The Pharmacologic Treatment of Chronic Congestive Heart Failure

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The management of the patient with congestive heart failure is a three-part process that includes the diagnosis of the underlying cardiac lesion(s), its severity, and precipitating factors; treatment; and prevention of cardiac disease, heart failure, and recurrences. Heart failure may result from abnormalities of left ventricular systolic function, diastolic function, or both. Abnormalities of left ventricular diastolic function commonly occur in association with the hypertrophied left ventricle; in some patients, it occurs after myocardial infarction. In left ventricular hypertrophy (for example, that associated with systemic hypertension), diastolic dysfunction may precede systolic dysfunction; in the stage of diastolic dysfunction, aggressive control of systemic hypertension, complemented if necessary by drugs that reduce ventricular filling pressure, may be adequate.

In everyday clinical practice, the diagnosis of heart failure and determination of its cause and treatment do not pose major difficulties. For example, systemic hypertension was the most common cause of heart failure in The Framingham Study, and in most patients heart failure is mild and is easily controlled. Toward the other end of the spectrum is a subset of patients in whom the cause of heart failure may not be so easy to determine or in whom the underlying cause cannot be corrected, who may have moderate-to-severe left ventricular systolic dysfunction, and who may be moderately to severely symptomatic; examples are patients with dilated congestive cardiomyopathy and advanced coronary artery disease with its complications. Referral centers that provide tertiary care or have specialized units of research in heart failure often have a high percentage of the latter subgroup of patients; in studies of chronic congestive heart failure, the majority of or nearly all of the patients have had coronary artery disease, dilated congestive cardiomyopathy, or both and the heart failure has usually been resistant to standard therapy. Although the experience at these centers may be unique and most valuable, one should be careful about extrapolating it without proof to all patients with heart failure. For example, it was recently suggested that the definition of heart failure should include a high incidence of ventricular arrhythmias. There is concern about such a definition because it implies that 1) in the absence of ventricular arrhythmias one cannot diagnose heart failure, which is incorrect, and 2) that one needs to seek or document ventricular arrhythmias if the other clinical features of heart failure are present. The practical significance is that one would have to perform ambulatory electrocardiographic monitoring frequently in such patients, and it is highly questionable whether this should be done routinely, particularly in this cost-conscious era when the diagnostic and therapeutic values of this test in patients with heart failure are unproven.

Forty years ago, when I entered medical school, most patients with heart failure were successfully treated with digitalis, intermittent intramuscular diuretics, and salt restriction; many such patients, particularly those with severe heart failure, would have died without such treatment. Subsequent introduction of oral diuretics into routine clinical practice made life much more comfortable and pleasant for the patient with heart failure and simplified the delivery of health care. The use of digitalis and diuretics was the mainstay of pharmacologic treatment of patients with heart failure; one reason was that they were the only therapies available. However, they also were and still are very effective in relieving the symptoms and signs of heart failure in most patients and, therefore, continue to be the mainstay of pharmacologic treatment of heart failure. Packer has recently provided excellent reviews of some of the results to be expected with some of the currently available pharmacologic agents in clinical use or under clinical investigation in the treatment of congestive heart failure.

During the past 2 decades, the effects of vasodilators have been widely studied; in the past 3 years, four reports have presented the results of three large randomized trials that have evaluated the role of vasodilators in improving survival, functional...
class, exercise time, and left ventricular function in
patients with chronic heart failure.4-7 It is my goal
to critically evaluate these trials and to provide the
perspective of one academically oriented clinical
cardiologist about the current pharmacologic treat-
ment of the patient with chronic congestive heart
failure who has left ventricular systolic dysfunction.

