The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria

PAUL R. MARANTZ, M.D., M.P.H., JONATHAN N. TOBIN, PH.D., SYLVIA WASSERTHEIL-SMOLLER, PH.D., RICHARD M. STEINGART, M.D., JOHN P. WEXLER, M.D., PH.D., NANCY BUDNER, M.P.H., LLOYD LENSE, M.D., AND JOSEPH WACHSPRESS, M.D.

ABSTRACT There is no uniformly accepted clinical definition for congestive heart failure (CHF), although criteria have been published by various groups. There is also no reference standard for CHF, although left ventricular ejection fraction (LVEF) gives a quantitative assessment of systolic function and is useful in predicting prognosis. To determine the relationship between LVEF and clinically diagnosed CHF, we compared resting LVEF determined by radionuclide ventriculography with diagnosis of CHF by clinical criteria in 407 patients, based on clinical data collected by a cardiology fellow. Of 153 patients with a low LVEF (≤0.40), 30 (20%) met none of the criteria for CHF. Conversely, of 204 patients with normal LVEF (≥0.50), 105 (51%) met at least one of the criteria. We conclude that different criteria for CHF will have varying utility depending on the population being examined, and that a combination of clinical features and an objective measure of cardiac performance is needed to diagnose CHF.


CONGESTIVE HEART FAILURE is among the most frequently encountered cardiac diagnoses. Prevalence of congestive heart failure is estimated to be 1% in the United States, and Framingham data gives an incidence rate of about 2 per 1000 persons per year. Only 50% of patients diagnosed as having congestive heart failure survive for 5 years. It also has major impact in terms of morbidity and hospitalization; among elderly patients, it is the most common medical indication for hospitalization.

Epidemiologic studies in congestive heart failure have been hampered by the lack of uniform diagnostic criteria, relying instead on physician diagnosis of the disease. The Framingham Study created clinical criteria for diagnosing congestive heart failure (table 1); however, these criteria have never been validated against a reference standard. A study performed at Duke derived another set of clinical criteria for congestive heart failure by a multivariate analysis of clinical variables against left ventricular end-diastolic pressure greater than 15 mm Hg in patients referred for cardiac catheterization with anatomic coronary artery disease. The criteria generated by this study were the presence of either an S₃ on examination or cardiomegaly on the chest x-ray (cardiothoracic ratio >0.48). A third group in Boston used clinical judgment to derive a set of diagnostic criteria (table 2), and then validated these against a pulmonary capillary wedge pressure greater than 12 mm Hg in patients undergoing nonemergency right heart catheterization.

To determine the relationship between the clinical diagnosis of congestive heart failure and objective measurement of systolic cardiac function, we compared the diagnosis of congestive heart failure, as determined by applying three different rating scales, with resting left ventricular ejection fraction, as measured by radionuclide wall motion studies. Although not a reference standard for the diagnosis of congestive heart failure per se, resting left ventricular ejection fraction has clinical significance as the most important predictor of prognosis in patients with coronary heart disease. It also can identify the subgroup of patients...
TABLE 1
Framingham criteria for congestive heart failure

Major criteria
- Paroxysmal nocturnal dyspnea or orthopnea
- Neck-vein distention
- Rales
- Cardiomegaly
- Acute pulmonary edema
- S3 gallop
- Increased venous pressure >16 cm of water
- Circulation time >25 sec
- Hepatogenous reflux

Minor criteria
- Ankle edema
- Night cough
- Dyspnea on exertion
- Hepatomegaly
- Pleural effusion
- Vital capacity decreased ½ from maximum
- Tachycardia (rate of >120/min)

For establishing a definite diagnosis of congestive heart failure in this study, two major or one major and two minor criteria had to be present concurrently.

with congestive heart failure who have normal systolic function, an important pathophysiologic mechanism that may require a different therapeutic approach.7

Materials and methods

Between July 1982 and June 1983, a study to evaluate the efficacy of cardiovascular nuclear medicine studies (CVNMS) was conducted at the Albert Einstein College of Medicine affiliated hospitals. The design of this study has been described in detail previously.8 During this period, radionuclide evaluation was performed on 2321 patients who were not on cardiotropic drugs. Physicians referring patients for CVNMS were required to complete a form before the test, specifying reason for the test, suspected heart disease, and predicted outcome. There were 1272 patients who underwent a standardized clinical assessment by a cardiologist fellow immediately before the nuclear scan as part of the CVNMS efficacy study. These patients were similar to those not examined by a study fellow with regard to reason for referral for the CVNMS and CVNMS results.

