Carvedilol Increases Two-Year Survival in Dialysis Patients With Dilated Cardiomyopathy
A Prospective, Placebo-Controlled Trial

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OBJECTIVES We sought to evaluate the effects of carvedilol on mortality and morbidity in dialysis patients with dilated cardiomyopathy.

BACKGROUND Several lines of evidence support the concept that therapy with beta-blocking agents reduces morbidity and mortality in patients with congestive heart failure (HF), but the demonstration of such a survival benefit in dialysis patients with dilated cardiomyopathy is still lacking.

METHODS A total of 114 dialysis patients with dilated cardiomyopathy were randomized to receive either carvedilol or placebo in addition to standard therapy. A first analysis was performed at one year and was followed by an additional follow-up period of 12 months.

RESULTS Two-year echocardiographic data revealed a significant attenuation of pathologic remodeling, with smaller cavity diameters and higher ejection fractions in the active treatment group than in the placebo group. At two years, 51.7% of the patients died in the carvedilol group, compared with 73.2% in the placebo group (p < 0.01). Furthermore, there were significantly fewer cardiovascular deaths (29.3%) and hospital admissions (34.5%) among patients receiving carvedilol than among those receiving a placebo (67.9% and 58.9%, respectively; p < 0.00001). The exploratory analyses revealed that fatal myocardial infarctions, fatal strokes, and hospital admissions for worsening HF were lower in the carvedilol group than in the placebo group. A reduction in sudden deaths and pump-failure deaths was also observed, though it did not reach statistical significance.

CONCLUSIONS Carvedilol reduced morbidity and mortality in dialysis patients with dilated cardiomyopathy. These data suggest the use of carvedilol in all dialysis patients with chronic HF. (J Am Coll Cardiol 2003;41:1438–44) © 2003 by the American College of Cardiology Foundation

The demonstration that therapy with beta-adrenergic blocking agents improves survival in congestive heart failure (CHF) (1–3) has recently prompted us to evaluate the effects of carvedilol, a third-generation beta-blocking drug endowed with vasodilator properties, in dialysis patients affected with dilated cardiomyopathy. Despite the routine pharmacologic therapy and the optimization of the dialysis regimen, such particular subset of patients exhibits an inexorable disease progression, with a very high mortality and morbidity (4–6).

After our initial investigation, which showed improved clinical status and left ventricular (LV) function in dialysis patients with dilated cardiomyopathy after 12 months of carvedilol therapy (7), we followed up the same patient population for an additional 12-month period. Not only clinical status and LV structure and function were evaluated, but also the mortality rate. The results of the current study provide the first demonstration that carvedilol can prolong survival in dialysis patients with dilated cardiomyopathy.

METHODS

Patients. Recruitment criteria were previously described (7). Briefly, from February 1996 to December 1998, we recruited 132 patients (89 men, 43 women; mean age, 55.1 ± 7.6 years) with uremia on periodic hemodialysis treatment and dilated cardiomyopathy. All patients were symptomatic for heart failure (HF) (New York Heart Association [NYHA] functional class II to III) for at least one year, with an left ventricular ejection fraction (LVEF) < 0.35 at echocardiography. To be included in the study, patients had to be clinically stable with no change in their usual medications in the last two weeks and should not have required intravenous inotropic drug therapy or experienced weight changes for at least 48 h before the enrollment (> 2.5 kg compared with the “dry weight”). Exclusion criteria included: current NYHA functional class IV; heart rate < 50 beats/min; sick sinus syndrome; first degree atrioventricular block with a PQ interval > 0.24 s, second- or third-degree heart block (unless controlled by a pacemaker); documented episodes of sustained ventricular tachycardia (> 30 s, > 120 beats/min); systolic blood pressure (BP) < 90 mm Hg; stroke, acute myocardial infarction (MI), unstable angina, coronary angioplasty, or aortocoronary bypass surgery in the three...
Abbreviations and Acronyms

ACE = angiotensin-converting enzyme
BP = blood pressure
CHF = congestive heart failure
CI = confidence interval
HF = heart failure
HR = hazard ratio
Kur = kurtosis
LV = left ventricle/ventricular
LVEDV = left ventricular end-diastolic volume
LVEF = left ventricular ejection fraction
LVESV = left ventricular end-systolic volume
MI = myocardial infarction
NYHA = New York Heart Association
Ske = skewness

Carvedilol Prolongs Survival in Dialysis Patients

The patients were checked with daily medical examinations during titration and every other day during the maintenance phase in concomitance with dialysis.