**Pharmacologic Treatment of Chronic Congestive Heart Failure**

**Severity of Congestive Heart Failure**

The severity of congestive heart failure has tra-
donically and commonly been assessed by clinical
criteria and graded according to New York Heart
Association functional Classes I-IV.11 Exercise test-
ing with measurement of maximum oxygen con-
sumption provides metabolic measurements and an
objective assessment of the degree of functional
impairment.12-16 It needs to be emphasized that in
general these studies have confirmed that the clinical
classification can be related to objective mea-
surements (Table 1), albeit not perfectly16; more-
over, the clinical classification also provides a guide
to mortality (see below and Table 2). Therefore,
exercise testing in patients with congestive heart
failure needs to be undertaken for clinical purposes
only in selected circumstances; however, it is im-
portant and may be essential for most research
studies.12-16

**Functional Class IV Patients**

In the Cooperative North Scandinavian Enalapril
Survival Study (CONSENSUS),6 a period of up to
14 days was allowed to stabilize Class IV patients
don digitals and diuretics; if the patients improved
to Class III during this period, they were excluded.
The number of patients who met the entry criteria
but were not randomized is not stated. The study
consisted of 253 randomized patients (average age,
70 years) of whom 70% were men; 73% had coro-
ary artery disease, 47% had a previous myocardial
infarction, 15% had cardiomyopathy, 22% had val-
cular heart disease, and 21% had systemic hyper-
tension. Of interest, 49% were on vasodilators other

### Table 1. Classification of Severity of Congestive Heart Failure

<table>
<thead>
<tr>
<th>NYHA functional class</th>
<th>Symptoms</th>
<th>Metabolic classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic on ordinary physical activity</td>
<td>*= A 21</td>
</tr>
<tr>
<td>II</td>
<td>Symptomatic on ordinary physical activity</td>
<td>= B 16-20</td>
</tr>
<tr>
<td>III</td>
<td>Symptomatic on less than ordinary physical activity</td>
<td>= C 10-15</td>
</tr>
<tr>
<td>IV</td>
<td>Symptomatic at rest or unable to perform any activity</td>
<td>= D 9</td>
</tr>
</tbody>
</table>

NYHA, New York Heart Association; maximum V02, maximum oxygen consumption.

* All equivalences are approximate.

Adapted and modified from References 11-16.

### Table 2. Mortality of Patients With Congestive Heart Failure

<table>
<thead>
<tr>
<th>Study</th>
<th>NYHA Class</th>
<th>Patients (n)</th>
<th>Patients (%)</th>
<th>Digitalis plus diuretics (%)</th>
<th>Digitalis plus diuretics plus vasodilators (%)</th>
<th>Diuretics plus vasodilators at 6 mon (%)</th>
<th>Diuretics at 6 mon (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONSENSUS*</td>
<td>IV</td>
<td>253</td>
<td>100</td>
<td>44</td>
<td>52</td>
<td>26</td>
<td>36</td>
</tr>
<tr>
<td>V-HeF†</td>
<td>III</td>
<td>459</td>
<td>48</td>
<td>52</td>
<td>20</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>and II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III‡</td>
<td>100</td>
<td>(12)</td>
<td>25</td>
<td>10</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>II‡</td>
<td>100</td>
<td>(6)</td>
<td>13</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Captopril-Digoxin MRG§</td>
<td>300</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
<td></td>
<td>80</td>
<td>7</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td>20</td>
<td></td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td>89-91</td>
<td></td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

NYHA, New York Heart Association; NA, not applicable.

Numbers are rounded off to exclude decimal points.

CONSENSUS Study: 49% of patients were also on vasodilators other than an ACE inhibitor.

‡ Class III based on group with maximum V02<14.5 ml/kg/min and Class II based on group with maximum V02≥14.5 ml/kg/min (see text).
( ), 6-month mortality assumed to be half of the reported annual mortality.
than an angiotensin-converting enzyme (ACE) inhibitor, and these vasodilators were continued in both groups during the period of the trial. The principal end-points of the study were the 6-month mortality and the cause of death.

