

# **Maintaining the Circulatory System when in a Critical State: ICU management for the Failing Circulation**

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*No conflicts of interest*



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# Objectives

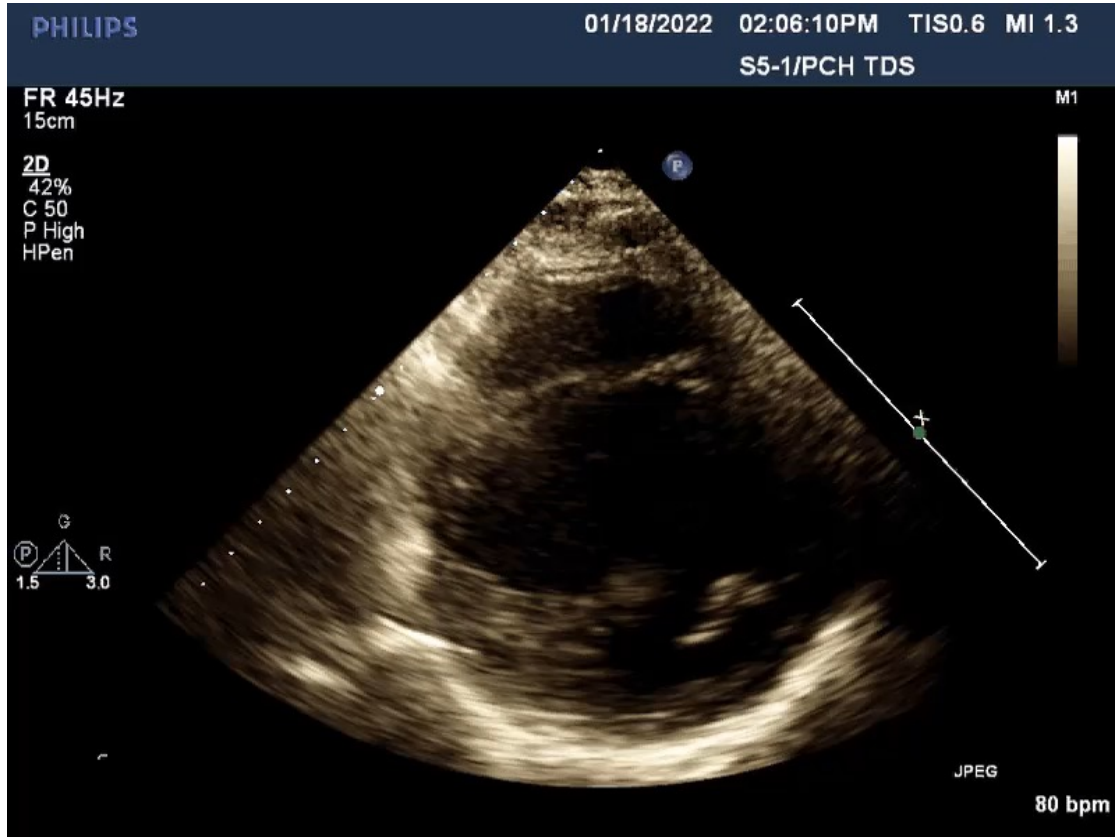
- Describe strategies to maintain the circulation
- Describe potential opportunities for and threats to optimal management
- Leverage adult data (and some pediatric) to improve understanding of potential therapeutic optimization



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# Two images are worth > 1000 words...

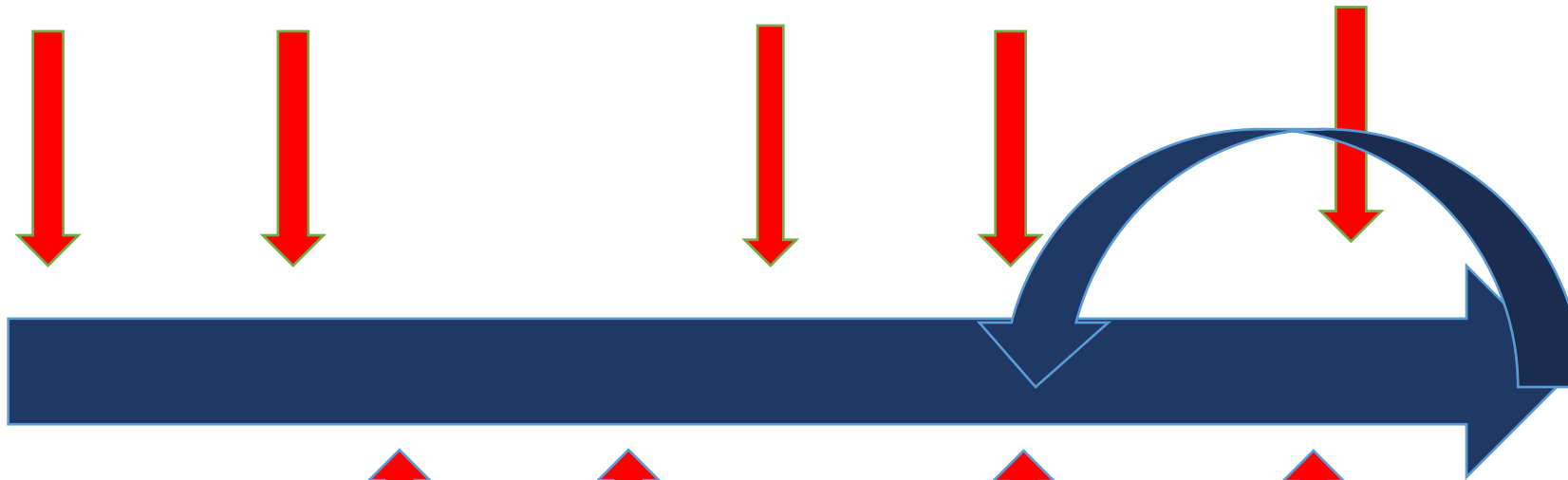


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# Course of the child with ADHF

