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Journal Club

**P:** In patients with acute congestive heart failure

**I:** Does the addition of a Beta-blocker

**C:** Compared with traditional therapy

**O:** Improve morbidity and mortality?

### **Three Part Question**

In [patients with acute congestive heart failure] does [addition of a beta-blocker to traditional therapy] improve [morbidity and mortality]?

### **Clinical Scenario**

A 55-year-old male presents to the emergency department in acute respiratory distress. Vital signs are BP 200/120 HR 110 SpO<sub>2</sub> 94% on a NRB mask. After appropriate physical exam and diagnostic testing you determine that he is in acute congestive heart failure. Diuretics and nitrates are being administered. You wonder if the addition of a beta-blocker will improve morbidity or mortality in this patient.

### **Search Strategy**

Medline 2000 – January 2008 using the Pubmed interface: “congestive heart failure”[Title] AND beta [Title] AND English[lang] AND Humans[MeSH Terms]

### **Search Outcome**

65 papers were found of which 55 were irrelevant to the study question.

### **Relevant Papers**

<b>Author, Date, Country</b>	<b>Patient Group</b>	<b>Subtype (level of evidence)</b>	<b>Outcomes</b>	<b>Key Results</b>	<b>Study Weaknesses</b>
Nagatomo, et al; 2007, Japan	52 patients with Mild – Mod CHF (EF <40%)	Open-label randomized	Metoprolol and Carvedilol effects on: 1. Exercise tolerance and 2D-Echo and ventriculography 2. CRP and LPO levels	EF increased at 16 wks; Carvedilol dec CRP and LPO in pt with high initial levels	Not blinded; No control; outpatient; did not measure QOL or mortality
Fauchier et al; 2007,	4 studies with 7250 pt	Meta-analysis	Mortality	Beta-blockers have a 38%	Only looked at chronic HF;

France	comparing beta-blocker with placebo in HF	Bisoprolol x2 Carvedilol* Metoprolol		reduction in RR of death in both ischemic and non-ischemic chronic HF	outpatient; meta-analysis  *Carvedilol had the lowest mort rates
Tate et al; 2007, USA	2708 pt with Class III or IV HF (EF $\leq$ 35%)	Randomized Double-blind Control Trial	Quality of Life	QOL improved with bucindolol in 2/4 surveys used	Used subjective surveys; Only half of surveys showed a change; Subset of BEST ; outpatient
Frantz, et al; 2007, USA	206 pt with Class III or IV HF (EF $\leq$ 35%)	Randomized Double-blind Control Trial	Big-ET, ET-1, BNP levels*  * strongest predictors of hospitalization or death	Bucindolol decreased Big-ET levels but not BNP	Subset of BEST; outpatient; morbidity and mort not directly measured
Frantz, et al; 2005, USA	55 pt with Class III or IV HF (EF $\leq$ 35%)	Open label trial	LVEF, NYHA class, BNP, NANP, Big-ET, norepi, Et-1, angiotensin II	Carvedilol improved LVEF & NYHA class and decreased BNP & angiotensin II	Only 46/55 pt followed up for 12 mos; No control; outpatient
Chan, et al; 2005, USA	950 adults > 65 yo	Longitudinal population based observational cohort study	Mortality, re-hospitalization	B-blocker treated pt had lower mort and re-hosp	Obs study; various initiation times, various B-blocker/dose
<b>Felix, et al; 2001, Germany</b>	<b>14 pt with decompensated HF</b>	<b>Open randomized intraindividual comparison</b>	<b>Hemodynamic Measurements</b>	<b>Celiprolol and esmolol dec HR; Celiprolol caused only a transient dec in CI</b>	<b>Not blinded; no control; Small Sample; only measured hemodynamics</b>
Aronow, et al; 2001, USA & Europe	3991 pt with Class II-IV HF (EF $\leq$ 40%)	Randomized double blind control trial	Mortality	Metoprolol caused 34% reduction in mortality	Outpatient study
The Beta-Blocker Evaluation of Survival Trial Investigators; 2001, USA	2708 pt with Class III or IV HF (EF $\leq$ 35%)	Randomized Double-blind Control Trial	Mortality	Bucindolol showed no significant survival benefit	Outpatient study; Terminated early secondary to no benefit
Packer et al; 2001, USA	2289 clinically euvolemic symptomatic pt with EF <25%	Randomized Double-blind Control Trial	Mortality and hospitalization	Carvedilol pt had 35% decrease in risk of death and 24%	Excluded those on IV vasodilators, inotropes and in the ICU

				decrease in hospitalization	
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### **Comments**

Although it makes sense physiologically that Beta-blockers may offer some benefit in acute diastolic heart failure, no studies found isolated patients who had diastolic failure from those with systolic failure. In fact, most major studies required patients have EF's below normal. Only one study found looked solely at patients in *acute* heart failure and it was very small – consisting of only 13 patients. It appears that there is a statistical difference among beta-blocker specificity when it comes to treating heart failure – those that offer some alpha-1 blocking/vasodilatory properties such as carvedilol clearly have a benefit on morbidity and mortality in chronic heart failure whereas the evidence does not support the use of pure Beta-1 blockers in chronic HF. Clearly, more studies need to be conducted on the use of Beta-blockers in acute HF (especially diastolic HF) to see if these patients may benefit from their use.

### **Clinical Bottom Line**

Do not initiate beta-blocker therapy in any patient with acute HF without cardiology consultation

### **References**

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6. Frantz, et al. Carvedilol therapy is associated with a sustained decline in brain natriuretic peptide levels in patients with congestive heart failure. *Am Heart J*. 2005 Mar;149(3):541-7.

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9. Packer, et al. Effect of carvedilol on survival in severe chronic heart failure. *N Engl J Med.* 2001 May 31;344(22):1651-8.
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