The CONSENSUS trial, which included only patients who were in NYHA functional Class IV, demonstrated a lower mortality at 6 months (26% compared with 44%; \( p = 0.002 \)) in the group of patients who had an ACE inhibitor, enalapril, added to the regimen of digitalis, diuretics, and other vasodilators that some were taking already (Table 2). The cause of death was cardiac in origin in almost all of the patients. The group treated with the addition of the ACE inhibitor also had an improved distribution of functional classes (\( p = 0.001 \)); for example, the improvement in functional class was greater in patients who received the ACE inhibitor enalapril (42% compared with 22%). It is of interest that the mortality from 6 to 12 months was similar in both groups (Table 3). In fact, review of Figure 1A strongly suggests that after 3 months there was no major difference in mortality between the groups during the 3–12 months of the trial. Whether there was continued or further benefit from enalapril during the last 3–12 months of the trial cannot be stated with certainty. Seventeen percent of patients in the ACE inhibitor group and 14% in the other group had to be withdrawn from the study because of side effects, medical reasons, or patient decision.

**Recommendation**

One can extrapolate the results of the CONSENSUS Trial to recommend that patients with congestive heart failure who are in functional Class IV should be treated with digitalis and diuretics and also should be given an ACE inhibitor at least for 3–6 months provided there is no contraindication to its use (Table 4).

**Functional Class III Patients**

In the Veterans Administration Heart Failure Trial (V-HeFT) study, 4,273 men were in the digitalis plus diuretics group and 186 men were randomized to receive in isosorbide dinitrate plus hydralazine (ISDN-Hyd) in addition to digitalis plus diuretics. There were 183 patients in the prazosin group; their results were no different from the digitalis plus diuretic group, and they will not be discussed further. The patients had to have clinical and exercise stability on digoxin plus diuretics for 2 weeks to

**TABLE 3. Mortality During Different Time Periods in Patients With Congestive Heart Failure**

<table>
<thead>
<tr>
<th></th>
<th>Digitalis plus diuretics (%)</th>
<th>Digitalis plus diuretics plus vasodilators (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CONSENSUS Study</strong> (n=253)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–6 mon</td>
<td>44</td>
<td>26</td>
</tr>
<tr>
<td>6–12 mon</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Total 12 mon</td>
<td>52</td>
<td>36</td>
</tr>
<tr>
<td><strong>V-HeFT (n=459)</strong>†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–12 mon</td>
<td>19.5</td>
<td>12.1</td>
</tr>
<tr>
<td>12–24 mon</td>
<td>14.8</td>
<td>13.5</td>
</tr>
<tr>
<td>24–36 mon</td>
<td>12.6</td>
<td>10.6</td>
</tr>
<tr>
<td>36–48 mon</td>
<td>6.7</td>
<td>13.5</td>
</tr>
<tr>
<td>Total 12–48 mon</td>
<td>34.1</td>
<td>37.6</td>
</tr>
<tr>
<td>0–48 mon</td>
<td>53.6</td>
<td>49.7</td>
</tr>
</tbody>
</table>


---

**FIGURE 1.** The mortality curves of the placebo and enalapril-treated groups from 3 to 12 months are parallel in the CONSENSUS Trial (Figure A). Similarly, the mortality curves of the placebo and Hyd-Iso in the V-HeFT Study are also parallel from 12 to 42 months (Panel B) (see text). Reproduced by permission from \( N \) Engl J Med 1987;316:1429–1435 and \( N \) Engl J Med 1986;314:1547–1552.
be included in the study; the number of patients who met the entry criteria but were not included in the study is not stated. The patients’ average age was 58 years and all were men; 44% had coronary artery disease, 42% had previous myocardial infarction, 38–43% had an excess of alcohol consumption, and 40–43% had systemic hypertension.

The V-HeFT study randomized patients who were in functional Classes III and II and demonstrated a reduction in mortality over the 4-year follow-up period in the group in whom ISDN-Hyd was added to standard digitalis and diuretic therapy (Tables 2 and 3). However, it must be recognized that this improvement had a p value of 0.093 on the log-rank test. The p value was 0.046 on the generalized Wilcoxon test; however, even “the Wilcoxon statistic was not [italics added] quite significant at the p = 0.05 level after adjustments were made for multiple tests over time for possible early stopping.”

In simple words, the overall improvement in survival in the V-HeFT study with the addition of ISDN-Hyd to digitalis plus diuretics was not statistically significant; therefore, one should be very careful about making inappropriate conclusions and extrapolations from this study.

