

# Independent and incremental prognostic value of left ventricular ejection fraction determined by stress gated rubidium 82 PET imaging in patients with known or suspected coronary artery disease

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**Background.** Whether left ventricular ejection fraction (EF) obtained by gated rubidium 82 positron emission tomography (PET) myocardial imaging can identify patients at risk for future cardiac events is unclear.

**Methods and Results.** Consecutive patients with known or suspected coronary artery disease who underwent dipyridamole stress gated Rb-82 PET imaging were evaluated. Scoring of perfusion was accomplished by use of a 17-segment model. EF was automatically generated. Patients were stratified based on summed stress scores (SSSs) (0-3, 4-8, or >8) and stress EF (>50%, 40%-49%, or <40%). All-cause mortality was determined by use of the Social Security Death Index. Of 1,441 patients, 132 (9.2%) died during mean follow-up of  $2.7 \pm 0.8$  years. Annualized mortality rates across SSS groups were 2.4% for SSS of 0 to 3, 4.1% for SSS of 4 to 8, and 6.9% for SSS greater than 8 ( $P < .001$ ). Similarly, annualized mortality rates were 2.4%, 6.2%, and 9.2% for the group with EF greater than 50%, group with EF of 40% to 49%, and group with EF lower than 40%, respectively ( $P < .001$ ). On multivariate analysis, the addition of EF to clinical and perfusion variables significantly increased the global  $\chi^2$  (73.3 to 107.7,  $P < .001$ ). Integration of EF with SSS significantly enhanced risk stratification.

**Conclusion.** EF assessed by stress gated Rb-82 PET imaging provides independent and incremental prognostic information and, hence, should be routinely incorporated in risk assessment. (J Nucl Cardiol 2008;15:745-53.)

**Key Words:** Rubidium radioisotopes • radionuclide imaging • positron emission tomography • exercise test • vasodilator agents • coronary arteriosclerosis • left ventricular function • prognosis • risk assessment

Left ventricular ejection fraction (EF), a major determinant of long-term survival in patients with known or suspected coronary artery disease (CAD),<sup>1-3</sup> can be

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accurately and reproducibly quantitated during electrocardiography (ECG)-gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI).<sup>4,5</sup> Because its quantification during SPECT imaging provides incremental prognostic information compared with perfusion assessment alone for stratifying individuals into various levels of cardiac risk,<sup>6-9</sup> it has become routine to acquire both perfusion and function information within a single session.<sup>10</sup>

Compared with SPECT, positron emission tomography (PET) provides higher-quality perfusion images because of enhanced spatial resolution, improved count density, and superior attenuation correction.<sup>11-13</sup> Rubidium 82 PET MPI, in particular, has a higher sensitivity and specificity than SPECT for diagnosing CAD.<sup>12,14-16</sup> Although the ability of PET perfusion to identify patients at risk for future cardiac events has been documented in a small number of studies,<sup>17,18</sup> none have yet determined

whether information on function adds to the modality's ability for risk stratification. The goal of this study was to assess whether EF measurements determined by gated Rb-82 PET MPI provide incremental prognostic value beyond perfusion data in patients with known or suspected CAD.

## METHODS

### Study Population

Consecutive patients with known or suspected CAD who underwent dipyridamole stress gated Rb-82 PET MPI between September 1, 2002, and December 31, 2005, were identified through electronic databases at Hartford Hospital (Hartford, Conn) and Saint Luke's Mid America Heart Institute (Kansas City, Mo). Eligible patients were excluded only if ECG gating was not possible or if the gated component of the study was technically compromised (typically <5% of all studies). Valvular disease and dilated cardiomyopathy were not specified as exclusion criteria. Approval for the study was obtained from the Institutional Review Boards of Hartford Hospital and Saint Luke's Hospital of Kansas City.

