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Interventions for Heart Failure

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Evidence-Based Practice

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IN DEPTH

Interventions for heart failure

Evidence-based answer

The following interventions improve important outcomes in patients with systolic heart failure (all SORs: A, based on meta-analyses):

- Angiotensin converting enzyme (ACE) inhibitors reduce mortality, repeat myocardial infarction (MI), and hospitalization rates
- Beta-blockers and aldosterone blockers reduce mortality and hospitalization rates
- Diuretics reduce mortality and hospitalization rates and improve exercise capacity
- Digitalis treatment decreases hospitalization rates and clinical deterioration
- Aerobic exercise rehabilitation of at least 6 months in duration decreases hospitalization rates and improves quality of life

The following intervention improves important outcomes in African American patients with systolic heart failure (SOR: B, based on a single RCT):

- Isosorbide dinitrate and hydralazine combination therapy reduces mortality and hospitalization rates and improves quality of life

Evidence summary

A systematic review of 5 RCTs involving 12,763 patients (mean age 61 years) with left-ventricular dysfunction or clinical heart failure assessed the effect of ACE inhibitors versus placebo. About half (6,928) of these patients developed heart failure due to recent MI, whereas the other patients had no history of MI.¹ Primary outcomes are given in the **TABLE** for this study as well as other studies discussed below.

A systematic review of 22 RCTS involving 10,480 patients (mean age 61 years) with chronic heart failure examined the effects of beta-blockers versus placebo.² Of the 22 trials, 2 used bisoprolol, 3 bucindolol, 8 carvedilol, 7 metoprolol, and 2 nebivolol in a double-blind randomized fashion and in a wide range of doses. Overall, the NNT with a beta-blocker to prevent 1 death was 20 and to prevent 1 hospitalization was 17.

A systematic review of 19 RCTs involving 10,807 patients with chronic heart failure or MI examined the efficacy of aldosterone blockade therapy.⁴ Spironolactone was the drug used most commonly, followed by eplerenone and canrenoate. Risk reduction in hospitalizations was mostly seen in the

TABLE

Outcomes from RCTs on interventions for heart failure

Medication	Papers (N)	NYHA class	Duration	Outcome	Magnitude of effect relative to placebo
ACE inhibitor ¹	5 (12,763)	Not provided	Mean 35 months	Mortality	OR 0.80 (95% CI, 0.74–0.87; <i>P</i> <.0001)
				Repeat MI	OR 0.79 (95% CI, 0.70–0.89, <i>P</i> <.0001)
				Hospitalizations	OR 0.67 (95% CI, 0.61–0.74; <i>P</i> <.0001)
Beta-blocker ²	22 (10,480)	Class I-IV	Mean 11 months	Mortality	OR 0.65 (95% CI, 0.57–0.74; <i>P</i> <.0001)
				Hospitalizations	OR 0.63 (95% CI, 0.56–0.71; <i>P</i> <.0001)
Diuretic ³	14 (525)	Class I-IV	Range 4–24 weeks	Mortality	OR 0.24 (95% CI, 0.07–0.83; <i>P</i> =.02)
				Hospitalizations	OR 0.07 (95% CI, 0.01–0.52; <i>P</i> =.01)
				Exercise capacity	SMD 0.72 (95% CI, 0.40–1.04; <i>P</i> <.0001)
Aldosterone blocker ⁴	19 (10,807)	Class I-IV	Range 2–24 months	Mortality	RR 0.8 (95% CI, 0.74–0.87; <i>P</i> <.00001)
				Hospitalizations	RR 0.77 (95% CI, 0.68–0.87; <i>P</i> <.00001)
Digitalis ⁵	13 (7,896)	Class I-IV	Range 7 weeks–5 years	Hospitalizations	OR 0.68 (95% CI, 0.61–0.75; <i>P</i> <.00001)
				Clinical deterioration	OR 0.31 (95% CI, 0.21–0.43; <i>P</i> <.00001)
Exercise ⁶	19 (3,647)	Class I-IV	Range 6 months–5 years	Hospitalizations	Fixed-effect RR 0.72 (95% CI, 0.52–0.99; <i>P</i> =.04)
				Quality of life ^a	Mean difference –10 (95% CI, –16 to –5; <i>P</i> <.0001)
Isosorbide dinitrate and hydralazine ⁷	1 (1,050)	Class II-IV	Mean 10 months	Mortality	HR 0.57 (<i>P</i> =.01)
				Hospitalizations	RR 0.66 (<i>P</i> =.001)
				Quality of life ^a	Mean difference, –2.9 (<i>P</i> =.02)

ACE=angiotensin-converting enzyme; CI=confidence interval; HR=hazard ratio; NYHA=New York Heart Association; OR=odds ratio; RCTs=randomized controlled trials; RR=relative risk; SMD=standardized mean difference.

^aQuality of life was measured with the 21-question, 105-point Minnesota Living with Heart Failure (MLWHF) questionnaire (where lower scores indicate better quality of life).

heart failure patients, while the post-MI patients had no significant change in hospitalization rate.

A Cochrane review of 13 double-blinded RCTs involving 7,896 participants (mean age 58–69 years) with congestive heart failure examined treatment with digitalis versus placebo.⁵ Of the 13 RCTs, mortality was measured in 8 studies, hospitalization was measured in 4 studies, and clinical deterioration was measured in 12 studies. Clinical deterioration was described in the various studies as chest pain, breathlessness, tiredness, and difficulty walking.

A Cochrane review of 19 RCTs involving 3,647 participants (mean age 43–72 years) with chronic heart failure examined exercise rehabilitation versus a control group for treatment of heart failure.⁶ Most studies used the 21-question Minnesota Living with Heart Failure (MLWHF) questionnaire to measure QoL. The questionnaire measured changes in physical and social functions, such as walking, climbing stairs, being able to leave home, and recreational activities. Each answer on the questionnaire receives 0 to 5 points (0–105 total), and higher scores indicated a poorer QoL.

An RCT involving 1,050 African American patients with chronic heart failure examined the effect of isosorbide dinitrate/hydralazine combination

therapy.⁷ Patients were randomly assigned a fixed dose of isosorbide dinitrate plus hydralazine or placebo, in addition to usual care. Mortality, hospitalizations, and HRQoL (MLWHF questionnaire) were measured. Mean duration of follow-up was 10 months. The study was terminated early (about 3 years later) due to a significantly higher mortality in the placebo group. **EBP**

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