The primary end points were the same as reported in the previous one-year investigation and included changes in LV end-diastolic volume (LVEDV), in LV end-systolic volume (LVESV), in ejection fraction, and in clinical status 24 months after randomization. Secondary end points were all-cause mortality, all-cause hospital admission, cardiovascular mortality, acute non-fatal MI, combined end point (cardiovascular mortality plus acute non-fatal MI), cardiovascular hospital admission, and permanent premature treatment withdrawals.

In the exploratory analyses regarding the cause of death, critical events were classified according to strict definitions. “Acute MI” was defined as a cardiac event requiring admission to the hospital, with development of new electrocardiographic changes and cardiac enzyme (troponin I) level increases. “Sudden death” was defined as death occurring within 1 h, without previous worsening of symptoms of HF. We also took unexpected deaths occurring during sleep to be “sudden” when patients were found deceased by family members in the morning when sharing the same room. We classified other unwitnessed deaths as “unknown.” We classified as “pump failure death” that which occurred as a consequence of progressive deterioration of HF, acute pulmonary edema, or cardiogenic shock. Fatal MI and fatal stroke were classified as “other cardiovascular deaths.” If cardiovascular events were excluded as the cause of a death, we recorded it as “non-cardiovascular death.” Death was classified as being due to an unknown cause when there was insufficient evidence to confirm a cardiovascular or non-cardiovascular cause.

We recorded a “permanent treatment withdrawal” whenever intolerance to study medication occurred, despite increases in baseline therapy, if study-drug dose was decreased or temporarily withdrawn, if patients experienced intolerance to first dose, and for all other circumstances in which study drug was permanently stopped.

The patients were informed in detail of the formalities and finality of the study. All patients provided written informed consent to participate. The institutional committee on human research approved the study protocol.

Among the 132 patients eligible for the inclusion in the trial, 18 were excluded during the run-in phase. Thus, 114 patients, whose clinical characteristics are reported elsewhere (7), started the maintenance phase.

Statistics. The analyses of primary and secondary end points included all the patients, according to the intention-to-treat principle. Descriptive statistical procedures were used to assess the distribution of each variable. The analyses

previous months; uncorrected valvular heart disease; active myocarditis; obstructive and restrictive cardiomyopathy; current treatment with verapamil, alpha/beta adrenergic agonists or antagonists; chronic obstructive airways disease; hepatic disease (serum transaminase > 3 times normal); drug or alcohol abuse; or any other life-threatening non-cardiac disease.

All patients were receiving digitalis; 128 patients (96.9%) were also receiving angiotensin-converting enzyme (ACE) inhibitors; four patients (3.1%) who were intolerant of the ACE inhibitors received angiotensin II receptor antagonists; 32 (25%) patients were taking nitrates.

All patients were dialyzed four times a week, for a mean time of 210 ± 30 min, with a middle quote blood of 260 ± 20 ml/min, using a cuprophan hollow-fiber hemodialyzer by 1.3 to 1.8 m² of surface and 7.5 μ of thickness. A personalized bath of dialysis was used, with variable concentration of potassium between 2 and 3.5 mEq/l. The concentration of sodium was variable between 144 and 150 mEq/l in relation to the BP. Monitors were used for computerized checking of ultrafiltration and real time monitoring of the loss of the weight, so as to have an exact and constant control of the weight reduction per hour. Furthermore, heart rate and BP were checked. The “dry weight” of all patients was stable for at least one month.

Design and study treatment. All inclusion criteria, the “run-in” phase, and the titration period are described in detail elsewhere (7). Upon completion of a one-year observation period, codes were broken, and the clinical and echocardiographic data were collected and reported in a previous publication (7). Subsequently, all patients were followed up for an additional 12 months. The current trial was, therefore, designed as a prospective, open-label, placebo-controlled, randomized clinical study. As previously described (7), at the end of the up-titration phase, the therapy with carvedilol or placebo was maintained for 24 months (maintenance phase), during which time carvedilol was administered at the maximum dose of 25 mg twice a day or to the highest dose tolerated. Concomitant therapy with digitalis, ACE inhibitors, angiotensin II receptor antago-
were performed by SPSS for Windows release 11.0 (Chicago, Illinois). Data are presented as mean ± SD.