On using the Cox life-table regression model, the lower cumulative mortality up to 2 years with ISDN-Hyd (25.6% compared with 34.3%) was significant (p < 0.028); however, for the same analysis, the log-rank statistic yielded a p value of 0.053.

Why is it that the CONSENSUS Trial easily demonstrated high statistical significance to the lowered mortality with an ACE inhibitor but in the V-HeFT study it was difficult to do so with ISDN-Hyd? There are probably many reasons but at least two can be reviewed. First, the CONSENSUS Trial included only functional Class IV patients with 1-year mortality on digitalis plus diuretics of 52%, which was reduced to 36% with the addition of an ACE inhibitor, whereas the V-HeFT study included patients in functional Classes III and II with a 1-year mortality on digitalis plus diuretics of 19.5%, which dropped to 12.1% with the addition of ISDN-Hyd. Because the annual mortality was much lower for patients in the V-HeFT study, a much larger number of patients and a greater drop in mortality may be required to demonstrate statistical significance. Second, the V-HeFT study used ISDN-Hyd as the vasodilators that were tested. In this study, 32% of the patients permanently discontinued one or both of these medications, and at the end of 6 months only 55% of the patients were prescribed full doses of both these drugs; in other words, a large number of patients were not taking the medications or not taking them in appropriate doses. Moreover, many patients are known to develop nitrate tolerance fairly rapidly, even those who receive it for the treatment of congestive heart failure.

It is of interest that in the V-HeFT study, the mortality from 12–24, 24–36, and 36–48 months and of the combined 12–48-month period was similar in both groups (Table 3; Figure 1B). In this study, patients with coronary artery disease also had a higher mortality than those without coronary artery disease.

There is no large study that has only evaluated functional Class III patients. However, subsequent subgroup analysis of the V-HeFT study provided information on patients with maximum total body oxygen consumption (Vo2) of less than 14.5 ml/kg/min (functional Class III, Table 1) and with maximum Vo2 of 14.5 ml/kg/min or more (functional Class II). Patients in functional Class III had an annual mortality rate of 25% in the digitalis plus diuretic group and of 20% in the group with ISDN-Hyd added to digitalis plus diuretics (Table 2). One could speculate that had the patients been given another vasodilator such as an ACE inhibitor, compliance with therapy and, therefore, the mortality in the group of Class III patients would have been lowered to a greater degree. Subgroup analysis also showed that the addition of ISDN-Hyd to digitalis plus diuretic resulted in greater absolute (and usually percent) reduction in annual mortality rate in patients with coronary artery disease, left ventricular ejection fraction of 0.28 or less, no history of excess alcohol, antiarrhythmic therapy, history of systemic hypertension, and age less than 60 years.

**Recommendation**

The functional Class III patient appears to have a higher mortality than the Class II patient when treated with only digitalis and diuretics (Table 2). The higher mortality in the Class III patient is slightly lower with the addition of vasodilators ISDN-Hyd. The combination of ISDN-Hyd has problems of side effects, compliance, and tolerance (see above); thus, at the present time, it would appear to be clinically prudent to recommend for the functional Class III patient the addition of an ACE inhibitor to digitalis plus diuretics for at least 12 months, provided there is no contraindication to its use.
Functional Class II Patients

The mortality of the functional Class II patient treated with digitalis plus diuretics (≤7% at 6 months and ≤13% at 1 year) is lower than for Class III and IV patients (Table 2). The V-HeFT study showed that the addition of ISDN-Hyd to digitalis plus diuretic reduced the mortality at 1 year to only 10%, but there are problems with the V-HeFT study (see above). On the other hand, the Captopril-Digoxin Multicenter Research Group (Captopril-Digoxin MRG) study showed no difference in survival at 6 months among the three groups that were studied, that is, digitalis plus diuretics, captopril plus diuretic, and diuretic (Table 2). Thus, the decision to use drugs or their combination in the functional Class II patients has to be based only on demonstrated benefits other than those of an improved survival.

A small randomized study demonstrated that an ACE inhibitor alone was not satisfactory for the control of heart failure; four of 14 patients so treated developed pulmonary edema. Another small study showed that the addition of an ACE inhibitor, captopril, to baseline diuretic and vasodilator therapy was inferior when compared with increasing doses of diuretic therapy in controlling heart failure. The Captopril-Digoxin MRG study showed digitalis plus diuretics as well as captopril plus diuretics to be better than diuretics alone in the treatment of patients in Class II. For example, patients treated with diuretics alone had significantly less improvement and greater deterioration in functional class; they also had no significant improvement in exercise time or left ventricular ejection fraction. Thus, single drug therapy with an ACE inhibitor or diuretics is not satisfactory in the treatment of the functional Class II patient. Digitalis therapy alone is unlikely to control heart failure; therefore, combination therapy has to be used even in the functional Class II patient.

In the Captopril-Digoxin MRG Study of 300 patients, the average age of the patients was 57 years and 83% were men; the etiology of the heart failure was coronary artery disease in 62% and idiopathic cardiomyopathy in 32%. The primary goal of the study was to determine an improvement in exercise tolerance; secondary goals included an assessment of left ventricular function (Table 5).

The Captopril-Digoxin MRG study provided a direct comparison of two drug combinations—captopril plus diuretics compared with digoxin plus diuretics. The captopril plus diuretic group had a statistically significant increase in exercise time when compared with the diuretic group (81 compared with 35 seconds; \( p < 0.05 \)); however, when the captopril plus diuretic group was compared with the digoxin plus diuretic group, the exercise times at baseline and at the end of the study were not significantly different. The number of patients who crossed over from one group to another and/or did not follow the protocol is not stated; when the data were analyzed by the intention-to-treat analysis, the increases in exercise times (captopril plus diuretic, 77 seconds; digoxin plus diuretic, 55 seconds; diuretics, 40 seconds) were not significantly different among the groups (\( p < 0.10 \); Table 5). On the other hand, the digitalis plus diuretic group had an increase of left ventricular ejection fraction of 4.4% that was

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**Table 5. Captopril-Digoxin Multicenter Research Group Study**

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Captopril plus diuretic</th>
<th>Digitalis plus diuretics</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.5</td>
<td>58.3</td>
<td>0.02</td>
</tr>
<tr>
<td>NYHA Class III (%)</td>
<td>9</td>
<td>20</td>
<td>...</td>
</tr>
<tr>
<td>Increase in exercise time (sec)*</td>
<td>77</td>
<td>55</td>
<td>NS</td>
</tr>
<tr>
<td>Increase in LVEF*</td>
<td>0.2</td>
<td>0.41</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Decrease in VPB per hour (%)*</td>
<td>48</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA Class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved*</td>
<td>42</td>
<td>33</td>
<td>NS</td>
</tr>
<tr>
<td>Deteriorated*</td>
<td>14</td>
<td>9</td>
<td>NS</td>
</tr>
<tr>
<td>Adverse drug reactions (%)</td>
<td>2.9</td>
<td>4.2</td>
<td>...</td>
</tr>
<tr>
<td>Possible adverse side-effects (%)</td>
<td>44.2</td>
<td>30.2</td>
<td>...</td>
</tr>
<tr>
<td>Withdrawal from study (%)</td>
<td>5.8</td>
<td>4.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hospitalization and ED visits (patients)</td>
<td>17 patients</td>
<td>15 patients</td>
<td>...</td>
</tr>
<tr>
<td>Mortality at 6 mon (%)*</td>
<td>7.7</td>
<td>7.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Intention-to-treat analysis.

NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; VPB, ventricular premature beats; ED, emergency department.

Note: Thirty patients not randomized because on withdrawal from digitalis; heart failure deteriorated. Patients only entered into study if they could tolerate captopril. Open-label captopril test-dose phase: 29% of patients experienced 20% or greater fall in systolic blood pressure; 11% had symptoms of hypotension; and 1% eliminated from study. Trough serum levels of digoxin >0.7–<2.5 ng/ml. Numbers of patients that crossed over and/or did not follow protocol not given.