ER/ICU   HF-ICU   OR   HF-ICU   Long term



Inotrope  
CPR

Resp-ETT

Complications  
Renal/GI/ID/CNS

Rehab  
Nutrition



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# The Bottom Line

- The main objectives of maintenance is:
  - Stabilization of organ function
  - Balance perfusion and congestion
  - Anticipation of complications
  - Preparation of mechanical support when needed
- It is getting the patient to be weaned of vasoactives into oral therapies or to be healthy enough to be an appropriate organ recipient



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# 2,058 Hospitalizations in 1,599 Pts

- Overall in hospital mortality = 11%
- Cardiac Tx occurred in 20% of hospitalizations
- MCS used in 13% of hospitalizations



**“HF-related ICU hospitalizations in children with cardiomyopathy are increasing”**



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*Shamszad P et al., J Cardiac Fail 2013;19:672e677*



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~80%  
Medical  
Management



“HF-related ICU hospitalizations in children with cardiomyopathy are increasing”



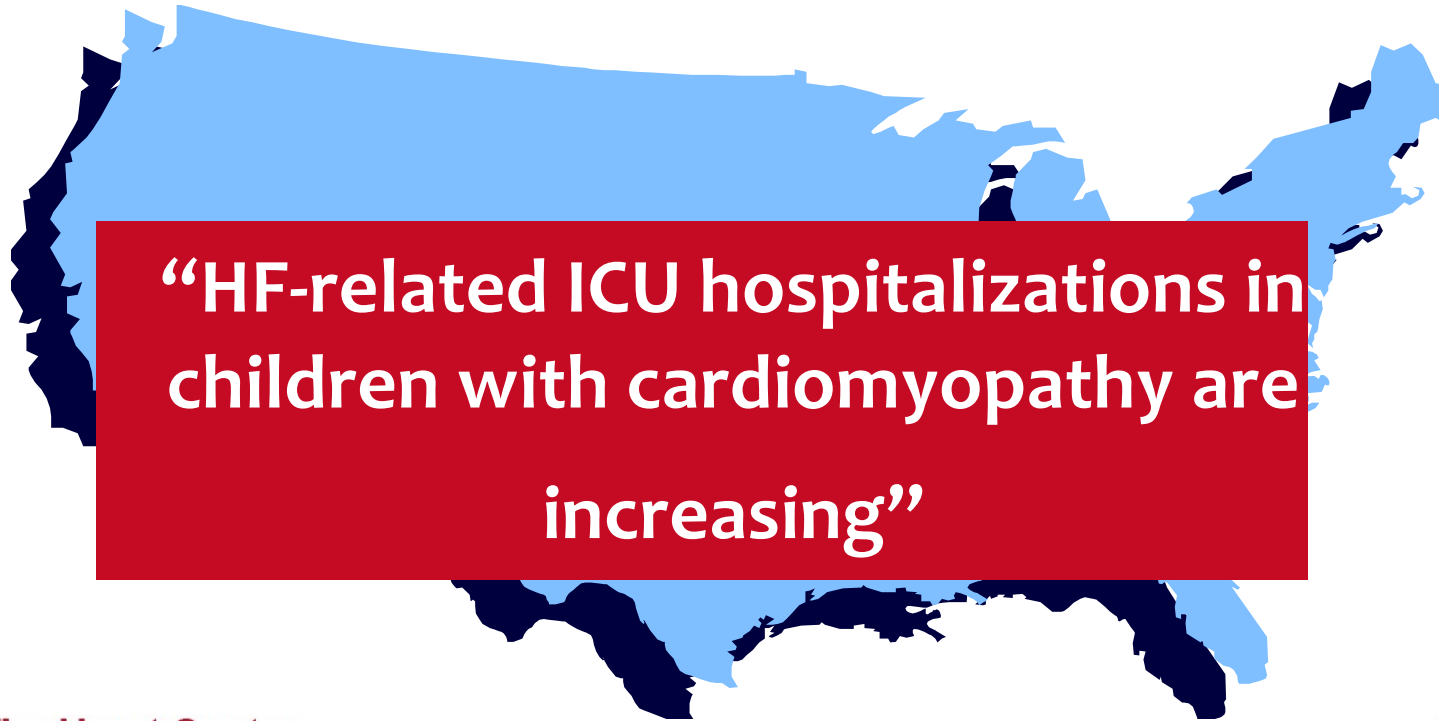
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“HF-related ICU hospitalizations in children with cardiomyopathy are increasing”

