

Evidence-based medicine

# Does nesiritide reduce mortality and readmission in decompensated heart failure?

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## INTRODUCTION

Heart failure (HF) is characterized by insufficient cardiac output to supply adequate perfusion to the peripheral demands. When decompensated, it can cause various systemic effects, depending on the type of presentation. The patient may have only a low cardiac output, or may have a large pulmonary vascular congestion, causing acute pulmonary edema and clinically important dyspnea.

Nesiritide is a recombinant form of brain natriuretic peptide (BNP), secreted when the walls of the heart's ventricles are dilated, and its use was approved in 2001 by the FDA for the treatment of decompensated HF. It has vasodilatory properties, causing reduced pre- and afterload, decreased pulmonary capillary pressure, and increased cardiac output without inotropic effects<sup>1,2</sup> and without causing arrhythmias<sup>3</sup>.

The objective of this review is to evaluate whether the use of nesiritide brings benefit or harm to patients presenting to the emergency department with dyspnea for HF decompensation.

## METHOD

A systematic review was conducted in the MEDLINE database to find the best evidence available with the following strategy: [(Natriuretic Peptide, Brain OR Nesiritide) AND (Dyspnea OR Heart failure)]. The Therapy/Narrow filter was used through the Clinical Queries interface.

Each retrieved study was evaluated by title and summary. The selected studies met the following inclusion cri-

teria: randomized clinical trial; use of nesiritide compared with placebo (both combined with standard therapy) in patients presenting to the emergency department with decompensated HF/dyspnea; and written in English, Spanish, or Portuguese. Only studies with a Jadad et al.<sup>4</sup> score greater than or equal to three were included in the final selection and data analysis.

All variables were analyzed through the CATmaker software, using the difference in absolute risk (AR), with 95% confidence interval (95% CI), and the number needed to treat (NNT) or number needed to harm (NNH). Meta-analysis was performed using the Review Manager 5.1.2 software.

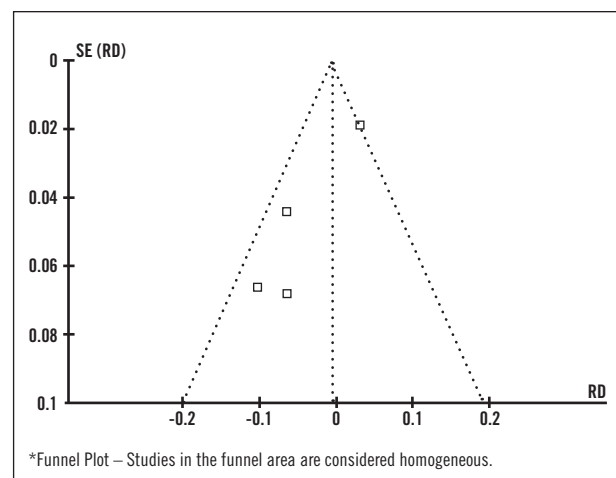


Figure 2 – Heterogeneity test.

Study or subgroup	Nesiritide		Placebo		Weight	Risk difference M-H, Fixed, 95% CI	Risk difference M-H, