Long-Term Survival of Patients with Viable and Nonviable Aneurysms Assessed by ^{99m}Tc-MIBI SPECT and ^{18}F-FDG PET: A Comparative Study of Medical and Surgical Treatment

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The prognostic value of myocardial viability assessment on left ventricular (LV) aneurysms remains undetermined. We aimed, first, to evaluate the long-term survival benefit of assessing the viability of the aneurysmal myocardium in patients with ischemic cardiomyopathy and, second, in the revascularization subgroup, to compare the short-term effects on LV function and clinical symptoms in patients treated by revascularization alone or by revascularization plus aneurysmectomy. **Methods:** Seventy consecutive patients with an LV aneurysm who underwent ^{99m}Tc-sestamibi SPECT and ^{18}F-FDG PET were followed up for a median of 6.8 y (range, 0.1–8.8 y). Only cardiac death during follow-up served as the endpoint. Patients were classified into 4 groups by aneurysmal viability and by treatment strategy (medical or surgical). Further, the effects of aneurysmectomy on LV function at 3 mo were evaluated by an analysis of revascularized patients grouped by aneurysmal viability and by aneurysmectomy. **Results:** Twenty-four patients were assigned to medical therapy, and 46 patients were assigned to surgery (18 revascularization alone and 28 revascularization plus aneurysmectomy). The annual cardiac mortality rate in patients with a viable aneurysm treated medically ($n = 10$) was significantly higher than that in patients with a viable aneurysm treated surgically ($n = 23$) (11.6% vs. 1.5%, $\chi^2 = 12.87$, $P < 0.0001$) and was also significant higher than that in patients with a nonviable aneurysm treated medically ($n = 14$) ($\chi^2 = 4.13$, $P < 0.05$) or surgically ($n = 23$) ($\chi^2 = 10.46$, $P = 0.001$). Multivariate analysis showed that the aneurysmal mismatch score ($P = 0.003$) and surgical therapy ($P = 0.001$) were independent predictors of cardiac death. Improvement of LV function and symptoms after revascularization ($P < 0.05$) was observed in patients with revascularization plus aneurysmectomy and in patients with a viable aneurysm and revascularization only. **Conclusion:** Viability in LV aneurysm in patients with ischemic cardiomyopathy was a negative independent predictor of survival. Compared with medical therapy, coronary revascularization was associated with improved long-term survival, symptoms, and LV function in patients with a viable aneurysm. These findings warrant further prospective investigations.

Key Words: coronary disease; aneurysm; myocardial viability; survival

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Leftventricle (LV) aneurysm is a complication of acute myocardial infarction that may lead to LV remodeling and to progressive congestive heart failure (CHF), thromboembolic events, arrhythmias, and sudden cardiac death (*1–4*). Patients with LV aneurysms and CHF-related symptoms have a poor prognosis if treated medically (*2*). Surgical resection of an aneurysm together with coronary artery bypass grafting can significantly improve LV function, clinical symptoms, and survival (*4,5*). However, because surgery is associated with a relatively high perioperative mortality, the identification of high-risk patients who are likely to benefit most from revascularization is desirable (*4,5*).

Previous investigations have focused on assessing myocardial viability and its prognostic value in patients with ischemic cardiomyopathy and LV dysfunction (*6–10*). Myocardial viability in these patients was found to be associated with a high risk of cardiac death, which was significantly reduced after revascularization (*6–10*). To date, relatively little information has become available on the prognostic implications of myocardial viability in LV

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aneurysms. Earlier studies either excluded patients with LV aneurysms (*11*) or did not specifically address the issue of myocardial viability in aneurysms (*9,12*). Aneurysmectomy together with revascularization has been reported to lead to an improvement in LV function that was attributed to a postrevascularization increase in contractile function in the nonaneurysmal myocardium (*13,14*). Because these investigations did not include comparison patients without aneurysmectomy, the effects of aneurysmectomy on prognosis have not been conclusively documented.

The aims of the current retrospective study were, first, to evaluate the long-term survival benefit of assessing the viability of the aneurysmal myocardium in patients with ischemic cardiomyopathy and, second, in the revascularization subgroup, to compare the short-term effects on LV function and clinical symptoms in patients treated by revascularization alone or by revascularization plus aneurysmectomy.

MATERIALS AND METHODS

Study Population

Patients were recruited from a study population referred to the Cardiovascular Institute and Fu Wai Hospital between March 1997 and December 1999 for viability assessment with ^{99m}Tc-sestamibi SPECT rest perfusion imaging and ^{18}F-FDG PET metabolic imaging. Inclusion criteria were prior myocardial infarction and symptoms of CHF, which was expressed by New York Heart Association heart failure class; diminished LV ejection fraction (LVEF) (≤50%); and LV aneurysm demonstrated by contrast ventriculography or echocardiography. Patients with recent myocardial infarction (<8 wk), rheumatic valvular disease, and acute pulmonary embolism were excluded. The study protocol was approved by the ethics committee of the Cardiovascular Institute and Fu Wai Hospital.

Coronary Angiography

Selective coronary angiography was performed within 4 wk of the myocardial viability study. Two experienced observers unaware of the clinical data visually assessed the angiograms. Significant coronary artery disease was defined as stenosis of at least 70% of the luminal diameter in at least 1 major coronary artery or a major branch. Biplanar left ventriculography was performed in the right and left anterior oblique projections. Regional wall motion was assessed visually in 7 LV segments (anterior, anterolateral, apical, inferior, posterior, septal, and posterolateral) and was graded on a 5-point scale (normal, moderately hypokinetic, severely hypokinetic, akinetic, or dyskinetic). In accord with the Coronary Artery Surgery Study (*15*), an LV aneurysm was defined as a discrete and thinned segment of the LV wall protruding from the angiographic outline of the LV chamber, with regional akinesis or dyskinesis. The presence of an LV aneurysm was verified intraoperatively by visual inspection and palpation, based on distinct bulging of the epicardial surface in the region of a prior myocardial infarction that was also associated with akinesis or dyskinesis.