There were 596 patients referred for exercise study, and 676 for resting radionuclide ventriculograms. We selected only those patients who were referred for resting wall motion study, since these patients are more likely to represent a population with suspected congestive heart failure than with suspected ischemia. Based on data from the standardized referral form, the referring physician suspected congestive heart failure in 66% of subjects referred for resting study, but in only 6% of those referred for exercise study. Among the resting study subjects, there were 407 for whom a complete history, physical data, and a chest x-ray were obtained, and in whom the wall motion study was technically adequate.

The Framingham and Duke scales are dichotomous with respect to the presence or absence of congestive heart failure, while the Boston scale classifies patients as having definite, possible, or unlikely congestive heart failure. Some modifications of the grading criteria had to be made for this study. Specifically, although cardiomegaly was a factor in all three scales, Framingham did not specify how cardiomegaly would be defined, the Duke scale required a cardiothoracic ratio on chest x-ray greater than 0.48, and the Boston scale required a ratio greater than or equal to 0.50. For our analysis, we accepted a radiologist’s reading of cardiomegaly on the chest x-ray, since explicit measures of cardiothoracic ratio were not in our data base. The Boston scale gave different point counts to “dyspnea on climbing,” “dyspnea on walking on level,” and “rest dyspnea”; we equated these with dyspnea on “extreme exertion,” “minimal/moderate exertion,” or “at rest,” respectively, as recorded during our clinical assessment. In adapting the Framingham scale, we excluded criteria that were either not entered in our data base (namely, night cough or weight loss) or that are not routinely used in the clinical diagnosis of congestive heart failure (venous pressure, circulation time, or vital capacity).

Once patients were classified, the groups were compared with respect to ejection fraction, by mean ejection fraction and by proportion with ejection fraction of 0.40 or less, 0.41 to 0.49, and 0.50 or more. These levels were selected to separate equivocal levels of ejection fraction from those that are more clearly normal or abnormal. We also related the clinical classification with patient’s medication history.

Ejection fractions are reported as the mean ± SEM. Statistical analysis was performed with computer software from Statistical Analysis Systems (SAS), with the use of analysis of variance to compare group means for continuous data, and where

TABLE 2
Boston criteria for congestive heart failure

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Point value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I: History</td>
<td></td>
</tr>
<tr>
<td>Rest dyspnea</td>
<td>4</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>4</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
<td>3</td>
</tr>
<tr>
<td>Dyspnea on walking on level</td>
<td>2</td>
</tr>
<tr>
<td>Dyspnea on climbing</td>
<td>1</td>
</tr>
<tr>
<td>Category II: Physical examination</td>
<td></td>
</tr>
<tr>
<td>Heart rate abnormality</td>
<td></td>
</tr>
<tr>
<td>(if 91–110 beats/min, 1 point; if &gt;110 beats/min, 2 points)</td>
<td>1–2</td>
</tr>
<tr>
<td>Jugular-venous pressure elevation</td>
<td></td>
</tr>
<tr>
<td>(if &gt;6 cm H2O, 2 points; if &gt;6 cm H2O plus hepatomegaly or edema, 3 points)</td>
<td>2–3</td>
</tr>
<tr>
<td>Lung crackles</td>
<td></td>
</tr>
<tr>
<td>(if basilar, 1 point; if more than basilar, 2 points)</td>
<td>1–2</td>
</tr>
<tr>
<td>Wheezing</td>
<td>3</td>
</tr>
<tr>
<td>Third heart sound</td>
<td>3</td>
</tr>
<tr>
<td>Category III: Chest radiography</td>
<td></td>
</tr>
<tr>
<td>Alveolar pulmonary edema</td>
<td>4</td>
</tr>
<tr>
<td>Interstitial pulmonary edema</td>
<td>3</td>
</tr>
<tr>
<td>Bilateral pleural effusions</td>
<td>3</td>
</tr>
<tr>
<td>Cardiothoracic ratio &gt;0.50</td>
<td>3</td>
</tr>
<tr>
<td>(posterolateral projection)</td>
<td></td>
</tr>
<tr>
<td>Upper zone flow redistribution</td>
<td>2</td>
</tr>
</tbody>
</table>

