Optimizing Risk Stratification in Cardiac Rehabilitation With Inclusion of a Comorbidity Index

Gilbert J. Zoghbi, MD; Bonnie Sanderson, PhD, RN; Jenny Breland, BSN, RN; Carla Adams, BSN, RN; Chris Schumann, MS; Vera Bittner, MD, MSPH

**PURPOSE:** The risk stratification criteria of the American Association of Cardiovascular and Pulmonary Rehabilitation include guidelines to be used in stratifying cardiac rehabilitation (CR) patients for risk of disease progression (long term) and clinical events (short term). Noncardiac comorbidities are not included as indicators in these criteria. This study was designed to ascertain the prevalence of noncardiac comorbidities among CR patients, and to assess their relation to the current risk stratification algorithm for clinical events.

**METHODS:** Patients were stratified into high-, intermediate-, and low-risk groups according to the American Association of Cardiovascular and Pulmonary Rehabilitation risk stratification criteria for clinical events (ARSE) at program entry. Within each risk group, age, gender, race, and noncardiac comorbidities were ascertained. Comorbidities were summarized in a comorbidity index (CMI). The relation between clinical events and risk status by ARSE and CMI was evaluated by logistic regression.

**RESULTS:** Among 490 patients (age, 60 ± 12 years; 35% women; 30% nonwhite) enrolled in CR with ischemic heart disease, the number of comorbidities ranged from 0 to 7 (median, 2; 75th percentile, 3). The patients categorized in the three ARSE groups differed significantly in age and comorbidities. Although ARSE tended to identify patients with a greater comorbidity burden, 38% of the patients with a comorbidity index exceeding the 75th percentile were not classified in the highest ARSE group. Clinical events increased across ARSE and CMI risk strata. Both ARSE and CMI were independent predictors of events in an age-, gender-, and race-adjusted logistic regression analysis (ARSE odds ratio [OR], 1.56; 95% confidence interval [CI], 1.14-2.12; CMI OR, 1.23, 95% CI, 1.03-1.47). Events were predicted best when both classifications were combined. Exploratory gender-specific analyses suggested that ARSE performed better among men than among women, whereas CMI was a more important predictor among women.

**CONCLUSIONS:** To appreciate more fully the overall complexity of disease among CR patients, ARSE should be supplemented not only with the inclusion of cardiac risk factors, as suggested in the current guidelines, but also with an assessment of noncardiac comorbidities.

Key Words: cardiac rehabilitation, risk stratification, comorbidity

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**EDITOR’S NOTE:** Beginning in 2004, JCR will publish an article in each issue for which continuing education credits can be earned. Test questions and instructions are provided at the end of this article.

Cardiac rehabilitation (CR) is a multifaceted program that focuses on risk factor modification1-3 and patient education and aims to slow coronary artery disease progression, reduce coronary heart disease events, enhance quality of life, and reduce mortality.1-6 Patients enrolled in CR are heterogeneous, with various degrees of illness severity, comorbid conditions, and cardiac disease.1-3 The American Association of Cardiovascular and Pulmonary Rehabilitation Association (AACVPR) has published risk stratification guidelines to help guide treatment...
plans and ensure patient safety through appropriate resource allocation during the supervised exercise sessions. These guidelines suggest a dual approach to risk stratification: (1) a stratification for long-term disease progression that takes into account prevalence and control of cardiac risk factors including smoking status, diet composition, dyslipidemia, diabetes mellitus, body weight, hypertension, depression, and physical activity level; and (2) a stratification for occurrence of clinical events in the near term (abbreviated as ARSE in this report) that considers extent of left ventricular dysfunction, presence of dysrhythmias, results of maximal exercise testing, symptoms of ischemia, and absence or presence of clinical depression. Noncardiac comorbidities such as those included in the D’Hoore comorbidity index (CMI) are known to affect prognosis in populations with cardiovascular disease.

Although one of the noncardiac comorbidities included in this index (diabetes mellitus) is captured in the two-component AACVPR stratification, a detailed assessment of such comorbidities is not currently recommended by the AACVPR guidelines.

The purpose of this study was to determine the prevalence of noncardiac comorbidities in a CR population and to assess their relation to ARSE. It was hypothesized that ARSE would not fully reflect the burden of disease as assessed by the authors’ CMI, and that a combined assessment of ARSE and comorbidities would better predict events during CR and thus serve as the foundation for more appropriate resource allocation in this era of limited resources.