~80%  
Medical  
Management

~86% had  
A Vasoactive  
Agent



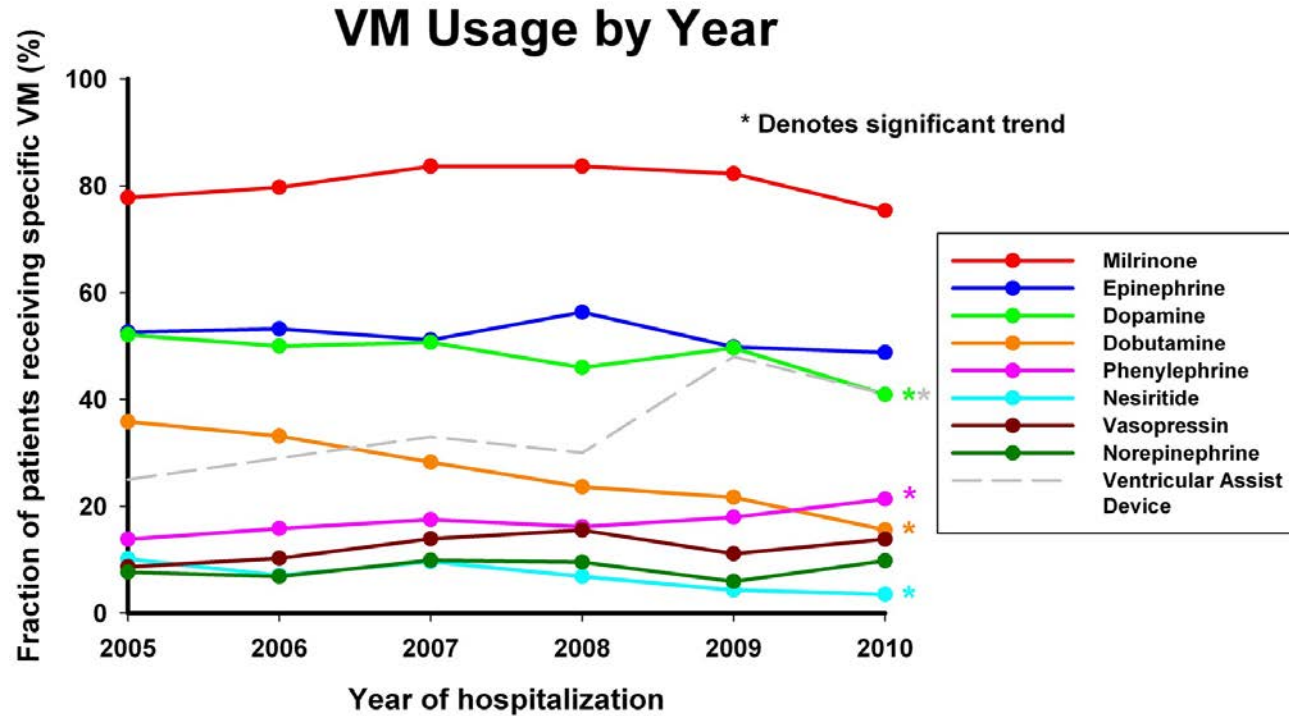
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# Vasoactive Medications Use



*P Shamszad, SCCM, 2013*

Circulation: Heart Failure

## ORIGINAL ARTICLE

### Epidemiology and Outcomes of Acute Decompensated Heart Failure in Children

Javier J. Lasa, MD; Michael Gaies, MD, MPH, MSc; Lauren Bush, MD; Wenying Zhang, MS; Mousumi Banerjee, PhD; Jeffrey A. Alten, MD; Ryan J. Butts, MD; Antonio G. Cabrera; Paul A. Checchia, MD; Justin Elhoff, MD; Angela Lorts, MD; Joseph W. Rossano, MD; Kurt Schumacher, MD; Lara S. Shekerdeman, MD; Jack F. Price, MD; for the Pediatric Cardiac Critical Care Consortium (PC<sup>4</sup>)



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$$\boxed{BP} = CO \times SVR$$

$$CO = SV \times HR$$

- SV= depends on preload, afterload and contractility

**Potential scenarios for normal BP**

**Low CO and high SVR**

**Low SVR and high CO**



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# Vasoactive Agents

- **Dopamine:**

- Synthetic precursor of NE. Effective treating hypotension in non-cardiac neonates
- Price (JCARD FAIL): children with advanced CHF. Use of Dopamine 2-3 mcg/kg/min alone or in combination with milrinone was well tolerated, increased EF, decrease HF symptoms and reduced readmissions after starting therapy

## Original Investigation

### Low-Dose Dopamine or Low-Dose Nesiritide in Acute Heart Failure With Renal Dysfunction The ROSE Acute Heart Failure Randomized Trial

Hong H, Chen, MD, PhD; Kavin J, Anderson, PhD; Michael M, Givertz, MD; Lynne W, Stevenson, MD; Marc J, Semigran, MD; Steven R, Goldsmith, MD; Bradley A, Bart, MD; David A, Bull, MD; Josef Sorliu, MD; Martin M, LeWinter, MD; Marwin A, Konstam, MD; Gordon S, Huggins, MD; Jean L, Rouleau, MD; Ellen O'Rourke, MD; W. H. Wilson Tang, MD; Randall C, Starling, MD; MPH; Javed Buttar, MD; MPH; Anita Deswal, MD; G, Michael Finkel, MD; Christopher M, O'Connor, MD; Raphael L, Bonita, MD; Scott, Kenneth B, Margulies, MD; Thomas P, Cappola, MD; Scott, Elizabeth O, Cobb, MD; Douglas L, Mann, MD; Victor G, Dilavio-Roman, MD; Steven E, McNulty, MD; Barry A, Borlaug, MD; Eric J, Velazquez, MD; Kerry L, Lee, PhD; Monica R, Shah, MD, MHS, MS; Adrian F, Hernandez, MD, MHS; Eugene Braunwald, MD; Margaret M, Redfield, MD, for the ROSE Acute Heart Failure Clinical Research Network

Supplemental content at [jama.com](http://jama.com)

**IMPORTANCE** Small studies suggest that low-dose dopamine or low-dose nesiritide may enhance decongestion and preserve renal function in patients with acute heart failure and renal dysfunction; however, neither strategy has been rigorously tested.

- Renal Optimization strategies in AHF
- Multicenter, double blind, placebo-controlled trial
- 360 hospitalized adults with AHF
- Dopamine 2 mcg/kg/min vs. Nesiritide 0.005 mcg/kg/min vs. placebo
- No difference

1035 mL;  $P = .491$  on the change in cystatin C level [nesiritide, 0.07 mg/L; 95% CI, 0.00-0.13 vs placebo, 0.11 mg/L; 95% CI, 0.06-0.16; difference, -0.04; 95% CI, -0.13 to 0.05;  $P = .36$ ). Compared with placebo, there was no effect of low-dose dopamine or nesiritide on secondary end points reflective of decongestion, renal function, or clinical outcomes.

**CONCLUSION AND RELEVANCE:** In participants with acute heart failure and renal dysfunction, neither low-dose dopamine nor low-dose nesiritide enhanced decongestion or improved renal function when added to diuretic therapy.