*No more than 4 points were allowed from each of three categories, and hence the composite score, the sum of the subtotal from each category, had a maximum possible of 12 points. The diagnosis of heart failure was classified definite for a score of 8 to 12 points, possible for a score of 5 to 7 points, and unlikely for a score of 4 points or less.
appropriate, the Scheffe test for multiple comparisons. Categorical data were evaluated by the use of chi-square tests. Values of \( p < .05 \) were considered statistically significant. Interscale agreement was measured by means of the kappa statistic, which takes observed agreement and corrects for agreement expected by chance alone.\(^5\)

**Results**

Of our 407 patients, 91\% were in-patients at the time of CVNMS. The mean age was 64 years, with 34\% age 70 or greater. Sixty-five percent of the study subjects were men. The reason for the test, as given by the referring physician, was to determine severity of disease in 61\%, to confirm the presence of disease in 25\%, to confirm absence of disease in 6\%, and in 8\% to monitor therapy.

**Ejection fraction.** For the total group, the mean left ventricular ejection fraction was 0.49, with a left ventricular ejection fraction less than 0.50 in 204 (50\%). Patients classified as having congestive heart failure by any of the scoring systems had significantly lower mean left ventricular ejection fractions when compared with those classified as not having congestive heart failure. Mean left ventricular ejection fraction for patients with congestive heart failure classified as present or absent according to the Framingham criteria was 0.45 ± 0.018 vs 0.53 ± 0.014 (\( p < .001 \)), and according to the Duke criteria 0.43 ± 0.015 vs 0.58 ± 0.016 (\( p < .0001 \)). The Boston scale classified patients as having definite, possible, or unlikely congestive heart failure; mean left ventricular ejection fraction in these patients was 0.41 ± 0.021 vs 0.51 ± 0.020 vs 0.55 ± 0.016, respectively (\( p < .0001 \)). The Scheffe test shows the significant difference to lie between those classified as having “definite congestive heart failure” and those with “possible or unlikely congestive heart failure.” Therefore, in the following discussion we will refer to the “definite” group as having congestive heart failure, and those classified as “possible or unlikely congestive heart failure” as not having congestive heart failure.

To determine the relationship between clinical classification of congestive heart failure and resting left ventricular ejection fraction, predetermined levels of left ventricular ejection fraction were used to classify patients into three distinct groups: low left ventricular ejection fraction (≤0.40), borderline (0.41 to 0.49), and normal left ventricular ejection fraction (≥0.50) (table 3). The data indicate significant associations on all three scales, with patients classified as having congestive heart failure more likely to have a low ejection fraction. Sensitivity and specificity of clinical diagnosis was calculated, setting left ventricular ejection fraction of 0.40 or less as the reference standard for clinically or prognostically important left ventricular dysfunction (table 3).

**Comparison of criteria.** We compared patients’ ratings among the various scales with results summarized in figure 1. We found that in patients with normal left ventricular ejection fraction (≥0.50) over half had congestive heart failure diagnosed by at least one of the criteria. Conversely, among subjects with low left ventricular ejection fraction (≤0.40), 20\% met none of the criteria for congestive heart failure.

Concordance among the three scales was measured by calculation of the kappa statistic. The value of kappa was 0.38 comparing Duke with Boston, 0.52 comparing Duke with Framingham, and 0.67 comparing Framingham with Boston criteria. These values show an interscale agreement that is fair, moderate, and substantial, respectively.\(^10\)

**Medication use.** It was found that substantial proportions of those subjects who did meet criteria for congestive heart failure were on \( \beta \)-blocking drugs (12\% to 20\%) (table 4). In addition, of those subject not meet-

<table>
<thead>
<tr>
<th>TABLE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relationship between clinical classification and left ventricular ejection fraction</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>LVEF category [% (n)]</td>
</tr>
<tr>
<td>≤40</td>
</tr>
<tr>
<td>41–49</td>
</tr>
<tr>
<td>≥50</td>
</tr>
<tr>
<td>Sensitivity(^a)</td>
</tr>
<tr>
<td>Specificity(^a)</td>
</tr>
</tbody>
</table>

+ = CHF present by criteria; – = CHF absent by criteria.