METHODS

Information from the patients enrolled in our phase 2 CR has been maintained in an outcomes database since the beginning of the CR program in January 1996 and has been described in detail elsewhere. Each patient’s baseline demographic and clinical information is obtained from a personal history, referral records, and hospital medical records, then entered into the database at the time of enrollment and tracked along with the outcome variables from enrollment to completion of the CR program. The data for patients enrolled in the CR program were reviewed retrospectively between January 1996 and December 2000. The demographic and clinical information pertinent to the purpose of this study was extracted. The patients were stratified into low-, intermediate-, and high-risk groups according to ARSE. Within each risk group, age, gender, and race were ascertained. Then a modified D’Hoore CMI was computed.

Comorbidity Index

The Charlson Comorbidity Index (CMI), a composite index of 19 comorbid conditions, has been used to measure the burden of comorbid diseases from administrative databases using the International Classification of Diseases 9, and to predict the short- and long-term mortality rate for a specific medical condition.

The D’Hoore CMI is an adaptation of the Charlson CMI applied to predict the short-term mortality rate for patients with ischemic heart disease, congestive heart failure, and other conditions. Each comorbidity is assigned a weight that represents the burden of the comorbid condition and approximates the 1-year relative risk of death for that condition. The D’Hoore CMI is the total of the comorbidity weights for each patient.

The different comorbid conditions for each patient were extracted from the outcomes database, and a modified D’Hoore CMI (Table 1) was computed excluding congestive heart failure and myocardial infarction because these are already included in ARSE. Mild liver disease also was excluded. The categories of “any tumor,” “leukemia,” and “lymphoma” were combined into a single category of “malignancy,” and patients with a history of stroke or cerebrovascular disease were assigned to the “cerebrovascular disease” category. The category “hemiplegia” was excluded from the original index because none of the patients were hemiplegic at the time of enrollment, although some had a history of strokes. Because the outcomes database does not have information about serum creatinine, only patients with end-stage renal disease were included in the renal disease category.

On the basis of the CMI score, the patients were classified into low-, intermediate-, and high-risk CMI strata.

Events

The CR program defines an event as any patient occurrence that may need medical intervention or necessitates a physician call by a staff member. The event log is maintained at the telemetry monitoring desk in the exercise area, and events are recorded by the CR nurse as they occur. Subsequently, the events are entered into the outcomes database according to the following categories: symptom (eg, chest pain, dizziness, shortness of breath, symptomatic hypotension, edema), condition change (eg, uncontrolled hypertension, fall, hypoglycemia, hyperglycemia), or electrocardiographic change (eg, bradyarrhythmia, tachyarrhythmia, ST segment changes, new conduction defect). The events are tracked to help determine the nature and volume of medical needs among the CR patients that necessitate a higher level of staff involvement during the group exercise sessions.

Statistical Analysis

Descriptive statistics (mean, standard deviation, percentile rank, median, and proportions) were used to summarize the patients’ baseline characteristics. The three ARSE risk groups were compared by analysis of
variance (ANOVA) or χ² statistics as appropriate with an alpha of 0.05. Exploratory subgroup analyses were performed comparing the performance of ARSE among women and men. The event data were summarized as the total number of events and the total number of patients with an event. Event occurrence was compared across ARSE risk strata, across CMI strata, and across both combined by determining events among patients classified as high risk on both, high risk on ARSE, intermediate or low risk by CMI, high risk by CMI, and intermediate or low risk by ARSE (9 categories in all for the combined classification). To determine independent predictors of events, an age-, gender-, and race-adjusted logistic regression analysis was performed using ARSE and CMI classification as independent variables. Gender differences were explored in stratified logistic regression analyses.

RESULTS

The mean age of the patients was 60.1 ± 11.6 years. In this patient group, 35.5% were women, 28.2% were nonwhite, and 27.6% had a left ventricular ejection fraction less than 40%. Only 14.9% were in the lowest ARSE stratum, whereas 45% were in the intermediate ARSE category and 40.1% were in the highest stratum.

ARSE and Comorbidities

The modified comorbidity index ranged from 0 to 7 (median, 2; 75th percentile, 3). Table 2 shows the characteristics of the three ARSE subgroups. The mean age increased progressively with increasing risk by ARSE classification from 56.6 ± 10.3 years in the low-risk group to 61.1 ± 11.3 years in the high-risk group. (P = .011). The prevalence of diabetes mellitus, chronic obstructive pulmonary disease, dementia, cerebrovascular disease, peripheral vascular disease, ulcer, and renal disease similarly increased in prevalence across the three ARSE risk groups, resulting in a statistically significant increase in CMI scores with increasing ARSE risk (Figure 1). Although ARSE tended to identify patients with a higher comorbidity burden, 38% of the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>THE MODIFIED D’HOORE COMORBIDITY INDEX</th>
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<tbody>
<tr>
<td>Weight</td>
<td>Condition</td>
</tr>
<tr>
<td>1</td>
<td>Myocardial infarct*</td>
</tr>
<tr>
<td></td>
<td>Congestive heart failure*</td>
</tr>
<tr>
<td></td>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td></td>
<td>Dementia</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular disease†</td>
</tr>
<tr>
<td></td>
<td>Chronic pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>Connective tissue disease</td>
</tr>
<tr>
<td></td>
<td>Ulcer disease</td>
</tr>
<tr>
<td></td>
<td>Mild liver disease ‡</td>
</tr>
<tr>
<td>2</td>
<td>Hemiplegia ‡</td>
</tr>
<tr>
<td></td>
<td>Moderate or severe renal disease‡</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
</tr>
<tr>
<td></td>
<td>Any tumor†</td>
</tr>
<tr>
<td></td>
<td>Leukemia</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td>3</td>
<td>Moderate or severe liver disease</td>
</tr>
<tr>
<td>6</td>
<td>Metastatic solid tumor</td>
</tr>
</tbody>
</table>