**TRIAL REGISTRATION** clinicaltrials.gov Identifier: NCT01328946

JAMA. 2013;310(23):2533-2543. doi:10.1001/jama.2013.282990  
Published online November 19, 2013.

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**Author Affiliations:** Author affiliations are listed at the end of this article.

**Group Information:** A complete list of the ROSE Acute Heart Failure Clinical Research Network appears in eAppendix 1 in the Supplement.

**Corresponding Author:** Hong H, Chen, MD, PhD, Mayo Clinic Cardiovascular Research, Guggenheim 9, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (chen.hong@mayo.edu).



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Rossano JW, Cabrera AG, et al. PCCM 2016  
*JAMA. 2013;310(23):2533-2543*



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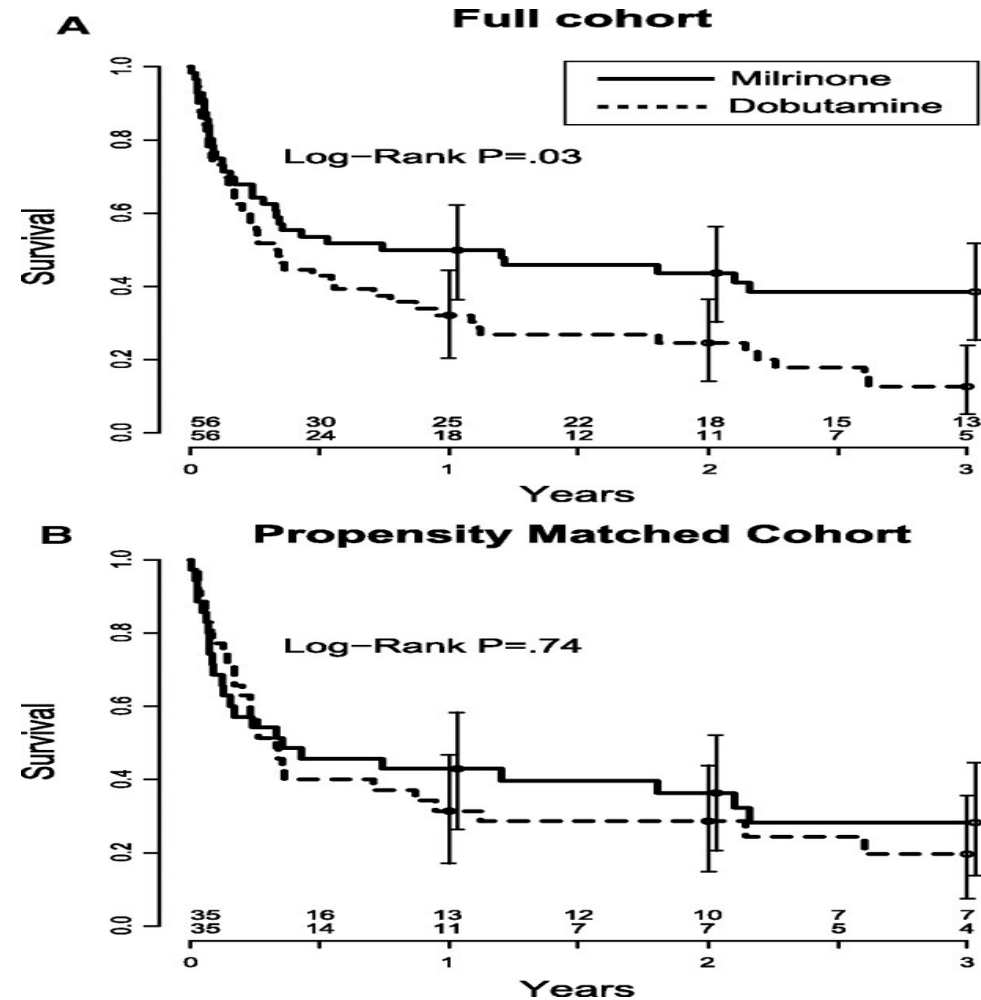
# Vasoactive Agents

- Epinephrine
  - At low doses ( $\sim 0.01$ - $0.03$  mcg/kg/min) can be used as a first or second agent when hypotension is present
- Dobutamine
  - Effective in treating hypotension in non-cardiac neonates
  - B-1 and B2 agonist
  - Tachyphilaxis after 2 weeks