### Rb-82 PET MPI Protocol

**Hartford Hospital protocol.** A Discovery LS PET/computed tomography (CT) scanner (GE Healthcare, Waukesha, Wis) was used for all patients undergoing imaging at Hartford Hospital. After a scout CT scan for positioning, a 17-second transmission was performed over the thorax for attenuation correction. Rb-82 (40-60 mCi) was then administered intravenously over a period of 30 seconds, with rest images acquired for 5 minutes after a delay of 105 to 135 seconds. Pharmacologic stress was achieved with the infusion of dipyridamole (0.56 mg/kg over a period of 4 minutes) and followed by an Rb-82 injection 4 minutes after its completion. Stress scans were finally obtained by use of the same protocol as in rest imaging. All acquisitions occurred in 2-dimensional gated mode (septa extended) with simultaneous evaluation of perfusion and function.

**Saint Luke's Mid America Heart Institute protocol.** All studies were performed on an ACCEL PET scanner (CTI, Knoxville, Tenn). This protocol involved a 4-minute scout transmission scan (germanium 68 rotating line sources) for both patient positioning and attenuation correction. Thereafter 40 to 60 mCi of Rb-82 was infused over a period of 30 seconds. After a 90-second delay for blood pool clearance, 2-dimensional rest images (septa extended) were acquired for a total acquisition time of 5 minutes. The detector septa were then retracted for 3-dimensional acquisition and Rb-82 infused once more. After a 150-second delay, a 3-minute ECG-gated acquisition was performed to assess resting cardiac function. Patients were then stressed with intravenous dipyridamole for 4 minutes (0.56 mg/kg) and scanned via the same protocol and parameters used for rest imaging.

In both laboratories, studies were corrected for emission/

transmission misalignment by use of the ImagenPro software application (Cardiovascular Imaging Technologies, Kansas City, Mo). Images were reconstructed with ordered-subset expectation maximization (6 iterations, 8 subsets) and post-filtered with a 3-dimensional isotropic Butterworth noise filter before reorientation to the short- and long-axis images. The resulting images were ultimately displayed in the AutoQuant environment (Cedars-Sinai Medical Center, Los Angeles, Calif) for interpretation and quantitation.

### Rb-82 PET Image Interpretation

Myocardial perfusion and function were interpreted without clinical data during daily clinical reading sessions by a consensus of 2 or more experienced readers using standardized myocardial segmentation and nomenclature. Visual scoring of perfusion images was accomplished by means of a 17- or 20-segment model. Patients from Mid America Heart Institute were initially scored according to a 20-segment model and later converted to a 17-segment score by determining the equivalent percentage of myocardial involvement.<sup>19</sup> Hartford Hospital patients were scored from the outset by use of a 17-segment model.

Left ventricular perfusion in each segment was graded according to a 5-point scale (0, normal uptake; 1, mildly reduced uptake; 2, moderately reduced uptake; 3, severely reduced uptake, and 4, no uptake). A global summed stress score (SSS) and summed rest score (SRS) were derived by adding together the segment scores for stress and rest images, respectively. A summed difference score (SDS), reflecting the presence and amount of ischemia, was calculated by subtracting the SRS from the SSS. For analysis, patients were stratified by SSS based on cutoff values (0, 1-3, 4-8, 9-13, and >13). An SSS of 4 or greater represented abnormal stress perfusion, whereas an SDS of 2 or greater signified ischemia.

Stress and rest EFs were determined by use of AutoQuant software.<sup>20-22</sup> EF reserve was calculated as the difference between the stress and rest EFs. Patients were arbitrarily stratified into groups according to stress EF ( $\geq 60\%$ , 50%-59%, 40%-49%, 30%-39%, and <30%).

### Patient Follow-Up

The primary endpoint of all-cause mortality was assessed by the Social Security Death Index (SSDI).<sup>23</sup> The SSDI is a large database containing vital information for individuals whose deaths have been reported to the US Social Security Administration. It is available as a free online database that is searchable by a person's name, social security number, birth date, death date, and last location of residence. For our study, the SSDI was queried to identify those patients in our population who had died during follow-up. The length of time to follow-up (ascertainment of vital status) ranged from 11 months to 4.4 years; 93% of patients had follow-up for longer than 18 months, whereas 80% of patients had follow-up for 2 years or longer. Patients not identified as dead through the SSDI were considered to be alive at the time of follow-up.

