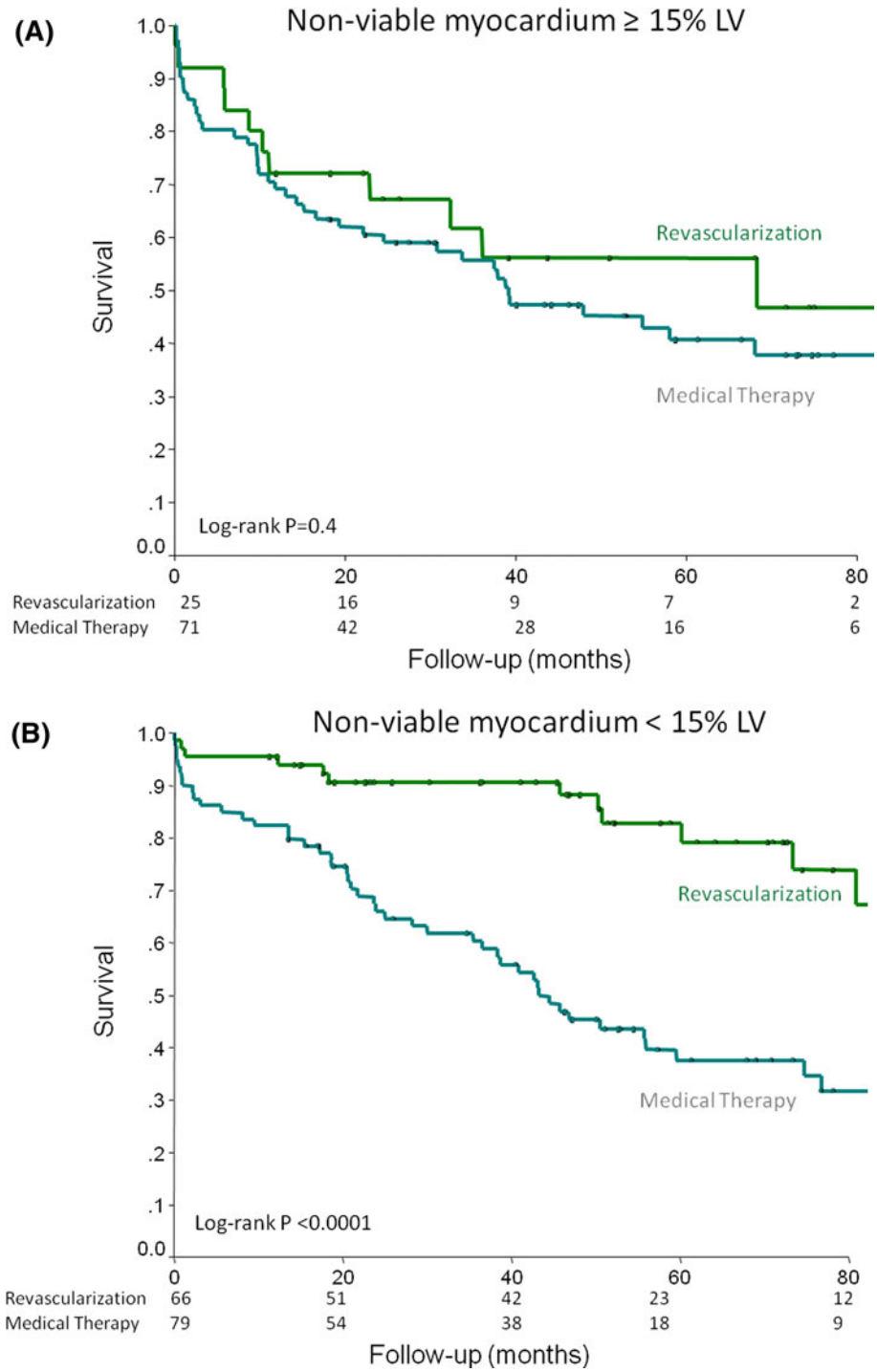

Figure 3. Kaplan-Meier analysis for survival according to management strategy and extent of nonviable myocardium. In patients with large area of nonviable myocardium (≥15% LV) the management strategy did not affect survival (**A**) but in those with smaller defects survival was better in those who underwent CR (**B**).

study, MT with carvedilol, was shown to improve LVEF in patients with viable myocardium.[25] Our results are in agreement with these findings but used automated analysis while most prior studies used visual analysis (visual scoring of either 17 or 20 segment models).[8] The automated analysis, though known and available for a long time, has only recently been advocated as a superior method to visual analysis.[7,26] Our quantitative analysis,