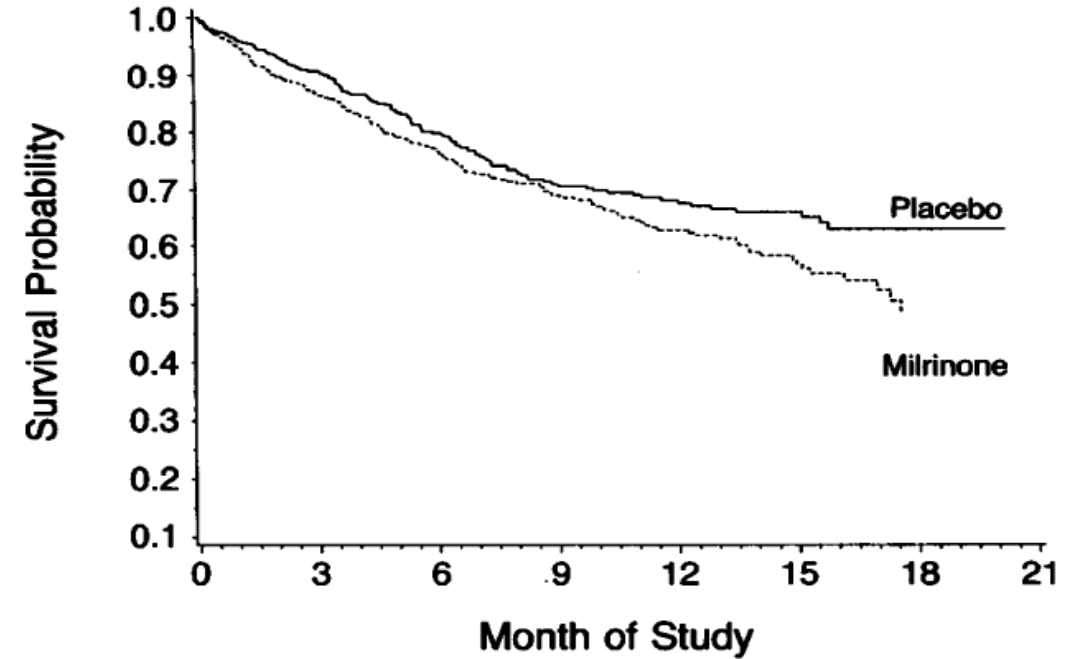
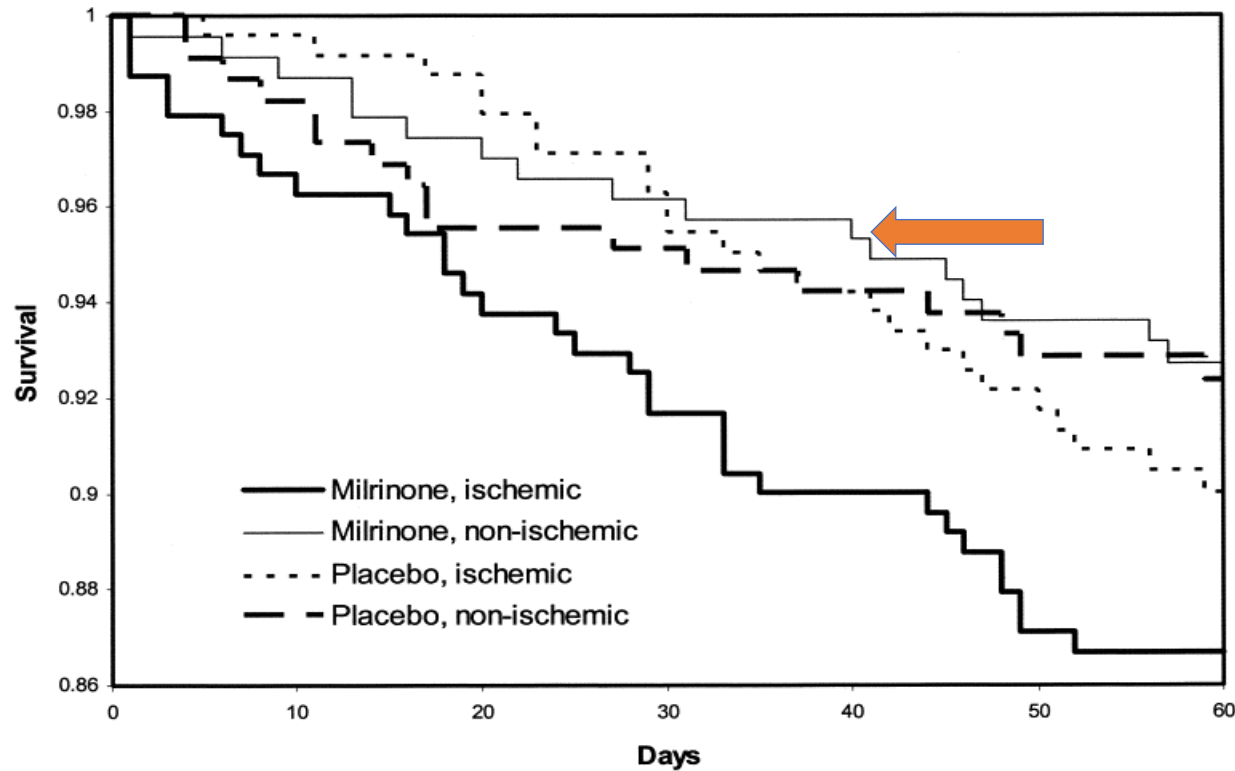


# Vasoactive Agents: Milrinone

- Onset of action: 5-15 min
- $T_{1/2}$  = 2.5 hours (prolonged if renal failure or CVVHD)
- ADHERE trial: higher mortality in adults with ADHF who received milrinone or dobutamine vs. nesiritide or nitroglycerine



# Milrinone and Cardiomyopathy



Milrinone may have a neutral to positive effect in patients with non ischemic cardiomyopathy



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OPTIME-HF trial Investigators, JACC 2003  
PROMISE Study Packer M, et al. NEJM. 1991





# Impact of Early Vasoactive Therapies

## ADHERE Registry (n=35,700)

- All patients tx with IV vasoactive therapy (<6 hrs vs >6 hrs)
- Within 48 hrs of admission
- **In-hospital mortality significantly lower in early tx group:**
  - (OR 0.87, CI 0.79-0.96, p=0.006)

Variable	< 6 hours n=22,788	> 6 hours n=12,912	P-value
Mortality	1166 (5.1)	847 (6.6)	<0.001
Time in ED (hr)	4.5 (3.1-6.5)	5.4 (3.8-7.6)	<0.001
LOS (days)	4.7 (3-7.6)	5.8 (3.8-9)	<0.001
ICU time (days)	2.4 (1.3-4)	3 (1.9-5.4)	<0.001
Asymptomatic at DC	10,016 (51.9)	5012 (46.7)	<0.001



# Macicek SM et al. Acute Heart Failure Syndromes in the ED

- 57 patient visits from 51 pts
- New onset symptoms: 25 (44%)
- Exacerbation of preexisting disease: 32 (56%)
- IV inotropes in the ED = 21% of all cases
- Time to initiation of inotropes:
  - ED= 7 hours vs ICU 11 hours





# Opportunities

- Early vasoactives possible better than late
- Vasoactive initiation should not be delayed based on location. Should be considered before arrival to the ICU
- Milrinone is not benign and has increased incidence of atrial and ventricular arrhythmias + worse outcomes. Have to make sure patient has symptomatic heart failure indication
- There is tachyphylaxis with Dobutamine but is not inferior to milrinone