\(^a\) Compared with LVEF ≤40\%.
ing criteria for congestive heart failure, about a third (31% to 36%) were being treated with digoxin. Similar results were found for patients without systolic dysfunction on nuclear scan: of subjects with normal left ventricular ejection fraction (≥0.50), 34% were being treated with digoxin, compared with 55% of those with low ejection fraction (<0.50).

Discussion

Our study indicates that although each of the three clinical scales identified patients with significantly lower ejection fractions, the three scales have varying sensitivities and specificities and could be expected to have different utilities depending on the goals of diagnosis (e.g., prognostication vs ruling out disease) and on the population being examined (e.g., high vs low prevalence of disease).

Evaluating the clinical diagnosis of congestive heart failure presents special problems due to the lack of accepted diagnostic criteria. Indeed, none of the three sets of criteria used in the present study is in wide use. In addition, there is not technologic reference standard for the diagnosis of heart failure. For example, pressure measurements (pulmonary capillary wedge pressure, left ventricular end-diastolic pressure) are not widely applicable. These measurements are extremely sensitive to therapeutic intervention, and may be normal despite severe ventricular dysfunction. Echocardiographic measurements are not easily quantified reproducibly, although the use of computer technologies is improving this situation. Nuclear studies provide a more quantifiable measure of cardiac function, but the resting left ventricular ejection fraction does not relate linearly to exercise capacity. Also, none of the measurements has a well-accepted cutoff level for "normal." For example, clinical trials in congestive heart failure use varying entry criteria of left ventricular ejection fraction, ranging from 0.30 to 0.49. In effect, then, a study of clinical criteria for congestive heart failure involves evaluating not only the criteria themselves but also the reference standard used.

Despite its usefulness in predicting prognosis, the major shortcoming of the left ventricular ejection fraction is its inability to identify diastolic dysfunction. The mechanism of diastolic dysfunction has been receiving increased attention, especially among the elderly. Given the high prevalence of elderly subjects in our study, it is possible that some of our subjects with clinical congestive heart failure had abnormalities in diastolic function, which we did not measure. In a previous study of patients with clinically diagnosed congestive heart failure (confirmed by a modification of the Boston criteria) referred for nuclear study, Soufer et al. found that 42% had intact systolic function (defined as left ventricular ejection fraction ≥0.45). This estimate is similar to that of Dougherty et al. (36%) and to our own (34% to 40%) (table 3). Of 58 such patients, 38% had diastolic dysfunction (defined as peak filling rate <2.5 end-diastolic volumes/sec), and an additional 24% had "probable diastolic dysfunction" (peak filling rate 2.5 to 3.0 end-diastolic volumes/sec). Objective measurement of diastolic function is not routinely obtained on radionuclide angiography, and even if available, would leave unexplained between 38% and 62% of patients with clinical congestive heart failure and normal systolic function. This implies that clinical judgment provides information about congestive heart failure that cannot be obtained from a nuclear scan.

Conversely, in our study, 23% to 28% of subjects

<table>
<thead>
<tr>
<th>Drug therapy and clinical classification of congestive heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Treated with [% (n)]</td>
</tr>
<tr>
<td>β-Blocker</td>
</tr>
<tr>
<td>Diuretic</td>
</tr>
<tr>
<td>Digoxin</td>
</tr>
</tbody>
</table>

+ = CHF present by criteria; - = CHF absent by criteria.
classified as not having congestive heart failure had depressed left ventricular ejection fractions (<0.40). In fact, of all patients with clearly low left ventricular ejection fractions, 20% were not diagnosed by any of the three sets of clinical criteria (figure 1). Since a left ventricular ejection fraction of 0.40 or less is generally accepted as abnormal, this indicates that an objective measure of left ventricular ejection fraction gives more information than can be obtained by clinical evaluation alone.