**Table 1.** Clinical and gated Rb-82 PET variables relative to mortality

Variable	Alive (n = 1,309)	Dead (n = 132)	P value
<b>Clinical</b>			
Age (y)	69 ± 12.1	75 ± 11.0	<.001
Male gender (%)	539 (41.2)	63 (47.7)	.146
Known CAD (%)	697 (53.2)	76 (57.6)	.342
Diabetes (%)	374 (28.6)	57 (43.2)	<.001
Hypertension (%)	1,030 (78.7)	112 (84.8)	.096
Elevated cholesterol level (%)	1,028 (78.5)	102 (77.3)	.737
History of smoking (%)	240 (18.3)	29 (22.0)	.307
<b>Site</b>			
Hartford Hospital	163 (12.5)	21 (15.9)	.257
Mid America Heart Institute	1,146 (87.5)	111 (84.1)	.257
<b>Gated Rb-82 PET</b>			
SSS	4.4 ± 7.2	8.1 ± 9.9	<.001
SSS ≥4 (%)	435 (33.2)	72 (54.5)	<.001
SSS >8 (%)	262 (20.0)	52 (39.4)	<.001
SDS	2.9 ± 5.2	4.4 ± 6.2	.002
SDS ≥2	528 (40.4)	69 (52.3)	.008
Stress EF	57.9% ± 14.3%	48.9% ± 17.7%	<.001
Stress EF <50% (%)	242 (18.5)	58 (43.9)	<.001
Stress EF <40% (%)	152 (11.6)	43 (32.6)	<.001
Rest EF	59.9% ± 15.1%	50.2% ± 18.0%	<.001
EF reserve	-2.0 ± 5.1	-1.3 ± 4.7	.115

Numbers in parentheses refer to the percentage of patients in the column who have the particular variable.

### Statistical Analysis

Comparisons between patient groups that did and did not experience mortality events were performed. Continuous variables were presented as mean ± SD and compared by use of a *t* test, whereas categorical variables were calculated as frequencies and compared by use of a  $\chi^2$  test. Time-to-event analyses were carried out by use of the Kaplan-Meier method to construct survival curves, which were then evaluated by use of the log-rank test. Annualized mortality rates were calculated as the number of events divided by the sum of each individual follow-up period in years.

Cox proportional hazards regression analysis was applied to determine independent predictors of all-cause mortality. The variables listed in Table 1 were considered, but only those that achieved statistical significance ( $P < .05$ ) by univariate analysis were entered into the multivariate analysis. Parameters for PET perfusion (SSS, SDS) and function (EF) were entered into the Cox regression as categorical covariates. Multivariate analysis was performed in a stepwise fashion, evaluating data on clinical characteristics, perfusion, and function. At each step, variables were entered by use of the forward Wald method until a final model comprising only significant independent variables was reached. To determine incremental value, we produced sequential Cox models, first analyzing clinical data, then adding perfusion results, and finally, adding functional information (EF). A statistically significant increase in the global

$\chi^2$  value of the models with the inclusion of a given variable (ie, perfusion or EF) defined incremental prognostic value.

Statistical significance was denoted by  $P < .05$ . Calculations were carried out by use of the SPSS statistical package (version 15.0; SPSS, Chicago, Ill).

## RESULTS

### Clinical and Gated Rb-82 PET Imaging Characteristics

A total of 1,441 consecutive, eligible patients were included in this study. The mean age of the population was 69.5 ± 12.1 years, and a majority (n = 839 [58.2%]) were women. Over half (n = 773 [53.6%]) of the patients had known CAD, whereas the others possessed known risk factors for its development. Risk factors were documented by clinical history and included diabetes (n = 431 [29.9%]), hyperlipidemia (n = 1,130 [78.4%]), hypertension (n = 1,142 [79.3%]), smoking (n = 269 [18.7%]), and a family history of CAD (n = 776 [53.9%]).

The mean SSS among all patients was 4.7 ± 7.6, with 507 (35.2%) having an SSS of 4 or greater. The

mean SDS was  $3.1 \pm 5.3$ , with ischemia ( $SDS \geq 2$ ) being noted in 844 individuals (58.6%).

All patients had peak stress EF and rest EF quantitated. Mean peak stress EF was  $57.1\% \pm 14.8\%$ , with a range of 5.0% to 91.0%. Mean rest EF was  $59.0\% \pm 15.6\%$ , with a range of 3.0% to 94.0%. Mean EF reserve was  $-1.9 \pm 5.1$ , with 358 patients (24.8%) showing an EF reserve of  $-6\%$  or worse.