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# Non-invasive Ventilation In Acute Cardiogenic Pulmonary Edema- 3CPO

- Multicenter randomized controlled trial
- Setting: Emergency Department
- Prospective 'open-label' trial
- Three treatment interventions in a 1:1:1 randomization:
  - 'Standard' oxygen therapy
  - CPAP
  - NIPPV



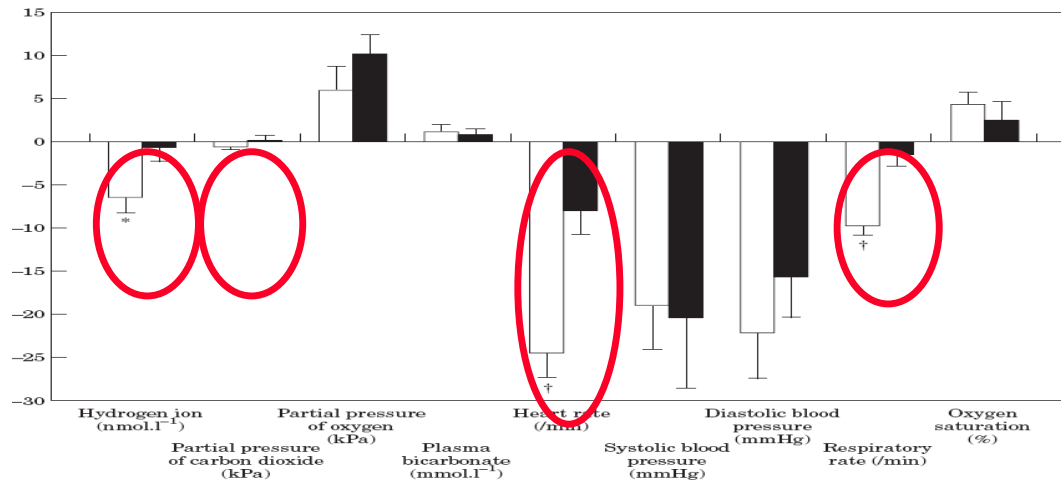
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Gray A et al, N Engl J Med. 2008 Jul 10;359

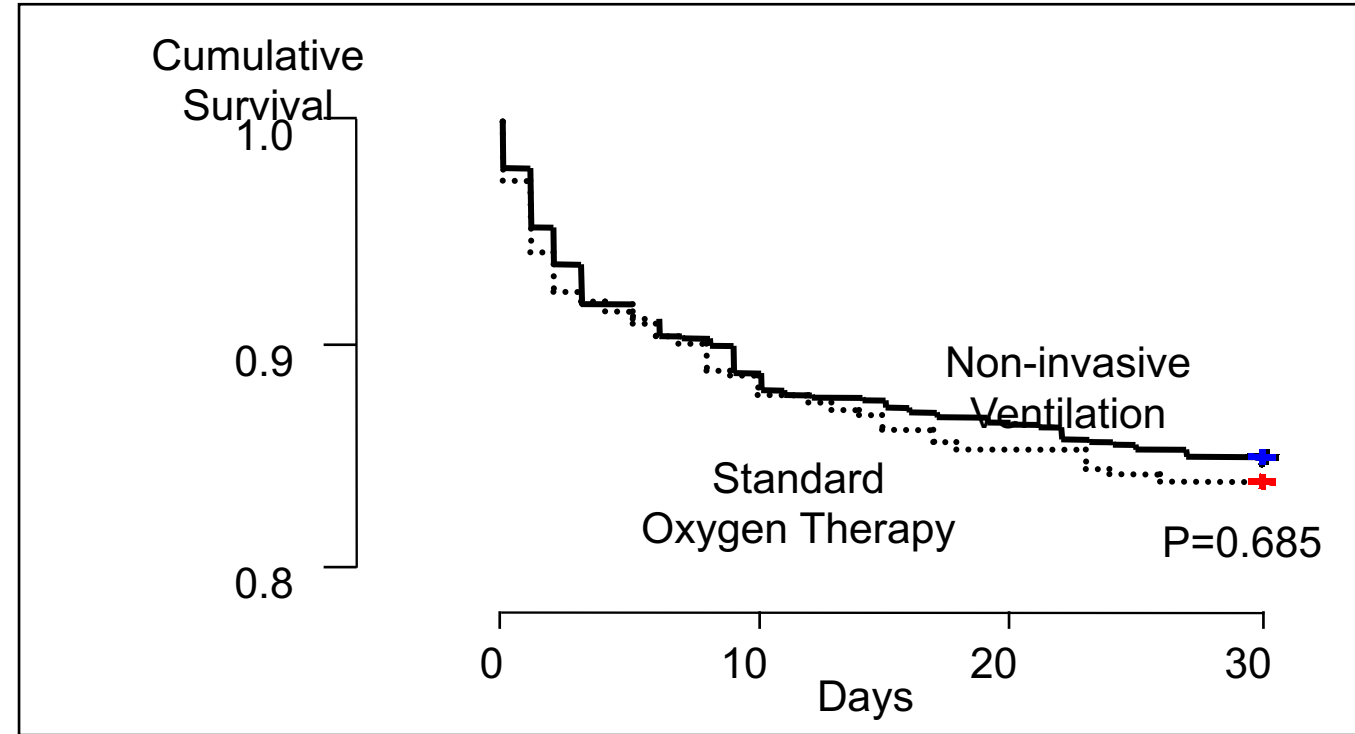
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# Physiological Improvement with CPAP in Patients with ACPO (Oedema)



**Reduced acidosis, respiratory rate and heart rate**



**No change in mortality**




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Gray A et al, N Engl J Med. 2008 Jul 10;359