Assessment of Myocardial Viability

Myocardial viability was assessed with ^{99m}Tc-sestamibi SPECT rest perfusion imaging and ^{18}F-FDG PET metabolism imaging, using a 2-d protocol (*7,16*). Two hours after injection of ^{99m}Tc-sestamibi (740–925 MBq) at rest, perfusion images were obtained over a 360° arc with a triple-head SPECT system (Siemens Medical Systems) equipped with a low-energy, all-purpose, parallel-hole collimator. Images were reconstructed with filtered backprojection and displayed as short-axis and horizontal and vertical long-axis slices.

Myocardial ^{18}F-FDG images were obtained as described previously (*7,16*), using a whole-body PET scanner (PET-B03; Beijing High Energy Institute) with 2 bed positions, providing 14 tomographic slices. Patients were studied with the glucose-loading method or a regular short-acting insulin injection according to the serum glucose level after an overnight fast (*7*). ^{18}F-FDG (296–370 MBq; Chinese Atomic Energy Institute) was administered intravenously; images were acquired after 1 h for 20–25 min (up to 20 million counts) and formatted into a 128 × 128 matrix. Transaxial images were reconstructed using the Butterworth-filtered backprojection method (order, 5; cutoff frequency, 0.30) and displayed as short-axis and horizontal and vertical long-axis slices. Because the PET slice thickness was only 3.33 mm, 2 contiguous PET slices were summed so that the PET and SPECT slice thicknesses were similar (6.7 and 6.4 mm, respectively).

Analysis of SPECT and PET Images

Two experienced observers, unaware of the clinical data, graded the myocardial activity in 9 segments (apex, anterior, anterobasal, inferior, posterior, anteroseptal, inferoseptal, anterolateral, and inferolateral) (Fig. 1). A 9-segment model was used rather than the standard 17-segment model of our prior study (*7,16*) and another study (*17*) because the 9-segment model better separated aneurysmal from nonaneurysmal regions and better corresponded to echocardiography. The LV contained the aneurysmal and nonaneurysmal regions (perianeurysmal plus remote aneurysmal). The aneurysmal segment was defined by left ventriculography, and all segments closely surrounding the aneurysmal region were considered perianeurysmal. The segment with the highest perfusion activity was defined as normal, and the relative perfusion and metabolic activity in the residual segments were graded on a 4-point scale where 0 is normal radiotracer activity, 1 is moderately reduced activity, 2 is severely reduced activity, and 3 is absence of activity.

To examine the prognostic value of viable myocardium in different myocardial regions, we determined myocardial viability, expressed as the summed mismatch score, separately for the aneurysmal segment, the aneurysmal plus perianeurysmal segments, and the nonaneurysmal segments. First, the summed perfusion and ^{18}F-FDG scores for the LV were obtained as the sum of scores in 9 segments. The mismatch score of the LV was calculated as the summed perfusion score minus the summed ^{18}F-FDG score. Further, the mismatch score was then calculated for the aneurysmal region, the aneurysmal plus perianeurysmal regions, and the

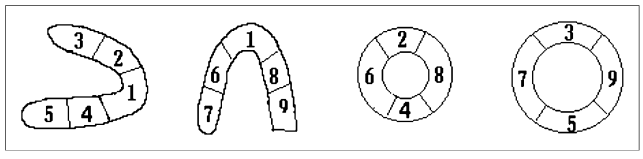

FIGURE 1. Nine-segment model of myocardial perfusion and metabolism (1 = apical; 2 = anterior; 3 = anterobasal; 4 = inferior; 5 = posterior; 6 = anteroseptal; 7 = inferoseptal; 8 = anterolateral; 9 = inferolateral).

nonaneurysmal regions. The mismatch score represents the extent and severity of myocardial viability, which was similar with the polar map approach (*18*). In accord with experience from our previous viability study (*7,16*), viability in aneurysms was defined as a mismatch score of 2.0 or greater. Two examples of a viable and a nonviable aneurysm are shown in Figure 2.

Echocardiography

Apical 2-chamber and 4-chamber views and parasternal short-axis and long-axis views on 2-dimensional echocardiography (Toshiba-380; Toshiba) were recorded on videotape. The LVEF was calculated from the apical 4-chamber view using Simpson's method, and the end-diastolic diameter of the LV was measured. Regional wall motion was graded in 9 LV segments (the same as for the SPECT and PET images) (*16*) as normal, mildly hypokinetic, severely hypokinetic, akinetic, or dyskinetic.

Follow-Up

LV function was reevaluated by 2-dimensional echocardiography 3 mo after revascularization. Symptoms related to CHF were followed at 3 and 6 mo after revascularization. Long-term follow-up was performed by review of patients' clinical records and by phone contact with patients or their relatives. The average follow-up time was 6.0 ± 2.7 y (median, 6.8 y; range, 0.1–8.8 y). The only endpoint was cardiac death, including sudden death (patient died within 1 h after onset of cardiac symptoms), due to recurrent myocardial infarction and CHF (with clinical records and documentation).

Statistical Analysis

Data were analyzed using SPSS software, version 13.0 (SPSS Inc.). Continuous data were expressed as the mean ± SD. Estimated survival was expressed as a percentage ± SE. The mean values of continuous variables were compared between groups by 1-way ANOVA followed by the Scheffé post hoc test. Intragroup differences with surgical therapy were analyzed by paired *t* tests. Categoric data were expressed as a percentage, and the χ^2 test was used (with Yates correction or the Fisher exact test in smaller sample sizes). The Cox proportional hazards regression analysis model was used to identify independent predictors of cardiac death. All variables were first assessed by univariate Cox proportional hazards regression analysis (Table 1). Only variables with a statistically significant ($P < 0.05$) association with survival were included in the multivariate model, which was created by a forward stepwise method. Cardiac survival curves were generated by the Kaplan–Meier method and compared by the log-rank test. Statistical significance was defined as a P value of less than 0.05.