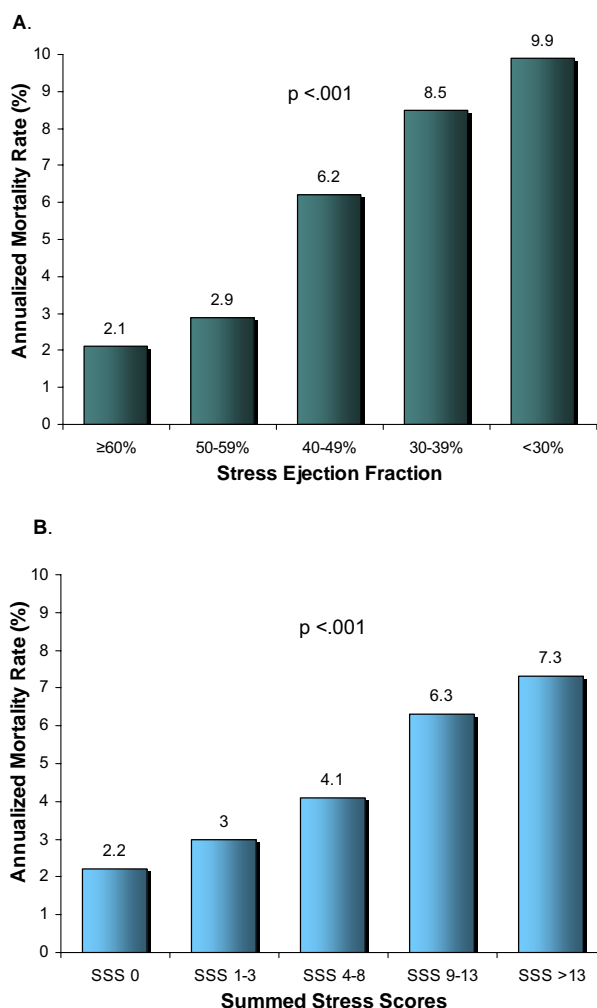
### Univariate Analysis

Over a mean follow-up of  $2.5 \pm 0.9$  years (maximum, 4.4 years) after PET imaging, 132 patients (9.2%) had died. As evidenced in Table 1, these patients were older and more likely to have diabetes compared with other individuals in the study. Perfusion and function results were significantly more abnormal in patients who had died compared with those who remained event free. Stress perfusion defects, in particular, were worse (SSS,  $8.1 \pm 9.9$  vs  $4.4 \pm 7.2$ ;  $P < .001$ ), whereas stress EF measurements were lower ( $48.9\% \pm 17.7\%$  vs  $57.9\% \pm 14.3\%$ ,  $P < .001$ ). Rest EF, in addition, was lower ( $50.2\% \pm 18.0\%$  vs  $59.9\% \pm 15.1\%$ ) in the individuals who had died. No difference in EF reserve, however, was noted between patients who had died and those who had not. Site location (Hartford Hospital or Mid America Heart Institute), in addition, had no impact on all-cause mortality ( $P = .257$ ).

### Gated Rb-82 PET Variables and All-Cause Mortality

Patients with an EF of 50% or lower had a cumulative mortality rate of 19.3% (58/300), as compared with 6.5% (74/1,141) in those with an EF greater than 50% ( $P < .001$ ). Annualized mortality rates are presented in Figure 1A. Individuals with a stress EF of 50% or lower had an annualized mortality rate of 8.2% compared with 2.4% in patients with a higher EF ( $P < .001$ ). Those with the most severe dysfunction (EF  $< 30\%$ ), however, had almost a 5-fold increase in the annual incidence of all-cause mortality (9.9% vs 2.1%,  $P < .001$ ). For comparison, the annual mortality rate in 2005 for Americans of a similar age cohort (65-74 years) was 2.1% (2,137 deaths per 100,000 population), with 31% of these deaths being attributable to major cardiovascular disease.<sup>24</sup>