For continuous variables, between-group comparisons were performed using the two-way analysis of variance (ANOVA), with treatment as one factor and time as the other factor. Comparisons to determine the significance of changes within the same group over time and between groups at each time point were performed with the Newman-Keul post-hoc test, using ANOVA models for repeated measures. Chi-square test was used for categorical variables like NYHA class.

Samples were tested for normal distribution by Box-Bartlett homogeneity test and by skewness (Ske) and kurtosis (Kur) analyses. In particular, Ske measured the asymmetry of the distribution, while Kur showed the extent to which observations clustered around a central point. By such analyses, continuous variables showed a normal distribution: heart rate (Ske, 0.3; Kur, 0.4), systolic BP (Ske, 0.4; Kur, 0.3), diastolic BP (Ske, 0.4; Kur, 0.3), LVEDV (Ske, 0.2; Kur, 0.3), LVESV (Ske, 0.3; Kur, 0.4), LVEF (Ske, 0.3; Kur, 0.2).

Hazard ratios (HR) and 95% confidence intervals (CI) for cardiac events were assessed by multivariable Cox proportional hazards regression models, in order to explore the effects of baseline variables on the estimated effects of carvedilol. Kaplan-Meier survival curves on cardiac events were assessed by use of the log-rank test (time to event). Comparisons to determine the significance of changes within the same group over time and between groups at each time point were performed with the Newman-Keul post-hoc test, using ANOVA models for repeated measures. Chi-square test was used for categorical variables like NYHA class.

RESULTS

Dropout patients. Of 132 patients entering the run-in phase, 18 (13.6%) were excluded due to side effects: hypotension (n = 3), dizziness (n = 1), bronchospasm (n = 5), bradycardia (n = 4), worsening HF (n = 4), and protocol violation (n = 1). Of 114 patients starting the titration phase, one was excluded. Of 114 patients entering the maintenance phase, 11 (9.6%) dropped out of the study. Four patients in the carvedilol group dropped out: one for the appearance of hypotension, one for bradycardia, one for second-degree heart block, and one because of acute MI. Seven patients in the placebo group dropped out: three for worsening HF, two because of protocol violation, one because of acute non-fatal MI, and one because of refractory hyperkalemia.

Echocardiographic parameters and clinical status asssessed as NYHA. The echocardiographic data and clinical status assessment (Tables 1 and 2) revealed that structural and functional benefits obtained by one-year carvedilol therapy were maintained also at year 2, insofar as LV cavity diameters and ejection fraction were similar in the active treatment group at both time points.

Mortality. Mortality was not significantly different between the two groups at one year (0.58 in carvedilol group vs. 3.56 in placebo group, p = NS). At two years in the carvedilol group, 30 patients (51.7%) died, compared with 41 (73.2%) in the placebo group (p < 0.01). There were significantly fewer all-cardiovascular deaths (29.3% vs. 67.9%, p < 0.00001) among patients receiving carvedilol than among those receiving placebo. In particular, the main reduction was observed in the number of other cardiovascular deaths (22.5% vs. 42.9%, p < 0.01). Also, the number of sudden deaths and pump failure deaths was reduced by carvedilol treatment, even if non-significantly differing between the two groups (Table 3).

By Cox proportional-hazards regression analysis, the use

| **Table 1. HR, Blood Pressure, and Echocardiographic Parameters in the Carvedilol and Placebo Groups** |
|---|---|---|---|---|---|---|---|---|---|
| **Carvedilol** | **Placebo** |
| **HR (beats/min)** | 93 ± 11 | 69 ± 7 † | 69 ± 7 † | 69 ± 7 † | 66 ± 5 † | 93 ± 12 | 92 ± 12 | 91 ± 12 | 92 ± 12 |
| **SBP (mm Hg)** | 134 ± 8 | 124 ± 7 † | 123 ± 7 † | 123 ± 8 † † | 120 ± 8 † † | 135 ± 9 | 134 ± 9 | 133 ± 10 | 133 ± 11 |
| **DBP (mm Hg)** | 75 ± 6 | 68 ± 6 † | 67 ± 6 † | 67 ± 6 † | 70 ± 5 † | 75 ± 6 | 74 ± 6 | 75 ± 6 | 73 ± 6 |
| **LVEDV (ml/m²)** | 100 ± 9 | 99 ± 8 | 94 ± 8 † | 94 ± 4 † | 94 ± 5 † | 97 ± 8 | 97 ± 8 | 99 ± 6 | 98 ± 6 |
| **LVESV (ml/m²)** | 74 ± 8 | 72 ± 8 | 62 ± 8 † | 62 ± 8 † | 64 ± 6 † | 72 ± 9 | 72 ± 8 | 72 ± 8 | 72 ± 8 |
| **LVEF (%)** | 26 ± 8 | 27 ± 7 | 35 ± 11 † † | 36 ± 11 † † | 37 ± 10 † † | 26 ± 8 | 26 ± 8 | 27 ± 8 | 26 ± 8 |