RESULTS

Of the 73 patients initially enrolled in the study, 3 could not be followed up and were excluded from the analysis. Accordingly, the final study population consisted of 70 patients with LV aneurysms (66 men and 4 women; mean age, 57 ± 10 y; mean LVEF, 36% ± 8% by 2-dimensional echocardiography and 32% ± 8% by radionuclide imaging). Demographics and clinical findings are summarized in Table 1. The aneurysm most frequently involved the LV apex ($n = 35$) and extended into the anterior wall ($n = 15$) or anterolateral wall ($n = 18$).

The patients were assigned to medical or surgical therapy by their clinicians. Twenty-four patients were assigned to medical therapy, 18 to revascularization alone (coronary artery bypass grafting in 10 and percutaneous coronary intervention in 8), and 28 to revascularization plus aneurysmectomy. Thus, 46 patients were treated by surgical therapy, which was performed 33 ± 23 d (median, 19 d) after the SPECT/PET viability study. Four patients had severe CHF and were assigned to medical therapy. Viability information was referred to by clinicians in 11.4% (8/70) of patients and did not influence decision making for most patients (87%, 61/70). The surgical plan was changed to medical therapy in 1 patient because of no viable myocardium and no angina symptoms.

Clinical characteristics did not significantly differ ($P > 0.05$) between patients treated medically and patients referred for revascularization with or without aneurysmectomy, except that patients in the medical group were older, and fewer had type 2 diabetes ($P < 0.05$), than patients in the surgical

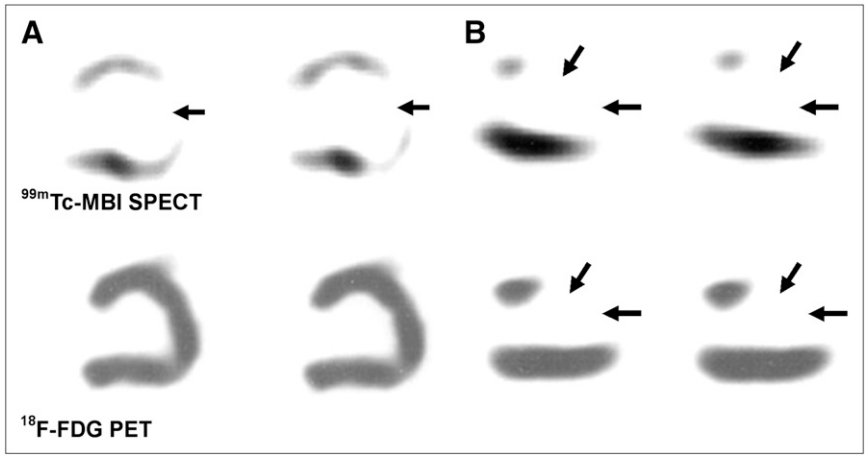

FIGURE 2. Examples of images obtained with ^{99m}Tc-MIBI SPECT and ^{18}F-FDG PET. (A) A 68-y-old man with history of anterior wall myocardial infarction. Coronary angiography shows left main artery disease, 2-vessel disease, and apical aneurysm. Perfusion–metabolism mismatch, which indicates myocardial viability, was observed in aneurysmal (apex), perianeurysmal (anterior and inferior), and remote aneurysmal (basal anterior and posterior) regions. Patient underwent coronary artery bypass grafting and aneurysmectomy, LVEF was improved from 30% to 50% after surgery. (B) A 48-y-old man with history of anterior wall myocardial infarction. Coronary angiography shows 2-vessel disease and anteroapical aneurysm. Perfusion–metabolism match, which indicates absence of myocardial viability, was observed in aneurysmal (apex and anterior) and nonaneurysmal regions.

TABLE 1
Clinical Characteristics of the Patients

Characteristic	Total (n = 70)	Medical (n = 24)	Revascularization alone (n = 18)	Revascularization plus resection (n = 28)
Age (y)	57 ± 10	61 ± 10	55 ± 10*	54 ± 9*
Male sex	66 (94)	25 (89)	16 (89)	25 (89)
Hypertension	35 (50)	11 (39)	9 (50)	15 (54)
Diabetes	7 (10)	0 (0)	3 (17)*	4 (14)*
Hyperlipidemia	11 (16)	5 (18)	3 (17)	3 (11)
Q-wave myocardial infarction	58 (83)	23 (82)	13 (72)	25 (89)
Prior PTCA	2 (3)	0 (0)	1 (6)	1(4)
New York Heart Association class III–IV	32 (46)	12 (50)	8 (44)	12 (43)
LVEF by echocardiography (%)	36 ± 8	37 ± 9	38 ± 7	35 ± 7
LVEF by radionuclide (%)	32 ± 8	32 ± 10	34 ± 11	32 ± 8
End-diastolic diameter (mm)	64 ± 7	67 ± 9	62 ± 7	64 ± 6
Mild mitral regurgitation	20 (29)	9 (38)	5 (28)	6 (21)
One-vessel disease	19 (27)	5 (21)	8 (44)	6 (21)
Two-vessel disease	25 (36)	8 (33)	5 (28)	12 (43)
Three-vessel disease	26 (37)	11 (46)	5 (28)	10 (36)
Distal disease	16 (23)	6 (25)	3 (17)	7 (25)
Aneurysmal size (% LV)	38 ± 13	40 ± 13	33 ± 12	40 ± 13
Location of aneurysm				
Apical	35 (50)	12 (50)	11 (61)	12 (43)
Anteroapical	15 (21)	7 (29)	3 (17)	5 (18)
Anterolateral	18 (26)	5 (21)	4 (22)	9 (32)
Posteroinferior	2 (3)	0 (0)	0 (0)	2 (7)
Summed perfusion score				
Aneurysm	4.7 ± 2.2	4.8 ± 2.2	4.4 ± 2.3	4.7 ± 2.3
Nonaneurysm	8.1 ± 3.4	8.3 ± 4.2	8.2 ± 3.4	8.0 ± 2.9
Aneurysm plus perianeurysm	9.9 ± 3.3	8.1 ± 2.6	7.3 ± 2.8	8.3 ± 2.4
LV	12.9 ± 3.6	13.2 ± 3.9	12.6 ± 3.3	12.8 ± 3.6
Summed mismatch score				
Aneurysm	1.6 ± 1.8	1.9 ± 2.4	1.6 ± 1.4	1.3 ± 1.4
Nonaneurysm	3.2 ± 3.4	3.1 ± 3.2	4.0 ± 4.5	2.7 ± 2.6
Aneurysm plus perianeurysm	3.3 ± 3.3	3.4 ± 3.4	3.4 ± 3.2	3.1 ± 3.3
LV	4.7 ± 4.3	4.9 ± 4.5	5.6 ± 5.0	3.9 ± 3.5

*$P < 0.05$ vs. medical group.
Data are number (with percentage in parentheses) or mean ± SD.

group. Importantly, the summed perfusion score and mismatch score of the aneurysmal and nonaneurysmal regions did not differ significantly among the 3 groups (Table 1).