*Myocardial infarct and congestive heart failure were omitted from the index because they are included in the AACVPR risk stratification for events.
†Includes patients with history of stroke or history of cerebrovascular disease as entered in our database.
‡Mild liver disease and hemiplegia were omitted from index because it could not be quantified in our database.
§Includes patients with end stage renal disease.
[Labeled as one category (malignancy)]

<table>
<thead>
<tr>
<th>Table 2</th>
<th>PREVALENCE OF COMORBIDITIES AMONG CARDIAC REHABILITATION PATIENTS BY ARSE CATEGORIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities</td>
<td>Total N = 490 n (%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>169 (33.7)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>5 (1.0)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>65 (13.3)</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>22 (4.5)</td>
</tr>
<tr>
<td>Dementia</td>
<td>6 (1.2)</td>
</tr>
<tr>
<td>Cerebrovascular disease/stroke</td>
<td>67 (13.6)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>74 (15.0)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>57 (11.6)</td>
</tr>
<tr>
<td>Ulcer disease</td>
<td>75 (15.3)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>7 (1.4)</td>
</tr>
</tbody>
</table>

ARSE, American Association of Cardiovascular and Pulmonary Rehabilitation risk stratification for events.

*P compares the proportion of patients with a given comorbidity across the 3 ARSE subgroups.
patients with a modified CMI above the 75th percentile were not in the high-risk ARSE group.

**Event Occurrence by Risk Group**

Among the 490 patients in this study, 137 had a total of 303 events (36% condition change and 48% symptoms) during 10,765 CR sessions (6 events in 100,000 participant sessions). The proportion of patients who had at least one event increased significantly across increasing-risk ARSE and comorbidity index subgroups and was highest in the subgroup of individuals classified as high risk by both ARSE and CMI (Figure 2). Both ARSE and CMI risk categories were independent predictors of events in an age-, gender-, and race-adjusted logistic regression analysis (ARSE odds ratio [OR], 1.56; 95% confidence interval [CI], 1.14-2.12; CMI OR, 1.23; 95% CI, 1.03-1.47). The $R^2$ of this age-, gender-, and race-adjusted event model containing both ARSE and CMI was 0.065, an improvement from 0.051 for a similarly adjusted model that contained only ARSE as the predictor variable.

**Exploratory Analyses by Gender**

The study population included 316 men and 174 women. The proportion of women in the low-, intermediate-, and high-risk strata of the ARSE was comparable with that for the men (12.6%, 50.0%, 37.4% versus 15.8%, 41.8%, 42.4%, respectively; $P = .204$). The average CMI score was $1.7 \pm 1.7$ for the men and $1.9 \pm 1.8$ for the women. In both gender subgroups, the CMI score was lowest in the low-risk ARSE stratum, intermediate in the intermediate stratum, and highest in the high-risk ARSE stratum (men: 0.8 ± 1.1, 1.5 ± 1.6, and 2.2 ± 1.8, respectively; women: 1.3 ± 1.3, 1.8 ± 1.7, and 2.2 ± 2.0, respectively; $P = .161$). However, high-risk status by ARSE was a better predictor of high-risk status by CMI (>75th percentile of CMI) among the men than among the women (66.7% correctly classified versus 55.6% correctly classified; $P = .02$).

There were 80 events among the men and 57 events among the women. Among the men, ARSE was a significant predictor of events during CR (OR, 1.69; 95% CI, 1.13-2.52) whereas there was no relation between CMI and events (OR, 1.04; 95% CI, 0.83-1.30). Among the women, CMI was a significant predictor of events (OR, 1.61; 95% CI, 1.19-2.17). Although the point estimate of the odds ratio magnitude among the women was similar to that among the men (OR, 1.51; 95% CI, 0.90-2.52), ARSE did not achieve statistical significance.