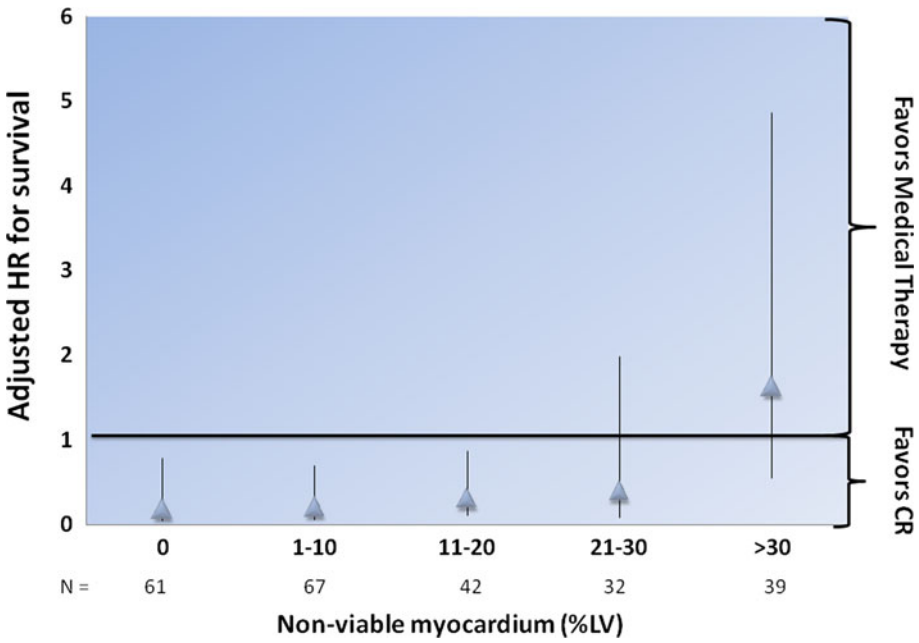

Figure 4. Hazard ratios for survival with CR according to the extent of nonviable myocardium. CR was associated with improved survival over medical therapy in patients with an area of nonviable myocardium ≤20% LV but not larger. HRs were adjusted for the covariates listed in Table 3. The number of patients in each category is indicated below the graph.

for example, allowed us to estimate a 5% increased risk of death in patients who underwent CR for every 1% LV increase in the extent of nonviable myocardium. Similar estimates were also possible for the effect of LVEF and LV volumes on mortality. Although our quantitative data were correlated with the traditionally used semi-quantitative data derived from the 17-segment model, and both models could be used to predict mortality, the associations were more robust for the quantitative model especially in its ability to identify a subset of patients who would not benefit from CR.

In addition to identifying predictors of mortality in this population, our study identifies factors associated with management decisions regarding CR vs MT. LV dilation is a known predictor of poor outcome after CR even in patients with myocardial viability.[27] In this study, LV volume was a predictor of poor outcome but not an independent factor in the decision for CR, likely because it was not systematically reported to the treating physician in a quantitative manner. Further, the presence of a large area of the LV that is nonviable also did not factor into the decision making (Table 2). As detailed above, the group of patients with a large area of nonviable myocardium did not benefit from CR (Figures 3a and 4) and those who did undergo CR had a much worse survival than patients with a small-sized nonviable myocardium (Figure 2a). Also, resting ischemia was not different between the CR and medical groups and did not affect outcome in either group, but rTID favored CR with an adjusted OR of 4.5. The extent of resting ischemia was small in our patients similar to the degree of flow-metabolism mismatch in the study by Beanlands et al[20] Both prior CABG and a history of ventricular arrhythmias favored MT over CR because of the known additional risk.[28-30] Another important factor that weighed in favor of proceeding with CR in our cohort was the presence of chest pain. The Coronary Artery Surgery Study showed a survival benefit for CABG in patients with depressed LVEF, this benefit was limited to patients who were symptomatic with chest pain.[31] The Surgical Treatment for Ischemic Heart Failure trial has recently finished enrolling patients and might help in defining the role of CABG in patients with low LVEF without chest pain.[32] The number of studies that have addressed the role of viability assessment on the decision-making process in patient management and on survival are limited.[33,34] The decision to proceed with CR might also depend on runoff of target vessels and a number of other factors that were not included in our analysis such as target vessels, associated conditions such as mitral regurgitation requiring repair or replacement, physiological age and wishes and expectations of the patients. It is hard to believe that imaging data alone could be the only decision maker for or against CR.

LIMITATIONS OF THE STUDY

There are several limitations to this study. Our sample population is derived from a single tertiary care academic institution and the study is observational with the inherent limitations of any study of this nature. It is inevitable that we have missed patients with ICM who were not referred for MPI. At our institution, however, the vast majority of viability assessment is performed with MPI. Unfortunately, an assessment of functional status was not available for the majority of these patients and therefore was not included in the analysis. Most of the patients in this report were ''too sick'' to undergo stress testing although stress testing with Tc-99m sestamibi has been part of the full protocol in our laboratory for many years in addition to the rest-redistribution thallium-201.[35] The stress results were not discussed here because they were available in a small subset of patients. The low prevalence of ischemia in our patients is related to patient selection and the fact that these studies were at rest and not with stress. It may also conceivably be due to the fact that automated methods may underestimate rest ischemia as the detection is subject to the need of a normal database, which is hard to define in this group of patients who often have LV dilatation and wall thinning.

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