During follow-up, there were 16 cardiac deaths, including 1 patient who died within 30 d of surgery (perioperative mortality, 2.6%). Two patients who were in the surgical group and died of cancer were censored. As depicted in Figure 3, the annual cardiac death rate was significantly higher in patients treated medically than in patients treated by revascularization with or without aneurysmectomy ($\chi^2 = 11.15$, $P = 0.004$) but did not differ significantly between treatment with revascularization alone and together with aneurysmectomy ($P > 0.05$).

Cardiac Survival by Aneurysmal Viability and by Treatment

According to aneurysmal viability and treatment strategy (medical vs. surgical), patients were divided into 4 groups (Fig. 4): no viability in aneurysm and treated medically (group 1, $n = 14$); no viability in aneurysm and treated surgically (group 2, $n = 23$); viability in aneurysm and treated medically (group 3, $n = 10$); and viability in aneurysm and treated surgically (group 4, $n = 23$).

Demographic and clinical characteristics did not reveal any significant difference among the 4 groups ($P > 0.05$), except that patients in group 3 were older, and fewer had hypertension ($P < 0.05$). However, differences in mismatch score existed between groups (Table 2), by definition. As shown in Figure 5, in patients with a viable aneurysm, the annual cardiac mortality in group 3 (11.6%) was significantly higher than that in group 4 (vs. 1.5%, $\chi^2 = 12.87$, $P < 0.0001$) and significantly higher than that in groups 1 (vs. 4.8%, $\chi^2 = 4.13$, $P < 0.05$) and 2 (vs. 2.2%, $\chi^2 = 10.46$, $P = 0.001$). Groups 1 and 2 did not differ significantly ($P > 0.05$).

Prediction of Cardiac Death by Cox Proportional Analysis

Variables significantly associated with cardiac death are listed in Table 3. Univariate Cox hazard regression

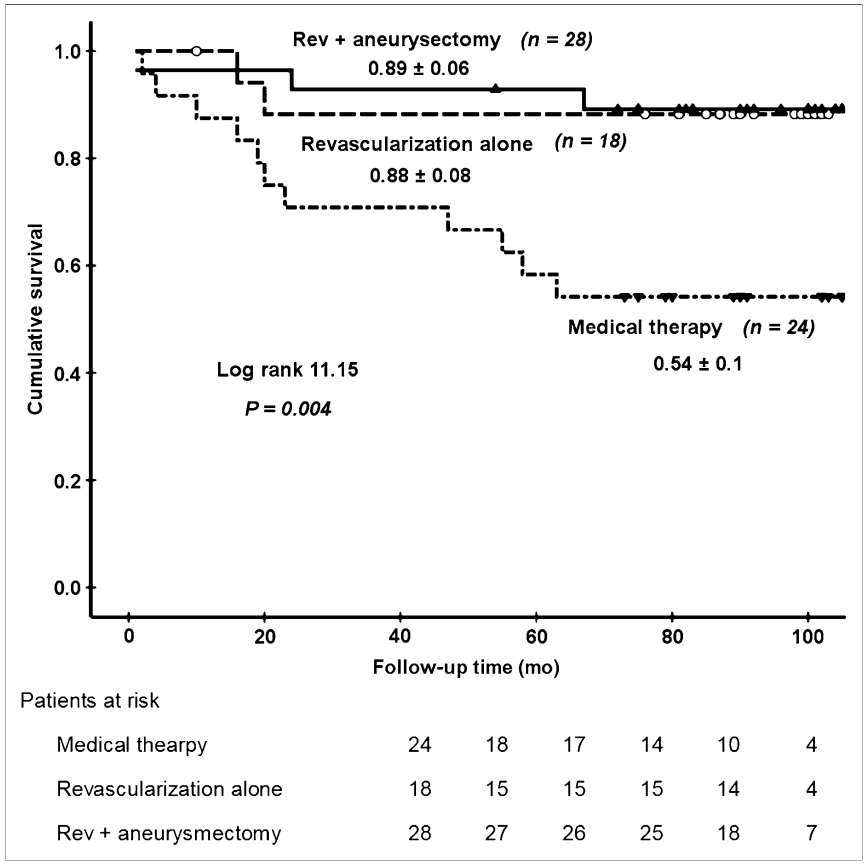

FIGURE 3. Kaplan–Meier cardiac survival curves show that estimated cardiac survival in patients treated medically was significantly lower than that in patients treated by revascularization alone or by revascularization plus aneurysmectomy ($P = 0.004$). Rev = revascularization.

analysis showed that LVEF ($P = 0.023$), mitral regurgitation ($P = 0.02$), mismatch score of aneurysm ($P = 0.005$), mismatch score of aneurysm plus perianeurysm ($P < 0.05$), mismatch score of LV ($P < 0.05$), and surgical therapy ($P = 0.003$) were independent predictors for cardiac death. Multivariate Cox analysis identified the aneurysmal mismatch score as an independent negative predictor of survival ($P = 0.003$), and surgical therapy was an independent positive predictor of survival ($P = 0.001$). Of interest, neither the mismatch score for the entire LV myocardium nor the mismatch score for myocardium outside the aneurysm proved to be a statistically significant independent predictor. Moreover, even when perfusion metabolism findings in myocardial segments adjacent to the aneurysm, that is, in the perianeurysmal region, were added to form a summed aneurysmal and perianeurysmal mismatch score reflecting a large, contiguous mismatch region, this parameter was found on multivariate analysis not to be significantly associated with survival.