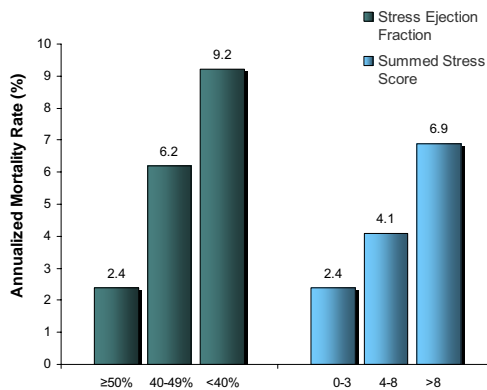
Abnormal PET perfusion also predicted death. The cumulative mortality rate was 14.2% (72/507) in patients with an SSS of 4 or greater, as compared with 6.4% (60/934) in individuals with lower scores ( $P < .001$ ). Annualized mortality rates gradually increased with the extent and severity of perfusion defects (Figure 1B). Overall, patients with an SSS of 4 or greater died at a rate



**Figure 1.** Annual incidence of all-cause mortality in relation to gated Rb-82 PET results. **A**, Event rates in relation to function (EF). **B**, Event rates in relation to perfusion (SSS).

of 5.8% per year, as compared with 2.4% for patients with an SSS lower than 4 ( $P < .001$ ). Those with the most abnormal perfusion scores (SSS  $> 13$ ) had an annualized mortality rate of 7.3% and were more than 3 times as likely to die as patients with an SSS of 0 (2.2%) ( $P < .001$ ).

On the basis of the annualized mortality rates shown in Figure 1, a 3-category risk stratification model was constructed. Ventricular function was separated into 3 groups: EF of 50% or greater, EF of 40% to 49%, and EF lower than 40%. For perfusion, patients were grouped in the following manner: SSS of 0 to 3, SSS of 4 to 8, and SSS greater than 8. Subsequent evaluation of these cohorts showed a progressive increase in annualized mortality rates as ventricular function deteriorated and as perfusion defects became more severe (Figure 2). Kaplan-Meier analysis, in addition, showed a similar



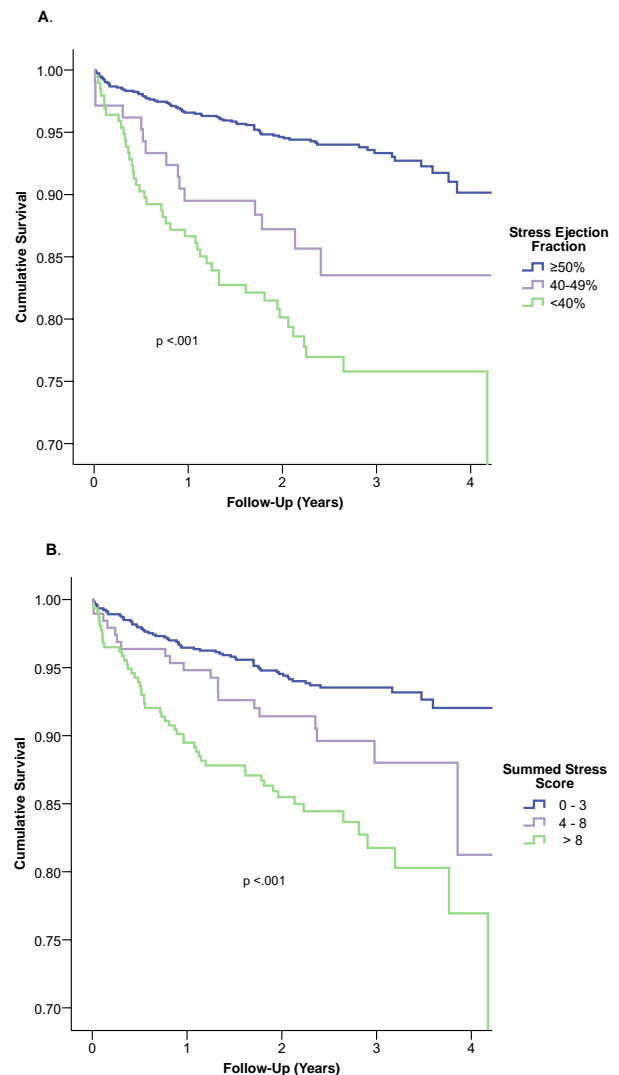
**Figure 2.** Annualized all-cause mortality rate across separate risk categories for both function (EF) and perfusion (SSS).  $P < .001$  across all perfusion and function groups.

decrease in survival with worsening function and perfusion (Figure 3). In each analysis (Figures 2 and 3) results were statistically significant across EF and SSS groups ( $P < .001$ ).