# The Ugly word: “Tracheostomy”

## Hospital outcomes for pediatric heart transplant recipients undergoing tracheostomy: A multi-institutional analysis

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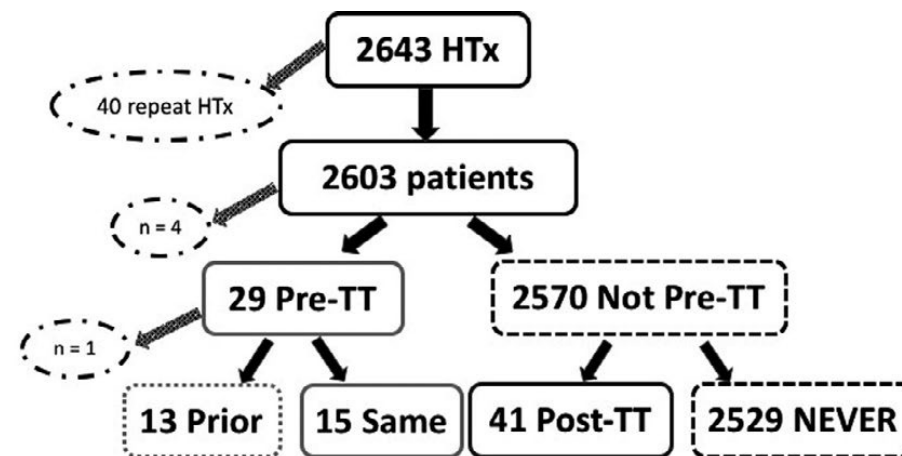
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### Abstract

Tracheostomy is associated with increased mortality and resource utilization in children with CHD. However, the prevalence and hospital outcomes of tracheostomy in children with HTx are not known. We describe the prevalence and compare the post-HTx hospital outcomes of pediatric patients with Pre-TT and Post-TT to those without tracheostomy. A multi-institutional retrospective cohort study was performed using the Pediatric Health Information System database. Hospital mortality, mediastinitis, LOS, and costs were compared among patients with Pre-TT, Post-TT, and no tracheostomy. Pre-TT was identified in 29 (1.1%) and Post-TT was identified in 41 (1.6%) of 2603 index HTx hospitalizations. Patients with Pre-TT were younger and more likely to have CHD, a non-cardiac birth defect, or an airway anomaly compared to those without Pre-TT. Pre-TT was not independently associated with increased post-HTx in-hospital mortality. Age at HTx < 1 year, CHD, and Post-TT were associated with increased in-hospital mortality. Pre-TT that occurred during the HTx hospitalization and Post-TT were associated with increased resource utilization. Tracheostomy was not associated with mediastinitis.

### KEYWORDS

outcome, pediatric heart transplant, tracheostomy



HTx: Heart Transplant; Pre-TT: Pre-transplant tracheostomy; Post-TT: Post-transplant tracheostomy

**Pre-HTx tracheostomy was present in 1.1% of children who underwent a first-time HTx, and it was not an independent risk factor for increased mortality**



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# Opportunities

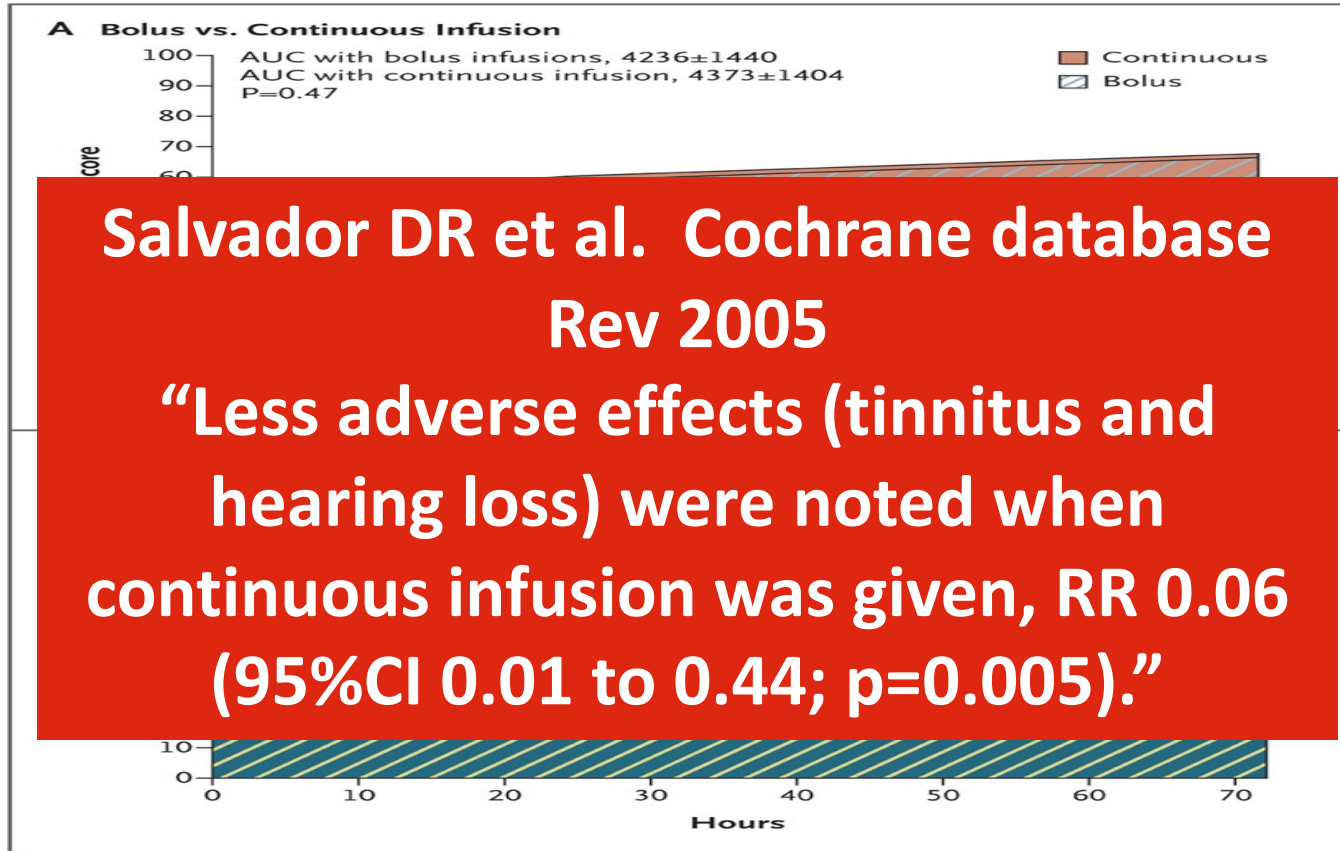
- Use of some sort of positive pressure will reduce the work of breathing and may stabilize the patient prior intubation or even at times prevent intubation
- Work of breathing does not improve unless pulmonary edema improves, be mindful about weaning because “the patient does not need it”
- Tracheostomy could be a potential alternative if VAD is not a good option (size, anatomy or parental preference)