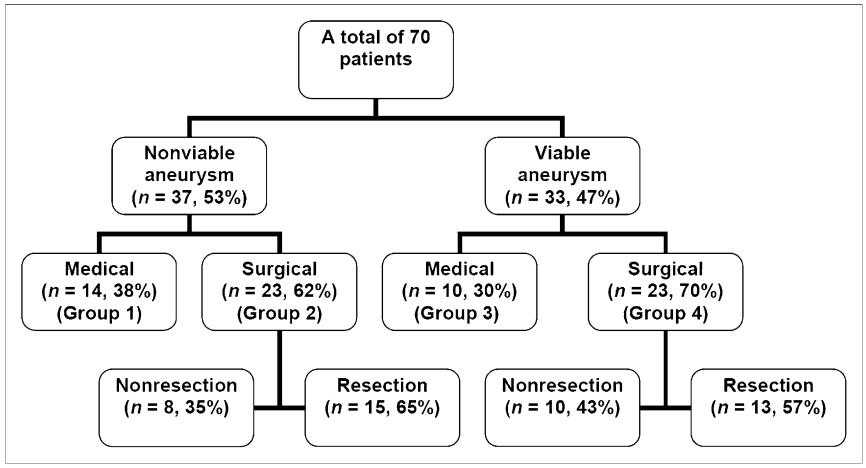

FIGURE 4. Flow diagram for group-outcome analysis.

TABLE 2
Clinical Characteristics of the 4 Groups

Characteristic	Nonviable aneurysm		Viable aneurysm		P
	Medical (group 1, $n = 14$)	Surgical (group 2, $n = 23$)	Medical (group 3, $n = 10$)	Surgical (group 4, $n = 23$)	
Age (y)	58 ± 11	54 ± 10	62 ± 8*	55 ± 9	0.017
Hypertension	7 (50)	9 (39)	2 (20)†	17 (74)	0.019
Diabetes	0 (0)	3 (13)	0 (0)	4 (14)	0.187
Prior percutaneous transluminal coronary angioplasty	0 (0)	0 (0)	0 (0)	2 (9)	0.080
LVEF by echocardiography (%)	38 ± 10	36 ± 7	36 ± 8	36 ± 7	0.947
End-diastolic diameter (mm)	67 ± 10	63 ± 6	67 ± 8	64 ± 7	0.475
Mitral regurgitation	5 (36)	8 (35)	4 (40)	3 (13)	0.106
New York Heart Association class III or IV	4 (29)	10 (44)	6 (60)	10 (44)	0.211
Two-vessel disease	5 (36)	9 (39)	3 (30)	8 (35)	0.828
Three-vessel disease	7 (50)	6 (26)	4 (40)	9 (39)	0.828
Distal disease	4 (29)	6 (26)	2 (20)	4 (17)	0.372
Summed perfusion score					
Aneurysm	4.9 ± 2.1	4.9 ± 2.3	5.0 ± 2.5	4.3 ± 2.2	0.783
Nonaneurysm	9.4 ± 3.5	8.2 ± 3.6	5.9 ± 3.9	8.1 ± 3.0	0.142
Aneurysm plus perianeurysm	8.4 ± 2.2	8.4 ± 2.6	7.7 ± 2.5	8.0 ± 2.6	0.545
LV	14.2 ± 3.3	13.0 ± 3.7	10.9 ± 3.8	12.5 ± 2.9	0.149
Summed mismatch score					
Aneurysm	0.2 ± 0.4	0.4 ± 0.4	3.7 ± 2.0†‡	2.5 ± 0.9‡	<0.0001
Nonaneurysm	2.1 ± 2.9	1.9 ± 3.1	4.5 ± 3.4	4.5 ± 3.5	0.022
Aneurysm plus perianeurysm	1.5 ± 2.0	0.7 ± 1.3	6.3 ± 2.9‡	5.6 ± 2.7‡	<0.0001
LV	2.5 ± 3.2	2.2 ± 3.2	8.5 ± 3.7§	7.0 ± 3.6‖¶	<0.0001

*$P < 0.05$ vs. groups 2 and 4.
†$P < 0.01$ vs. group 4.
‡$P < 0.0001$ vs. groups 1 and 2.
§$P < 0.01$ vs. groups 1 and 2.
‖$P < 0.01$ vs. group 1.
¶$P < 0.001$ vs. group 2.
Surgical = patients with revascularization alone and patients with revascularization plus aneurysmectomy.
Data are number (with percentage in parentheses) or mean ± SD.

Effect of Aneurysmectomy on Survival, Clinical Symptoms, and LV Function

The effects of aneurysmectomy on LV function at 3 mo and on long-term survival were evaluated by a subgroup analysis of revascularized patients grouped by aneurysmal viability and by aneurysmectomy (Fig. 4). Summed perfusion scores were similar in the 4 subgroups, whereas mismatch scores of aneurysm, by definition, were higher in the patients with than without myocardial viability (Table 4). CHF-related symptoms were comparable (Fig. 6) among the 4 subgroups at baseline but had significantly improved 3 mo after revascularization and aneurysmectomy in the nonviability group and in the patients with aneurysmal viability but without resection ($P < 0.05$). CHF-related symptoms further improved in 2 subgroups with viability at 6 mo. LVEF (Fig. 7) had significantly increased in the 2 subgroups with aneurysmectomy but also in patients with aneurysmal viability and with aneurysmectomy ($P < 0.05$). Finally, the long-term estimated cardiac survival did not differ statistically among these 4 subgroups ($P > 0.05$).

DISCUSSION

This study addressed the value of viability assessment in aneurysmal and nonaneurysmal myocardial regions for predicting the long-term cardiac survival of patients with ischemic cardiomyopathy and diminished LV function. The main findings were as follows: First, the aneurysmal mismatch score, used as a measure of the extent and severity of viability in the LV aneurysm, was a negative independent predictor for long-term cardiac survival. Second, surgical therapy was a positive independent predictor for long-term cardiac survival. Third, revascularization together with aneurysmectomy was associated with an improvement in CHF symptoms and in LVEF, and similar improvements were also observed in patients with a viable aneurysm who underwent revascularization alone, without aneurysmectomy.