There are several limitations that must be considered in interpreting these data. The first is the population studied, which was a referral population with a high prevalence of cardiac disease. History of hypertension was present in 53%, 37% had a confirmed history of prior myocardial infarction, and 49% had typical angina. Although our study population is subject to a referral filter bias, the noninvasive nature of the procedure would make our sample more representative of patients with suspected congestive heart failure in clinical practice than were the catheterized populations previously studied.\footnote{Circulation 77: 183, 1988}

Another limitation was the need to categorize patients according to congestive heart failure criteria through the retrospective application of a database that was not designed to answer this question. The problems were minor in categorizing subjects on the Duke and Boston criteria, involving simply substituting radiologist’s reading of cardiomegaly for a specific value of cardiothoracic ratio, and applying slightly different terminology in the assessment of dyspnea. This limitation was more serious with regard to the Framingham criteria, where entire major and minor criteria had to be eliminated, such as circulation time and vital capacity. Inclusion of other criteria, however, could only serve to diagnose more subjects as having congestive heart failure. This might increase sensitivity, but at the probable expense of a loss of specificity from the values we derived of 0.63 and 0.63, respectively.

The effect of drug therapy in this population is difficult to assess. Large proportions of the subjects were taking medications such as digoxin (45%), diuretics (61%), and β-blockers (26%) (table 4). The impact of drug therapy on left ventricular ejection fraction is unclear in previous reports. For instance, there are two randomized double-blind placebo controlled crossover studies of digoxin that measured systolic left ventricular function. Fleg et al.\footnote{Am Heart J 128: 1441, 1990} found no clinical response to digoxin, but did show a small but statistically significant rise in echocardiographically determined velocity of circumferential fiber shortening with digoxin (0.90 circ/sec) compared with placebo (0.82 circ/sec) (p < .05). Conversely, Lee et al.\footnote{Circulation 77: 183, 1988} found clinical benefit with digoxin use, but no change in resting radionuclide left ventricular ejection fraction with digoxin (0.30) compared with placebo (0.29) (p = .49). In a study of digoxin use after myocardial infarction there was a statistically significant but clinically insignificant rise in left ventricular ejection fraction with digoxin use (0.29 ± 0.09 vs 0.33 ± 0.11, p < .03).\footnote{Circulation 77: 183, 1988} A study of propranolol showed no effect on resting left ventricular ejection fraction in normal subjects or in patients with coronary artery disease.\footnote{Circulation 77: 183, 1988}

Our data indicate that many subjects without congestive heart failure by clinical criteria are being treated with digoxin. This finding is consistent with those of Carlson et al.\footnote{Circulation 77: 183, 1988} who devised the Boston criteria. However, some of our subjects received digoxin for indications other than congestive heart failure. For example, of 183 subjects taking digoxin, 27 had atrial fibrillation or flutter (15%), compared with seven of 224 subjects not taking digoxin (3%). Significant left ventricular dysfunction frequently coexisted with the arrhythmia: 13 of the 27 subjects (48%) with atrial arrhythmias on digoxin had a left ventricular ejection fraction of 0.40 or less. The use of digoxin for atrial arrhythmias would not account for the fact that only 84 of 183 subjects taking digoxin in our study (46%) met the Boston criteria for congestive heart failure.

There are no uniformly accepted criteria for the diagnosis of congestive heart failure, and there is no “gold standard” for the diagnosis. The inability of resting left ventricular ejection fraction to serve this function has been well demonstrated.\footnote{Circulation 77: 183, 1988} We do not suggest that our data can be used to validate clinical criteria with left ventricular ejection fraction as a gold standard. Rather, they indicate that a combination of clinical diagnosis and an objective measure of cardiac performance is necessary to definitively diagnose congestive heart failure, since each provides information not available from the other.

We thank Ms. Mindy Ginsberg for computer programming, and Ms. Sheila Reyes for the preparation of the manuscript.

References


The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria.
P R Marantz, J N Tobin, S Wassertheil-Smoller, R M Steingart, J P Wexler, N Budner, L Lense and J Wachspress

_Circulation._ 1988;77:607-612
doi: 10.1161/01.CIR.77.3.607

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/77/3/607

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/