From JAMA 1988;259:539–544.
significantly greater than that seen in the captopril plus diuretic (1.8%; p<0.05) and diuretic groups (0.9%; p<0.01). Moreover, when the data were analyzed by the intention-to-treat analysis, the improvement in left ventricular ejection fraction in the digoxin plus diuretic group was still significantly greater (4.1%; p<0.05) than that seen in the captopril plus diuretic and diuretic groups in whom left ventricular ejection fraction increased by 2% and 1.3%, respectively.

A comparison of results between the captopril plus diuretic and digoxin plus diuretic groups from the Captopril-Digoxin MRG study is shown in Table 5. The two groups were not identical: The patients were older in the digoxin plus diuretic group; the number of Class III patients was twice as high in the digitalis plus diuretic group as in the captopril plus diuretic group; at least 30 patients were not randomized because they deteriorated when digoxin was withdrawn, thus biasing the study against digitalis; patients were only entered into the study if they could tolerate captopril, thus biasing the study in favor of captopril; and trough digoxin levels were kept as high as 2.4 ng/mL, increasing the likelihood of digoxin side effects and toxicity.

Recommendation

In the functional Class II patient, monotherapy with an ACE inhibitor, diuretics, and probably digitalis is not satisfactory. Treatment with an ACE inhibitor plus diuretic and digoxin plus diuretic is superior to use of diuretics alone. Digoxin plus diuretic may be superior to ACE inhibitor plus diuretic based on my interpretation of the available data, and therefore my recommendation is that functional Class II patients should be treated with digitalis plus diuretic therapy.

There may be several advantages to using digitalis rather than an ACE inhibitor: digitalis is given orally (once daily which is expected to improve patient compliance); it is easily tolerated; side effects are infrequent; and ACE inhibitor therapy is much more expensive than digitalis.

It has been suggested that the Class II patient should receive a vasodilator in addition to digitalis plus diuretic because vasodilators have been shown to prolong survival in heart failure. The CONSENSUS Trial after 3–6 months and in the V-HeFT study after 12 months, the additional mortality in those treated with vasodilators was similar to those not treated with vasodilators (Table 3). Thus, the evidence for routine use of vasodilators in the Class II patient does not seem persuasive.

Not all Class II patients will be adequately controlled with digitalis plus diuretic; therefore, it can be recommended that an ACE inhibitor be added to digitalis plus diuretic therapy if the response to the latter is not adequate.

Functional Class I Patient

The functional Class I patient is by definition asymptomatic on ordinary activity, which implies these patients have impaired left ventricular systolic function that is usually not accompanied by any significant hemodynamic abnormality. There is no data at the present time to suggest any therapy improves survival or quality of life or has other beneficial effects in these patients.

Need for Additional Studies

We do not possess all the information needed to manage all patients with chronic congestive heart failure ideally and many questions remain. For example, is there benefit to continuing vasodilator therapy beyond 6 months in the Class IV patient and beyond 12 months in the Class III patient? Is there any benefit to adding vasodilator therapy to digoxis plus diuretic in the Class II patient? Is the combination of digitalis plus vasodilator therapy superior to digitalis plus diuretic therapy in the Class II patient? Is any therapy better than no therapy in the Class I patient; if it is, which drugs or combination are the best? There is a need for many additional studies and extensive research in this field.

It is also clear that future studies should study specific patient groups separately. For example, Class III patients should be studied separately from Class II patients. Preferably, the patients should be characterized by exercise testing; the data from the V-HeFT Study suggest patients with coronary artery disease may need to be studied separately from those without coronary artery disease.

Need for Additional Measures

In patients with chronic congestive heart failure, even with the use of digitalis, diuretics, and vasodilators, the 1-year mortality (Table 2) of the Class IV patient is very high (36%) and that of the Class III patient is high (20%). In the Class II patient, the 6-month mortality is not low (7%). Thus, there is a need to continue to evaluate use of other pharmacologic agents and interventions and, in the appropriate patient, to consider cardiac transplantation early and to emphasize the importance of preventive measures (both primary prevention of heart disease and heart failure and secondary prevention, that is, recurrences of heart failure).
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S H Rahimtoola

Circulation. 1989;80:693-699
doi: 10.1161/01.CIR.80.3.693

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