Cardiac Survival by Aneurysmal Viability and by Treatment

Patients with an LV aneurysm usually have LV remodeling and hemodynamic changes and represent a high-risk

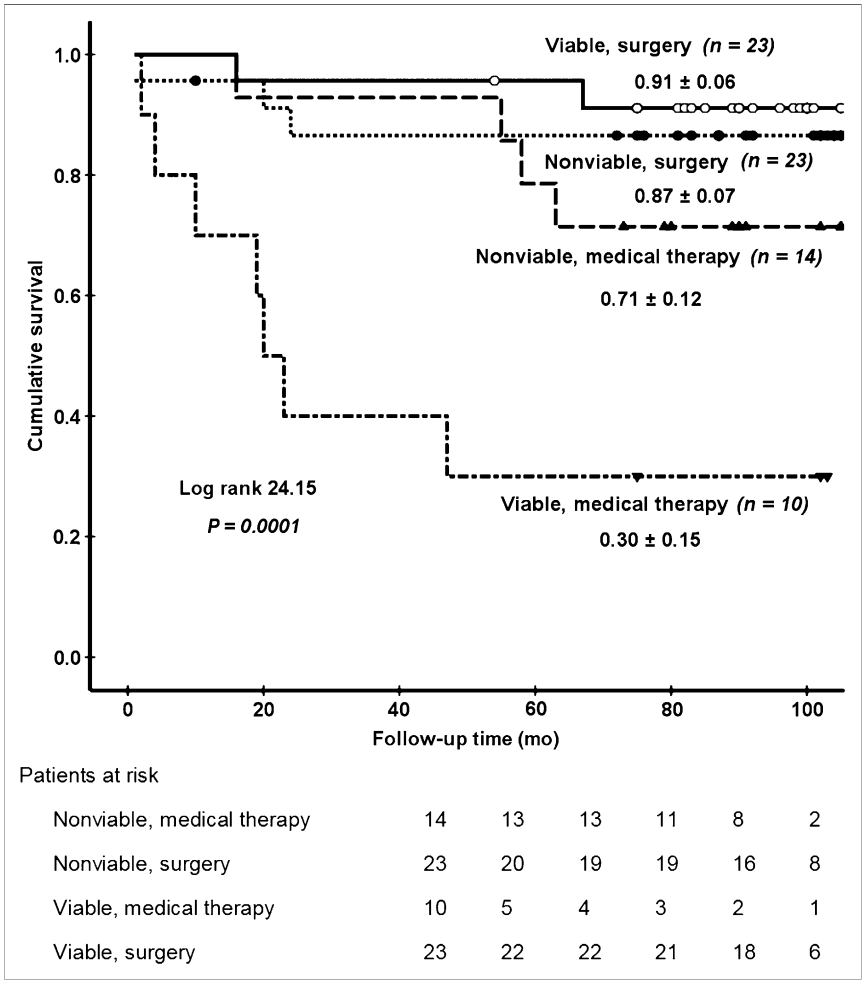

FIGURE 5. Kaplan–Meier cardiac survival curves for 4 groups. Estimated cardiac survival in group 3 was significantly lower than that in group 4 ($P < 0.0001$) and lower than that in group 1 ($P < 0.05$) and group 2 ($P < 0.01$). No significant survival difference was observed in the other 3 groups ($P > 0.05$).

population. Previous clinical studies addressed the prognostic value of the LV aneurysm, as determined by angiography (*2,4,15,19*), radionuclide angiography (*3*), or echocardiography (*1*). However, viability in aneurysmal regions was not determined in these studies. Whether viability in aneurysmal, nonaneurysmal, or aneurysmal-plus-perianeurysmal regions has different effects on survival has not been investigated yet. Some studies demonstrated that early formation of an aneurysm after acute myocardial infarction carries a high risk for cardiac death within 1 y that is independent of LVEF (*1,3*). In contrast, some studies reported that in patients with chronic coronary artery disease and LV aneurysm, the outcome was primarily related to age, extent of coronary disease, LV function and severity of heart failure, and residual nonaneurysmal contractility, whereas the presence of an aneurysm itself was not an independent predictor of survival (*4,15,19*). These different results and conclusions may be related to differences in how the aneurysm was defined and in patient populations and diagnostic techniques.

In our current population, traditional risk factors including age, New York Heart Association class, and diseased vessels were not significantly predictive of survival. Conversely, a statistically significant association was found between cardiac death and LVEF, mitral regurgitation, the mismatch score for the aneurysm, the mismatch score for aneurysmal-plus-perianeurysmal myocardium, and the mismatch score for the entire LV myocardium. Yet, on multivariate analysis, only the mismatch score for the aneurysm itself remained a significant predictor of cardiac death (in addition to the negative predictive value of surgical therapy).

Thus, as current and new findings indicate, in patients with ischemic cardiomyopathy and an LV aneurysm, the amount of viable myocardium in the aneurysmal region is indeed an independent predictor for cardiac death. The observations were consistent with earlier findings in patients with ischemic cardiomyopathy (*6–9*). One study has reported a direct association between the amount of viable myocardium and the incidence of cardiac death (*9*). Different, however, from that study was our finding that only viability localized in the aneurysmal myocardium, not in the remainder of the LV, contained statistically significant and independent prognostic information.

