**THERAPEUTICS**

**Carvedilol reduced mortality and hospital admission in severe chronic heart failure, regardless of pretreatment systolic BP**


Clinical impact ratings IM/Ambulatory care ✿ ✿ ✿ ✿ ✿ Internal medicine ✿ ✿ ✿ ✿ ✿ Cardiology ✿ ✿ ✿ ✿ ✿

**Q How does pretreatment systolic blood pressure (SBP) affect the efficacy and safety of carvedilol in patients with severe chronic heart failure (HF)?**

More patients in the carvedilol group than in the placebo group reported dizziness (24% v 17%, \(p<0.0001\^{*}\)), hypotension (15% v 9%, \(p<0.0001\^{*}\)), syncope (8% v 5%, \(p=0.0045\^{*}\)), and bradycardia (12% v 3%, \(p<0.0001\^{*}\)), whereas fewer patients reported HF (28% v 34%, \(p=0.002\^{*}\)), to a similar extent in each BP subgroup. The risk of a serious adverse event increased as pretreatment BP decreased \(p<0.001\). However, patients in the carvedilol group were less likely to have a serious adverse event than those who received placebo (39% v 46%, \(p=0.002\^{*}\)). This benefit increased as pretreatment SBP decreased (interaction \(p=0.03\^{*}\)).

**CONCLUSION**

In patients with severe chronic heart failure, carvedilol reduced the risk of all cause mortality and combined mortality and general and cause specific hospital admission regardless of pretreatment systolic blood pressure.

*Calculated from data in article.

**Rx**

**Main Results**

Overall, carvedilol reduced all cause mortality by 35%, combined death or cardiovascular admission by 27%, combined death or admission for HF by 31%, and combined death or admission for any reason by 24% (all \(p<0.0001\)). Regardless of treatment, the lower the pretreatment SBP, the higher the risk of a major clinical event. However, the relative magnitude of treatment benefits did not vary as a function of SBP (all interaction, \(p>0.1\)).

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**Methods**

**Design:** randomised controlled trial (Carvedilol Prospective Randomized Cumulative Survival [COPERNICUS] study).

**Allocation:** concealed \(^{*}\).

**Blinding:** blinded (patients and outcome assessors).

**Follow up period:** mean 10.4 months at early termination of study.

**Setting:** 334 centres in 21 countries.

**Patients:** 2289 patients (mean age 63 y, 80% men) with severe chronic HF because of ischaemic or non-ischaemic cardiomyopathy; \(>2\) months of dyspnoea or fatigue at rest or an minimal exertion; left ventricular ejection fraction <25%; and SBP >85 mm Hg. Exclusion criteria: correctable cause of HF, heart transplant; severe primary pulmonary, renal, or hepatic disease; contraindications to \(\beta\) blockers; major cardiac event within 2 months; use of \(\alpha\) adrenergic blockers, calcium channel blockers, or class I antiarrhythmic drugs within 4 weeks; heart rate <68 beats/minute, serum creatinine concentration >2.8 mg/dl or an increase of >0.5 mg/dl, serum potassium <3.5 or >5.2 mmol/l. Patients were retrospectively grouped according to pretreatment SBP: 85–95 mm Hg (n = 132), 96–105 mm Hg (n = 264), 106–115 mm Hg (n = 468), 116–125 mm Hg (n = 472), or >125 mm Hg (n = 953).

**Intervention:** in addition to usual medication for HF, oral carvedilol, initial dose 3.125 mg twice daily for 2 weeks, which was increased as tolerated at 2 week intervals to 6.25, 12.5 mg, and finally 25 mg twice daily (n = 1156), or matching placebo (n = 1133).

**Outcomes:** included all cause mortality, combined death or hospital admission for HF; combined death or cardiovascular admission; combined death or hospital admission; and adverse events.

**Patient follow up:** 100% (intention to treat analysis).

\(^{*}\)See glossary.