### Multivariable Analysis and Risk Stratification

All-cause mortality was independently predicted by age, diabetes, poor ventricular function, and severe perfusion abnormalities (Table 2). In particular, stress EF and SSS were significant PET imaging predictors. These parameters provided incremental value in the assessment of patient prognosis. By use of sequential Cox regression models, the addition of perfusion data to clinical variables significantly increased the global  $\chi^2$  (46.6 to 73.3,  $P < .001$ ), as did the addition of ventricular function data to both clinical and perfusion variables (73.3 to 107.7,  $P < .001$ ) (Figure 4). Notably, rest EF and SDS were not significant predictors of outcome.

The integration of EF measurements with SSS perfusion data enhanced patient risk stratification for all-cause mortality. As shown in Figure 5, annualized mortality rates based initially on SSS were further refined with the inclusion of EF. Among individuals with normal perfusion (SSS of 0-3), the annualized mortality rate increased from 2.0% to 4.2% for an EF of 40% to 49%, with a further increase to 7.1% for an EF lower than 40% ( $P < .001$ ). Those with an SSS greater than 8 had an annualized mortality rate of 4.1% if the EF was 50% or greater but died at a rate of 10.7% annually if the EF fell below 40% ( $P < .001$ ). There were similar findings in patients with an SSS of 4 to 8; however, comparisons between the group with an EF of 40% to 49% and the group with an EF lower than 40% were not statistically significant because of small event numbers in the former ( $P = .166$ ). Of note, risk stratification by use of gated PET variables (SSS alone, EF alone, and



**Figure 3.** Kaplan-Meier event-free survival curves in relation to gated Rb-82 PET perfusion and functional results. **A.** Cumulative survival with stratification by function (EF). **B.** Cumulative survival with stratification by perfusion (SSS).

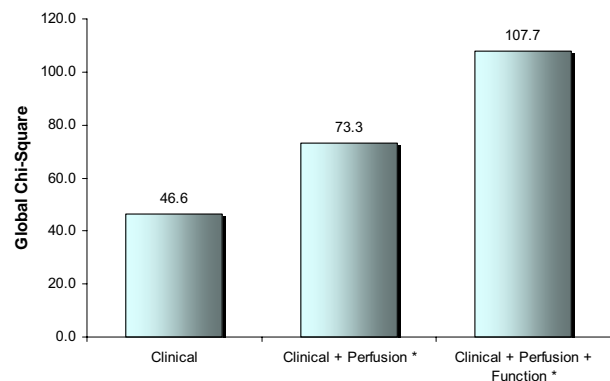
their combination) was equally and highly effective in both women and men.

The prognostic value of gated PET in both diabetic patients and the elderly was separately examined, as Cox regression analysis identified each as high-risk subpopulations. Within these cohorts, perfusion as measured by SSS effectively predicted all-cause mortality. Moreover, the integration of EF significantly enhanced risk stratification across perfusion (SSS) categories. A subanalysis performed in diabetic patients ( $n = 431$ ) showed that EF measurements lower than 50% provided significant incremental prognostic information in an already high-risk cohort, further refining patient risk for all-cause mortality beyond perfusion data alone. EF determined by PET

**Table 2.** Multivariate Cox regression analysis: Predictors of death

Predictors	Wald $\chi^2$	OR	95% CI	P value
Age	36.61	1.05	1.04–1.07	<.001
Stress EF	28.10	0.97	0.96–0.98	<.001
Diabetes mellitus	11.59	1.84	1.30–2.62	.001
SSS	5.02	1.02	1.00–1.04	.025

OR, Odds ratio; CI, confidence interval.