*p < 0.05 vs. basal; †p < 0.05 vs. placebo; ‡p < 0.05 vs. control at one month.

DBP = diastolic blood pressure; HR = heart rate; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; SBP = systolic blood pressure.
of carvedilol appeared to be a strong independent predictor of both all-cause mortality (HR, 0.51; 95% CI, 0.32 to 0.82; p < 0.01) and cardiovascular mortality (HR, 0.32; 95% CI, 0.18 to 0.57; p < 0.0001).

The cumulative two-year mean survival time was 20.37 months in the carvedilol group and 18.33 months in the placebo group (log-rank, 8.58; p < 0.005) (Fig. 1). Of interest, 12-month mortality rate was 0% in the carvedilol group versus 5.2% in the placebo group (p = NS), but it increased, respectively, to 51.7% and 73.2% (p < 0.01) at two-year follow-up. In addition, patients receiving carvedilol showed increased two-year survival time free of cardiovascular deaths compared with placebo patients (21.7 vs. 18.1 months, respectively; log-rank, 17.14; p < 0.00001) (Fig. 2).

**Hospital admissions.** Significantly fewer patients receiving carvedilol were admitted to the hospital for all causes (20 patients, 34.5%) than placebo patients (33 patients, 58.9%) (p < 0.005). In particular, the difference in hospital admission for worsening HF was 43.3% (8 patients, 13.8%, in carvedilol group vs. 32 patients, 57.1%, in placebo group; p < 0.00001). Conversely, the number of hospital admissions for acute non-fatal MI, combined end point, or pump failure did not significantly differ between the two groups.

### Table 3. Secondary End Points and Exploratory Analyses

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 56)</th>
<th>Carvedilol (n = 58)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary End Points</strong></td>
<td></td>
<td></td>
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<tr>
<td>All-cause mortality</td>
<td>41 (73.2%)</td>
<td>30 (51.7%)</td>
<td>0.51 (0.32–0.82)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>All-cause hospital admission</td>
<td>33 (58.9%)</td>
<td>20 (34.5%)</td>
<td>0.44 (0.25–0.77)</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>All cardiovascular deaths</td>
<td>38 (67.9%)</td>
<td>17 (29.3%)</td>
<td>0.32 (0.18–0.57)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Non-fatal myocardial infarction</td>
<td>1 (1.8%)</td>
<td>0 (0%)</td>
<td>0.81 (0.61–1.34)</td>
<td>0.31</td>
</tr>
<tr>
<td>Combined end point</td>
<td>39 (69.6%)</td>
<td>17 (29.3%)</td>
<td>0.76 (0.47–1.22)</td>
<td>0.22</td>
</tr>
<tr>
<td>Permanent treatment withdrawals</td>
<td>15 (26.8%)</td>
<td>17 (29.3%)</td>
<td>1.12 (0.84–1.42)</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Exploratory Analyses</strong></td>
<td></td>
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<tr>
<td>Sudden deaths</td>
<td>6 (10.6%)</td>
<td>2 (3.4%)</td>
<td>0.76 (0.52–1.13)</td>
<td>0.12</td>
</tr>
<tr>
<td>Pump-failure deaths</td>
<td>8 (14.4%)</td>
<td>2 (3.4%)</td>
<td>0.23 (0.05–1.23)</td>
<td>0.056</td>
</tr>
<tr>
<td>Other cardiovascular deaths</td>
<td>24 (42.9%)</td>
<td>13 (22.5%)</td>
<td>1.13 (0.82–1.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Non-cardiovascular deaths</td>
<td>2 (3.6%)</td>
<td>12 (20.7%)</td>
<td>0.76 (0.44–1.33)</td>
<td>0.02</td>
</tr>
<tr>
<td>Unknown cause of death</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>0.95 (0.55–1.3)</td>
<td>0.98</td>
</tr>
<tr>
<td>Hospital admission for worsening heart failure</td>
<td>32 (57.1%)</td>
<td>8 (13.8%)</td>
<td>0.19 (0.09–0.41)</td>
<td>&lt; 0.00001</td>
</tr>
</tbody>
</table>

CI = confidence interval.