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# Decongestion-myths and legends



Cardiac Failure

Loop Diuretic Administration

Negative Sodium Balance

RAAS

Sec-Hyperaldosteronism

↓ Distal Sodium Delivery

Hypertrophy of Distal Nephron; Increased Expression of NaCl Transporter

Loop Diuretic Resistance

Low Urinary Sodium  
High Urinary Potassium  
High BUN  
High RA pressure



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Felker GM et al. *N Engl J Med* 2011;364:797-805.

Bansal S., *Circ Heart Fail.* 2009; 2:370-376



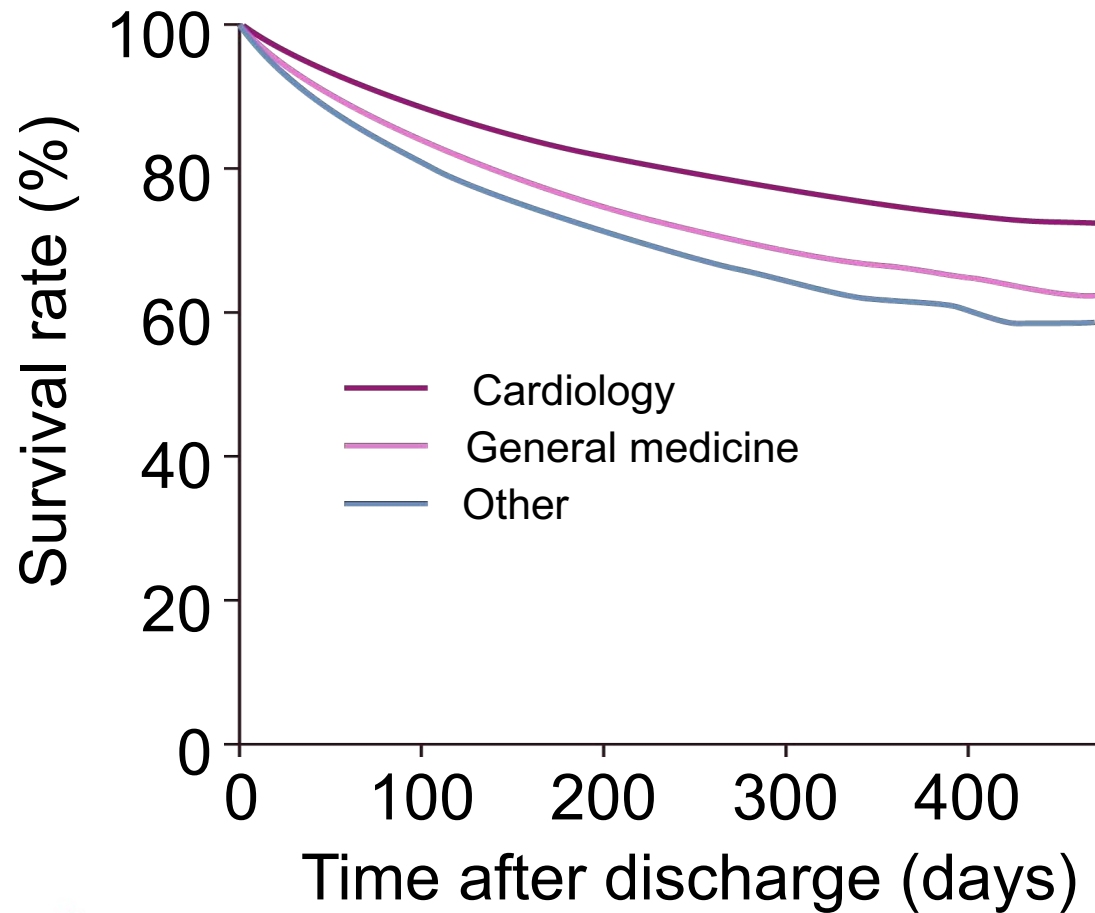


# Other Systems cautionary tales/Threats

- **GI-** feeds could be the kiss of death. Feeding tolerance is a frequent issue. Patient becomes snacker+vomiting=check RV congestion  
Sometimes TPN and some feeds is better than NEC or no feeds. The true value and risk of trophic feeds on this population needs to be carefully studied
- **ID-** the Achilles heel of maintaining/waiting. Many patients lymphopenic but without discernible immunodeficiency. Fevers with negative blood cultures potentially mean partially treated CVL infections
- **HEME:** anticipation of potential thrombus or management of stroke risk
- **CNS:** agitation $\neq$ delirium $\rightarrow$  could be changes in cardiac output



# Care in specialist units reduces the likelihood of death in hospital or soon after discharge



- Teamwork between cardiologists and other physicians and nurses is essential
  - Emergency department
  - Internal medicine
  - Intensive care
  - Outside hospital
- Patients and public alike can recognize 'good care'



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# The Bottom Line

- The main objectives of maintenance are:
  - Stabilization of organ function
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# Thank YOU



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