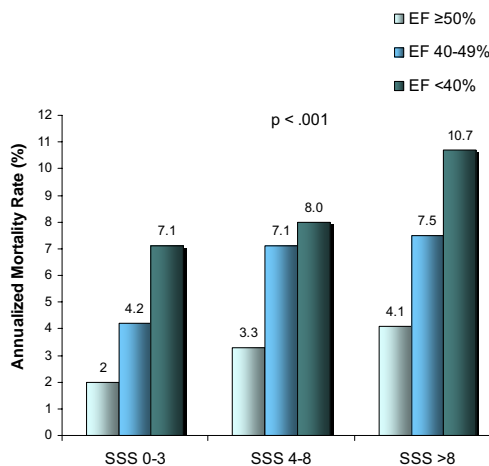
**Figure 4.** Incremental prognostic value of gated Rb-82 PET functional data. A significant increase in global  $\chi^2$  ( $P < .001$ ) was noted with the subsequent addition of perfusion as well as function.

imaging likewise improved risk stratification in elderly patients aged over 65 years ( $n = 947$ ); the annualized mortality rate increased significantly in these patients across all SSSs once EF fell below 50%.

### DISCUSSION

Given its diagnostic advantages and unique technical characteristics, it is not surprising that the use of Rb-82 PET imaging has steadily grown, even amid an overwhelming SPECT presence in most nuclear laboratories.<sup>11,25</sup> Rb-82 PET MPI has been widely used to diagnose CAD in many challenging situations and has been particularly valuable in the evaluation of patients with obesity, equivocal SPECT scans, and borderline coronary stenoses.<sup>12-16,18,26-28</sup> The resulting perfusion data, moreover, have provided clinicians with the ability to identify patients at high risk for future cardiac events.<sup>17,18</sup> Whether similar prognostic information could be gained from the assessment of ventricular function, however, has remained unclear.

This study examined the prognostic value of EF measurements determined by gated Rb-82 PET stress



**Figure 5.** Incremental prognostic value of functional data (EF) across perfusion risk groups (SSS).  $P < .001$  across all perfusion groups.

imaging in patients with known or suspected CAD. The results show that ventricular function is an independent predictor of all-cause mortality, with reductions in EF leading to progressively higher annualized mortality rates. Information on EF also adds significant incremental value to both clinical and perfusion data. In particular, the integration of function with perfusion was shown to improve risk stratification. Even in high-risk cohorts such as diabetic patients and the elderly, functional assessment by gated PET imaging proved quite valuable in estimating patient mortality risk.

One advantage of gated PET lies in its ability to assess ventricular function at peak stress rather than after stress, because of the timing of image acquisition.<sup>29</sup> As such, it more accurately reflects EF during stress and may provide functional information of greater sensitivity with regard to prognosis than gated SPECT imaging. Unfortunately, until this study, only limited data have been available describing the efficacy of stress gated PET EF assessment in predicting death. Recent work by Dorbala et al<sup>30</sup> focused on the value of EF in the diagnosis and exclusion of multivessel CAD. Using PET/CT imaging, they noted increases in EF from rest to peak stress in patients with normal myocardial perfusion. The change between the 2 values, or EF reserve, was inversely related to the magnitude of jeopardized myocardium and the extent of angiographic CAD. A positive EF reserve of more than 5% had an excellent negative predictive value (97%) for excluding severe left main or 3-vessel disease. A severely reduced EF reserve, in contrast, may be indicative of severe left main or 3-vessel disease despite the absence of any perfusion

abnormalities (balanced ischemia). Clearly, the diagnostic accuracy of gated PET imaging can be appreciably enhanced with the inclusion of EF and EF reserve in the final interpretation of perfusion studies. However, we were not able to adequately address this finding in our study.

Our study, nonetheless, suggests that EF reserve is not an independent predictor of all-cause mortality and, thus, does not have a significant impact on prognosis. This result is not surprising, as reversible wall motion abnormalities indirectly identify myocardial ischemia—a variable that correlates rather poorly with death and that, itself, was not an independent predictor of death in our multivariate analysis.<sup>18,30,31</sup> Future studies in which ischemic and cardiac events are determined, however, may provide a more complete answer. Information on stress EF, nonetheless, provided significant prognostic value beyond clinical variables and perfusion scans in the risk stratification of patients. This, along with the diagnostic value acquired by calculating EF reserve, underscores the importance of measuring EF during PET perfusion imaging.