**Figure 1.** Kaplan-Meyer curves for all-cause mortality during 24-month follow-up cumulative survival rate according to use of carvedilol. Solid lines = carvedilol group; dashed lines = placebo group.
The number of permanent treatment withdrawals was similar in the two groups.

By use of Cox regression analysis, treatment with carvedilol was independently associated with both reduced all-cause hospital admission (HR, 0.44; 95% CI, 0.25 to 0.77; \( p < 0.005 \)) and hospital admission for worsening HF (HR, 0.19; 95% CI, 0.09 to 0.41; \( p < 0.00001 \)).

By Kaplan-Meier analyses, patients receiving carvedilol showed increased two-year mean survival time free of hospital admissions compared with patients receiving placebo (20.9 vs. 16.2 months, respectively; log-rank, 8.8; \( p < 0.005 \) ) (Fig. 2). Of note, two-year mean survival time free of hospital admissions for worsening HF was 21.26 months in the carvedilol group and 13.98 months in the placebo group (log-rank, 22.7; \( p < 0.00001 \)).

**DISCUSSION**

Several lines of experimental evidence support the concept that therapy with beta-blockers reduces morbidity and mortality in CHF, but the demonstration of such a survival benefit in specific subgroups of patients is still lacking. In this regard, dialysis patients with CHF have been reported to have a higher mortality rate than non-uremic subjects (8–10). In a recently published study (7), we have demonstrated that carvedilol therapy attenuates the echocardiographic signs of pathologic remodeling, insofar as LV cavity diameters were reduced and ejection fraction increased after one year of carvedilol therapy, compared with baseline evaluation and placebo-treated subjects.

Herein, we report two-year data from the same patient population. In addition to the maintenance of LV structural and functional benefits, carvedilol therapy significantly reduced mortality compared with standard therapy. Specifically, all-cause mortality, all-cause hospital admission, all-cardiovascular mortality, fatal MIs and stroke, and cardiovascular hospital admission were all significantly improved in the carvedilol group compared with the placebo arm.

**CHF in dialysis patients.** Cardiovascular mortality ranks as the principal cause of death in dialysis patients (1–3). In the current study, we not only document beneficial effects of carvedilol on survival and LV function, but we also report novel data about mortality in dialysis patients with dilated cardiomyopathy. Specifically, we observed a dramatic and unexpected rise of mortality rate in our placebo arm from 5.2% to 73.2%, and in the carvedilol group from 0% to 51.7%, in the first and second years of observation, respectively. In this regard, few studies have described survival curves in dialysis patients with CHF. The landmark study by Harnett et al. (9) identified the primary determinants for the development of CHF in a patient population of 432 dialysis patients followed up for a mean of 41 months. Independent predictors were systolic dysfunction, older age, diabetes mellitus, and ischemic heart disease, while potentially reversible abnormalities included anemia, hypertension, and hypoalbuminemia. Compared with the observations of Harnett et al. (9), which reported a median survival in the CHF group of 36 months, the current study displays a considerably higher mortality rate. This discrepancy may be explained by the worse clinical status and pathologic remodeling of our patients at the study entry. Specifically, we recruited only patients with NYHA functional classes II and III, and with an ejection fraction lower than 0.35 at echocardiography. As a consequence, almost two-thirds of our patient population was in NYHA class III at the study entry, with an average ejection fraction of 0.26 and an indexed end-diastolic volume of 100 ml/m², compared with a mean fractional shortening and LV end-diastolic diameters of 0.30 and 53 mm in Harnett’s study, respectively. In other words, all our patients displayed the typical features of...
dilated cardiomyopathy, whereas, in the Canadian study, patients with minor degrees of HF were also included in the analysis.