However, the exact reason for the independent predictive value of viable aneurysmal myocardium for an increased risk of cardiac death is uncertain. Two possible mechanisms

TABLE 3
Independent Predictors of Cardiac Death by Cox Univariate and Multivariate Analyses

Variable	Univariate analysis		Multivariate analysis	
	Hazard ratio	*P*	Hazard ratio	*P*
Age	1.02 (0.97–1.08)	0.45		
Sex	2.12 (0.48–9.32)	0.32		
Hypertension	0.40 (0.14–1.14)	0.085		
Diabetes	1.24 (0.28–548)	0.77		
Hyperlipidemia	0.68 (0.16–3.01)	0.62		
New York Heart Association class	1.60 (0.84–3.04)	0.151		
Vessel	1.54 (0.80–2.98)	0.197		
Distal disease	1.64 (0.57–4.74)	0.357		
Aneurysmal size (% LV)	1.01 (0.97–1.06)	0.34		
LVEF (%)	0.91 (0.85–0.98)	0.023		
End-diastolic diameter (mm)	1.05 (0.98–1.12)	0.196		
Mitral regurgitation	3.21 (1.20–8.59)	0.02		
Surgical therapy	0.19 (0.07–0.57)	0.003	0.16 (0.06–0.48)	0.001
Mismatch score of LV	1.13 (1.01–1.26)	0.023		
Mismatch score of aneurysm	1.42 (1.11–1.85)	0.005	1.40 (1.11–1.75)	0.003
Mismatch score of aneurysm plus perianeurysm	1.17 (1.03–1.34)	0.013		
Mismatch score of nonaneurysm	1.11 (0.98–1.27)	0.113		
Viability of aneurysm × surgery	0.25 (0.06–1.11)	0.069		
Mismatch score of aneurysm × surgery	0.64 (0.37–1.10)	0.107		

Data in parentheses are 95% confidence intervals.

might account for the independent predictive value, observed in the current study, of the mismatch score in LV aneurysms. The first relates to the arrhythmogenic potential of the aneurysmal border zone (*20*). The second relates to LV remodeling with "increased ventricular stretch" as a "possible mechanistic source of ventricular arrhythmia" (*21*). The high arrhythmogenic potential of viable myocardium is supported by heterogeneous remodeling of cells,

TABLE 4
Clinical Characteristics of Patients with Viable and Nonviable Aneurysms Treated Surgically

Characteristic	Nonviable		Viable		*P*
	Nonresection (*n* = 8)	Resection (*n* = 15)	Nonresection (*n* = 10)	Resection (*n* = 13)	
Male sex	7 (88)	13 (87)	9 (90)	12 (92)	0.618
Age (y)	53 ± 13	54 ± 8	54 ± 11	57 ± 8	0.810
Diabetes	1 (13)	2 (13)	2 (20)	2 (15)	0.780
Hypertension	3 (38)	6 (40)	6 (60)	9 (69)	0.342
New York Heart Association class	2.0 ± 0.8	2.8 ± 0.9	2.6 ± 0.5	2.1 ± 0.8	0.033
LVEF (%)	40 ± 7	34 ± 6	36 ± 7	37 ± 8	0.263
One-vessel disease	4 (50)	4 (27)	4 (36)	2 (15)	0.182
Two-vessel disease	2 (25)	7 (46)	3 (27)	5 (39)	0.854
Three-vessel disease	2 (25)	4 (27)	3 (27)	6 (46)	0.262
Summed perfusion score					
LV	12.1 ± 4.2	13.5 ± 3.5	12.4 ± 2.6	11.6 ± 3.2	0.626
Aneurysm	4.8 ± 2.9	4.8 ± 1.9	4.1 ± 2.1	4.5 ± 2.7	0.933
Nonaneurysm	7.8 ± 4.3	8.5 ± 3.4	8.0 ± 3.1	7.3 ± 2.2	0.726
Summed mismatch score					
LV	3.4 ± 4.9	1.5 ± 1.7	7.5 ± 4.4*	6.7 ± 3.1*	<0.0001
Aneurysm	0.4 ± 0.5	0.1 ± 0.4	2.6 ± 1.0†	2.5 ± 1.1†	<0.0001
Nonaneurysm	2.9 ± 4.7	1.4 ± 1.6	4.9 ± 4.3	4.2 ± 2.9	0.055
Estimated cardiac survival (%)	86 ± 13	87 ± 9	90 ± 10	92 ± 7	0.964

*$P < 0.01$ vs. nonviable aneurysm with resection.
†$P < 0.0001$ vs. nonviable aneurysm with and without resection.
Data are number (with percentage in parentheses), mean ± SD, or (for estimated cardiac survival) mean ± SE.

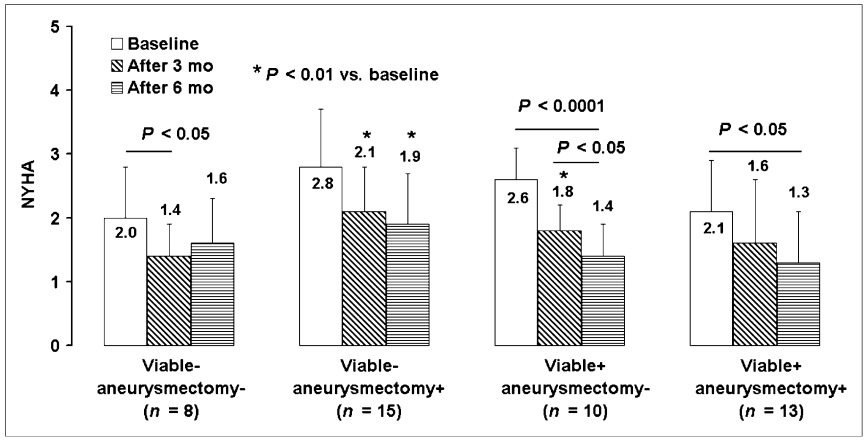

FIGURE 6. New York Heart Association (NYHA) class at baseline, 3 mo, and 6 mo after surgical therapy in 4 subgroups. Significant improvement of class after surgery was observed in all subgroups except patients without viability in aneurysm and without aneurysmectomy.

sympathetic dysinnervation, and increased susceptibility to sympathetic activation for ventricular arrhythmia in the border zone of hibernating myocardium as observed in animal experimental studies (*22–24*). Regional alterations in contractile function, including increased muscle fiber stretch and reduced contractility at the border zone (*25*), may exacerbate the vulnerability of the myocardial viability border, assuming it overlaps or extends beyond the aneurysmal border. Increased ventricular stretch associated with LV remodeling may also account for the high mortality of patients with a viable aneurysm. There may indeed be an interaction between LV remodeling and perfusion–metabolism mismatches in patients with poor LV function that is highly predictive of poor survival (*26*). It is possible that progressive cell loss in viable and remote myocardium as demonstrated both in animal experimental studies and in patients with ischemic cardiomyopathy (*27,28*) resulted in progressive LV remodeling, with increases in arrhythmogenic potential, and in the deterioration of CHF symptoms. Whether such progressive LV remodeling is accelerated in patients with LV aneurysms with residual viability remains uncertain. If, however, the magnitude of LV remodeling depends on the size of the infarct, and if progression of hibernating myocardium to scar tissue formation leads to infarct expansion, continued LV remodeling may have occurred in our patients with viable aneurysms.

