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Q/ What is the best beta-blocker for systolic heart failure?

EVIDENCE-BASED ANSWER

A/ **Three beta-blockers—carvedilol, metoprolol succinate, and bisoprolol**—reduce mortality equally (by about 30% over one year) in patients with Class III or IV systolic heart failure. Insufficient evidence exists comparing equipotent doses of these medications head-to-head to recommend any one over the others (strength of recommendation [SOR]: **A**, systematic review/meta-analysis).

Evidence summary

A 2013 network meta-analysis compared beta-blockers with placebo or standard treatment by analyzing 21 randomized trials with a total of 23,122 patients.[1] Investigators found that beta-blockers as a class significantly reduced mortality after a median of 12 months (odds ratio=0.71, 95% confidence interval [CI], 0.64-0.80; number needed to treat [NNT]=23).

They also compared atenolol, bisoprolol, bucindolol, carvedilol, metoprolol, and nebivolol with each other and found no significant difference in risk of death, sudden cardiac death, death resulting from pump failure, or tolerability.

Three drugs are more effective and tolerable than others

A 2013 stratified subset meta-analysis used data from landmark randomized controlled trials (RCTs) that evaluated beta-blockers vs placebo in patients with systolic heart failure to compare metoprolol succinate (MERIT-HF) vs placebo with bisoprolol (CIBIS-II), carvedilol (COPERNICUS), and nebivolol (SENIORS-SHF) vs placebo (**TABLE**).[2]

Three of the drugs—bisoprolol, carvedilol, and metoprolol succinate—showed similar reductions relative to placebo in all-cause mortality, hospitalization for heart failure, and tolerability. Investigators concluded that the 3 drugs have comparable efficacy and tolerability, whereas nebivolol is less effective and tolerable.

Carvedilol vs beta-1-selective beta-blockers

Another 2013 meta-analysis of 8 RCTs with 4563 adult patients 18 years or older with systolic heart failure compared carvedilol with the beta-1-selective beta-blockers atenolol, bisoprolol, nebivolol, and metoprolol.[3] Investigators found that carvedilol significantly reduced all-cause mortality (relative risk=0.85; 95% CI, 0.78-0.93; NNT=23) compared with beta-1-selective beta-blockers.

However, 4 trials (including COMET, N=3029) compared carvedilol with short-acting metoprolol tartrate, which may have skewed results in favor of carvedilol. Moreover, 2 trials comparing carvedilol with bisoprolol and 2 trials comparing carvedilol with nebivolol found no significant difference in all-cause mortality.[3]

Recommendations

The 2010 Heart Failure Society of America Comprehensive Heart Failure Practice Guideline notes that the marked beneficial effects of beta blockade with carvedilol, bisoprolol, and controlled- or extended-release metoprolol have been well-dem-

TABLE

How metoprolol succinate vs placebo compares with other beta-blockers vs placebo[2]

Comparison	Randomized controlled trials	RRR*
Bisoprolol	CIBIS-II (N=2647; 95% CI,19-46; *P*<.0001; NNT=23)	34%
vs	vs	vs
Metoprolol succinate	MERIT-HF (N=2002; 95% CI, 24-56; *P*<.0001; NNT=16)	42%
Carvedilol	COPERNICUS (N=2289; 95% CI,19-48; *P*=.0014; NNT=14)	35%
vs	vs	vs
Metoprolol succinate	MERIT-HF (N=795; 95% CI, 11-58; *P*=.0086; NNT=14)	39%
Nebivolol	SENIORS-SHF (N=1359; NS; NNT=63)	16%
vs	vs	vs
Metoprolol succinate	MERIT-HF (N=985; 95% CI, 2-53; *P*=.038; NNT=21)	32%

CI, confidence interval; EF, ejection fraction; CIBIS-II, Cardiac Insufficiency Bisoprolol Study II (EF<35%); COPERNICUS, Carvedilol Prospective Randomized Cumulative Survival trial (EF<25%); MERIT-HF, Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (EF<40%); NNT, number needed to treat; NS, not significant; RRR, relative risk reduction; SENIORS-SHF, Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors with Heart Failure trial.

* Relative risk reduction of annual mortality rates from placebo to beta-blocker arms.

onstrated in large-scale clinical trials of symptomatic patients with Class II to IV heart failure and reduced left ventricular ejection fraction.[4]

The 2013 American College of Cardiology Foundation/American Heart Association heart failure guideline recommends the use of one of the 3 beta-blockers proven to reduce mortality (bisoprolol, carvedilol, or sustained-release metoprolol succinate) for all patients with current or previous symptoms of heart failure with reduced ejection fraction, unless contraindicated, to reduce morbidity and mortality.[5] JFP

Carvedilol, metoprolol succinate, and bisoprolol all reduce mortality by about 30% over one year in patients with Class III or IV systolic heart failure.

References

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