**DISCUSSION**

As expected, a high prevalence of noncardiac comorbidities was found in this university-based CR population. Although the ARSE high-risk stratum identified many of these patients, approximately 40% of the patients with CMI scores above the 75th percentile were not classified as high risk by ARSE. Both ARSE and CMI were independent predictors of events in analyses adjusted for demographic characteristics, but the current model explained only a small proportion of the variability in events. Exploratory subgroup analyses suggested that the addition of CMI to the standard risk assessment may be more important for women than for men.
Several professional organizations have set risk stratification guidelines for supervised exercise among CR patients to facilitate rational allocation of CR resources.11-15 Some have suggested limited medical supervision and electrocardiographic monitoring for intermediate- and low-risk patients, whereas others have recommended neither of these services for low-risk patients. When current risk stratification algorithms and monitoring are used, the rate of major cardiovascular complications is low, ranging from approximately 1 per 60,000 participant exercise hours for cardiac arrest or acute myocardial infarction16-18 to 1 per 320 exercise hours for prolonged chest pain, dyspnea, and arrhythmias.19 Although ARSE has been shown to correlate with major complications during exercise, Paul-Labrador et al20 found a positive predictive value of only 3% to 7% for serious complications during exercise, suggesting that an expanded risk assessment could be useful. Although the definition of events differed between this study and the current study, the current modeling of ARSE as a predictor of events is consistent with Paul-Labrador's findings.

Little is known about the prevalence of noncardiac comorbidities among CR patients and the effect of these comorbidities on prognosis. The Charlson CMI has been validated by D'Hoore et al8,9 to predict short-term mortality for patients with ischemic heart disease, and by Ghali et al21 and Roos et al,22 respectively, to predict short- and long-term mortality in relation to coronary artery bypass graft. Although most patients enrolled in CR have ischemic heart disease or have undergone prior revascularization, the D'Hoore index has not been previously applied in the CR setting. D'Hoore found a twofold increase in short-term mortality if the score increased from 1-2 to 3-4, with a progressive 10-fold increase in mortality as the score increased from 0 to more than 6.9 Although caution should be observed in direct extrapolation of these mortality figures to CR patients, the current study has shown that patients with a greater CMI are clearly more seriously ill and more likely to have an event during CR sessions. Ideally, such patients should be identified at entry into the CR program and assigned staffing to permit close medical surveillance throughout enrollment.

In contrast to previous studies, the current study did not find a significantly higher burden of comorbidities overall among women than among men.23,24 The current data suggest, however, that there are significant gender differences in the ability of ARSE to identify individuals who have a greater comorbidity burden and thus are potentially at greater risk for recurrent events. Supplementation of ARSE with additional assessments of comorbidities may be more important among women than among men.

**Study Limitations**

Although the D'Hoore CMI has been validated for inpatients with ischemic heart disease and congestive heart failure, it has not been validated for outpatients enrolled in a CR population. However, the impact of comorbidities is likely to be similar in the inpatient and outpatient settings. The comorbidities in the current study were determined from a hospital chart review and were not based on formal International Coding of Diseases-9. However, good to very good correlations have been observed between administrative databases and chart reviews.25

The D'Hoore index was modified to avoid overlap with ARSE. Such overlap would have resulted in artificially high correlations between the two indices and potentially unstable modeling of highly correlated variables. The descriptive analyses detailed earlier were repeated after congestive heart failure and myocardial infarction were included in the CMI calculation with similar results (data not shown). We therefore do not think that exclusion of these two comorbidities represents a significant limitation of the study. Data on some conditions such as malignancies and extent of renal dysfunction were limited. Scores in the current index are thus lower than those reported in the literature and may underestimate the true comorbidity burden. It is unlikely that complete ascertainment of comorbidities would have changed the study conclusions because underestimation of comorbidity would have led to overestimation of ARSE's ability to capture the patients' comorbidity burden. The modified index awaits validation as a predictor of “hard ischemic heart disease events” and mortality outside the CR setting. Because power was limited after stratification, the gender-specific analyses should be considered preliminary until confirmed by others.

**CONCLUSION**

According to this study, noncardiac comorbidities are highly prevalent among CR patients. Conventional ARSE fails to identify a large subgroup of patients with a high burden of such comorbidities. The observed differences between women and men in the performance of ARSE suggest that a single tool may not be sufficient to assess the broad spectrum of patients enrolled in contemporary CR programs. We therefore believe that ARSE stratification should be supplemented not only by assessment of cardiovascular risk factors, as suggested by current guidelines, but also by assessment of comorbidities to help guide decisions about intensity, type, and duration of therapy as well as allocation of staff during the supervised exercise sessions. The data also suggest that the training for CR staff should be broadened to ensure that
the staff is competent to handle the multitude of noncardiac comorbidities among their patients. Further studies are needed to validate the modified CMI for CR populations in a variety of care settings, and to explore further relations to short- and long-term cardiovascular events and complications during exercise.

References