Effects of Aneurysmectomy on LV Function and Cardiac Survival

The effects of aneurysmectomy together with revascularization on LV function were studied in only a small population. Consistent with prior studies (*5,13,14*), LV function and heart failure symptoms improved significantly after revascularization of the nonaneurysmal region in conjunction with aneurysmectomy, independent of the viability of the aneurysmal region. In patients with aneurysmectomy, LV function may have improved because of a decrease in LV volume, wall stress, or myocardial oxygen consumption or in part because the contractility of residual myocardium in the nonaneurysmal region was improved or

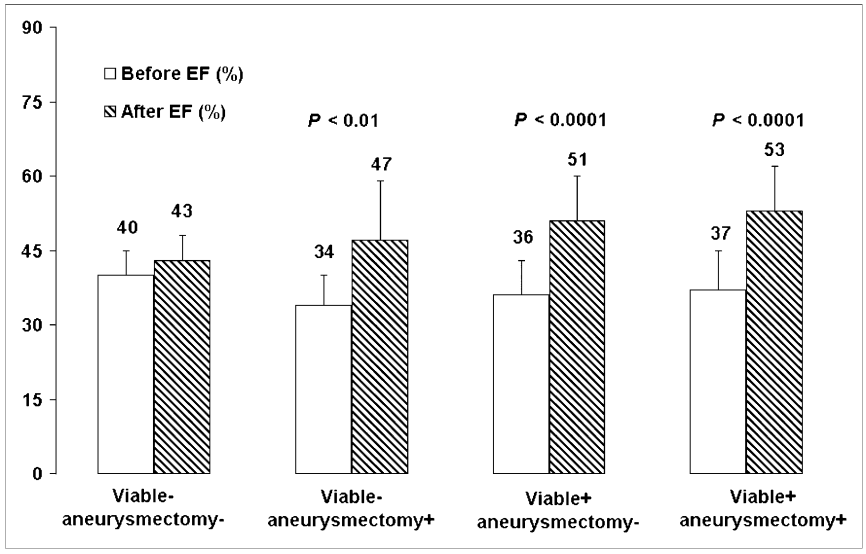

FIGURE 7. LVEF (%) at baseline and 3 mo after surgical therapy in 4 subgroups. Significant improvement of LVEF after surgery was observed in all subgroups except patients without viability in aneurysm and without aneurysmectomy.

protected by restoration of myocardial blood flow through revascularization (*14,29*). This improvement in LV function and heart failure symptoms was also noted 3 mo after revascularization of the viable myocardium in the aneurysmal and nonaneurysmal regions, rather than the aneurysmectomy region. Most likely, it resulted from a postrevascularization improvement in contractile function of the aneurysmal and nonaneurysmal portions of the LV. Thus, higher amounts of both aneurysmal and nonaneurysmal viable myocardium recovered their regional function after revascularization, contributing to the improvement of global function.

In addition, in view of the relatively small sample size, with the 3-mo follow-up to determine LV function after revascularization with and without aneurysmectomy, the current subgroup analysis does not provide definite answers but raises an intriguing hypothesis that revascularization of a viable aneurysmal region may be associated with an improvement of LV function comparable to that after revascularization together with aneurysmectomy. This warrants further investigations in larger populations and with long-term follow-up of LV function. Whether salvage rather than resection of viable myocardium affects long-term outcome remains uncertain. We found that, compared with revascularization alone, aneurysmectomy plus revascularization did not significantly affect long-term outcome, but the number of patients in our study was too small to allow us to draw definitive conclusions.

Study Limitations

Our study had several limitations. First, it was retrospective; the same limitation as for all available prognostic viability studies applies to the current study (*9*). Assignment of patients to medical treatment and revascularization alone or together with aneurysmectomy was not random and, thus, might have introduced a possible selection bias. However, 3 groups revealed similar clinical findings at baseline, except that renal function was not considered in the current study and patients treated by medical therapy were older, and fewer had diabetes. Further, viability information did not influence decisions about the treatment of most patients. A second limitation was the size of the study population, although to our knowledge, it represents the largest patient cohort reported to date with a long-term follow-up. Such information might be forthcoming from the Surgical Treatment for Ischemic Heart Failure trial currently in progress (*30*). A third limitation was that a 9-segment rather than the standard 17-segment model was used for image-based analysis of regional radiotracer activity concentrations and wall motion. The same segmentation approach had been used in our prior studies (*7,16*), as well as by another group (*17*), and afforded adequate evaluation and grading of perfusion and metabolism and of wall motion in LV aneurysms. A fourth limitation was that our study had the intrinsic technical limitation of SPECT perfusion imaging. Thus, the degrees of mismatch score may have been overestimated, particularly in the inferior wall. However, 50% (24/48) of segments showed viability in the inferior wall—a prevalence similar to that in the whole population (47%). Myocardial PET perfusion imaging and ^{18}F-FDG PET metabolism will overcome the technical limitation in further studies. Finally, the end-diastolic wall thickness of the aneurysmal region was not quantitatively measured in the current study. However, MRI and echocardiography studies have shown that dysfunctional segments with an end-diastolic wall thickness of less than 6 mm reflect areas with significant scarring (*31*). Further investigation is needed of the relationship between viability in the aneurysmal region and end-diastolic wall thickness.

CONCLUSION

LV aneurysmal viability in patients with ischemic cardiomyopathy was a negative independent predictor of survival. Compared with medical therapy, coronary revascularization was associated with improved long-term survival, symptoms, and LV function in patients with a viable aneurysm. These findings warrant further prospective investigations.

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