The causes of excess mortality in dialysis patients with CHF are not entirely elucidated. They include volume overload with consequent hypertension, anemia, impaired renal function (20), and non-uremic (13) CHF patients. In particular, in chronic hemodialyzed patients that usually show a peculiar neurohumoral status (14–16), these benefits are justified by the adequate management of systemic hypertension, arrhythmias, and “silent” angina (17–19). Moreover, among other beta-blocking agents, in such patients carvedilol is endowed with favorable kinetic characteristics, in view of its prevalent hepatic metabolism that does not require dose adjustment in case of impaired renal function (20).

The echocardiographic data show that anti-remodeling actions exhibited by carvedilol at one year were maintained after 12 months of therapy, with no evident signs of disease progression as assessed by LV cavity diameters, ejection fraction, and NYHA class. These findings were associated with a 23% absolute reduction of mortality rates in the carvedilol group, whose use resulted as a strong and independent predictor of all-cause and cardiovascular mortality.

The exploratory analyses revealed that both “other cardiovascular deaths” and “hospital admissions for worsening HF” were lower in the carvedilol group than in the placebo group. Furthermore, a reduction in sudden deaths and pump-failure deaths was also observed, even if it did not meet statistical significance.

Our findings emphasize carvedilol efficacy in determining a significant reduction both of fatal MIs and of fatal strokes, which represent the main causes of cardiovascular mortality in uremic patients (5). These benefits may be related to the well-known anti-ischemic properties of carvedilol: the ability to reduce systemic BP, heart rate, and myocardial oxygen demand; to decrease the risk of plaque rupture; and to reduce the frequency and the complexity of ventricular arrhythmias (13). In addition, carvedilol exerts antioxidant effects that may further protect the heart from ischemia or reperfusion damage (21), independent of its actions as an adrenergic receptor blocker.

As for the effects of carvedilol treatment on LV pump function, data from the first year of the study documented improvement in remodeling and systolic parameters after six months of carvedilol therapy. However, most of the deaths in both groups occurred in the second year of the study, despite these effects on pump function. Intermediate time points of analysis between 12 and 24 months would have detected significant worsening of clinical and echocardiographic parameters before the fatal episodes of pump failure. On the other hand, anti-apoptotic, anti-inflammatory, and antiproliferative effects of carvedilol have just begun to be elucidated and might be at play, particularly in dialysis patients with CHF, in whom the cytokine system is maximally activated (22,23).

It must be stressed that the limited sample size does not allow us to draw definite conclusions, insofar as sudden deaths were lower in the active treatment group (two deaths) than in the placebo group (six fatal events), making it possible that in a larger patient population significant differences would have been detected. Future studies are needed to clarify this issue.

Although the cost evaluation is not one of the aims of our study, a final comment regarding the significant reduction of all-cause hospital admission and admission for worsening HF observed in our population may be of interest. Considering that during the last 10 years the annual number of hospitalizations has increased from approximately 1.7 to nearly 2.6 million for HF as a primary or secondary diagnosis, these data suggest that carvedilol therapy may lead to a remarkable reduction of health care costs.

Study limitations. The main limitation of this study is the small sample of the study group. However, it should be underlined that our population represents a very selected group of dialysis patients with dilated cardiomyopathy in advanced NYHA class, exhibiting, despite routine pharmacologic therapy and optimization of the dialysis regimen, a very high mortality and morbidity. Furthermore, to the best of our knowledge, no previous reports have analyzed carvedilol effects on mortality rate in such a particular subset of patients.

The lack of a double-blind design might be viewed as a potential limitation of the study. Maybe it influenced several measurements, especially NYHA class. However, it appears unlikely that this exerted a significant impact on the mortality curves of the study groups.

Conclusions. In summary, the data of the current investigation demonstrate that dilated cardiomyopathy in dialysis patients is characterized by a very poor prognosis, with a two-year mortality rate of 71%, and that carvedilol therapy prolongs survival in addition to providing a significant improvement in LV function and clinical status. Such beneficial effects were obtained independent of the cause of HF and of the patients’ clinical status at the study entry.

In conclusion, even admitting the intrinsic limitations of our study (open-label, unblinded trial), the main finding is to have shown the feasibility of carvedilol therapy in dialysis patients with dilated cardiomyopathy and its efficacy in determining a significant reduction of morbidity and mortality. Further double-blinded, placebo-controlled trials may
be necessary to confirm such beneficial effects of carvedilol in this subset of patients with such a poor prognosis.

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REFERENCES