The perfusion data, themselves, play a similar key role in assessing prognosis. Previous PET studies have focused on the usefulness of perfusion imaging in estimating cardiac risk. Marwick et al,<sup>17</sup> for instance, examined the relationship between Rb-82 PET perfusion defects and adverse events such as death and myocardial infarction. In their study patients who had normal scans had a cardiac mortality rate of 0.9% annually, as compared with a rate of 4.3% in patients with abnormal perfusion ( $P < .003$ ). Recent work by Yoshinaga et al<sup>18</sup> likewise has shown the independent prognostic value of Rb-82 PET SSS. Normal scores predicted a yearly event rate of 0.4%, whereas higher scores signaled a much poorer prognosis (7.0% annually for SSS  $\geq 8$ ). Similar findings were noted in our study, as the all-cause mortality rate rose with worsening perfusion. Annualized mortality rates were dependent on defect severity (assessed by SSS), and this remained true even in high-risk subgroups such as diabetic patients and the elderly. In contrast to previous studies, however, these rates were appreciably higher because of the selection of an all-cause mortality endpoint.

Taken together, these data put forward a strong argument for the continued use of Rb-82 PET MPI in everyday practice. Although perfusion was not the primary focus of the study, our data do represent the largest follow-up series to date on the prognostic value of PET perfusion. In addition, the evidence presented here with regard to the benefits of EF assessment should hopefully prompt routine gating of such studies in the future. At a minimum, they serve to further validate the clinical

efficacy of Rb-82 PET imaging, in general, as an alternative to SPECT.

### Limitations

This study was a retrospective analysis of a prospectively collected database and, thus, was subject to errors of confounding and bias inherent in such a design. It examined a population that was heterogeneous and consisted of some patients who had valvular heart disease and/or dilated cardiomyopathy. The extent to which this may have influenced our findings is unclear. Because the protocol involved only pharmacologic stress, conclusions on the incremental value of PET EF measurements in patients undergoing exercise stress could not be made. In addition, the protocols at both sites were different, namely in the use of a PET versus a PET/CT scanner. Although this may represent a minor limitation, having 2 separate protocols does serve to broaden the applicability of our findings. The study, moreover, relied on data obtained during the clinical workup of patients and was not completely blinded during the interpretation and scoring of perfusion images. The automated assessment of EF, however, would not have been affected.

All-cause mortality as reported by the SSDI was used as the primary endpoint instead of cardiac death.<sup>23</sup> Although this may have led to the inclusion of deaths unrelated to cardiac disease, it reduced the influence of any bias seen from the misclassification of cause of death. Unlike cardiac death, all-cause mortality is an objective measure with a specificity exceeding 99%.<sup>32,33</sup> Its efficacy as an endpoint is evidenced by our results, which correlated EF with mortality risk and are in accord with published literature for other modalities.<sup>1,7-9,34-36</sup> Comparisons between the group with an EF of 40% to 49% and the group with an EF lower than 40%, however, were not statistically significant, given the low event numbers in the former. In addition, 20% of our patients had an EF lower than 50%, possibly highlighting a more selective population than those seen in past SPECT studies.

Information on patient therapy subsequent to PET imaging was not available. To the extent that individuals underwent revascularization, the cardiac mortality rate may have decreased.<sup>19,37-40</sup> Such a confounder, though, would have weakened the predictive value of EF (and SSS), but this was not seen. Finally, it should be pointed out that none of our patients underwent fluorine 18 fluorodeoxyglucose PET imaging, which has been shown to provide incremental prognostic value in patients with ischemic cardiomyopathy.<sup>41</sup> Whether inclusion of F-18 fluorodeoxyglucose PET parameters would have affected

the prognostic value of Rb-82 PET EF assessment cannot be determined, given the design of this study.

## Conclusions

The assessment of ventricular function during gated Rb-82 PET stress MPI, thus, provides clinicians with key information regarding all-cause mortality. The functional data have significant incremental value in the evaluation of patient prognosis, supplementing information gained from both clinical and perfusion variables. As a result, consideration should be made for the routine determination and reporting of EF during Rb-82 PET MPI, not only to improve patient risk stratification but also to optimize their care.

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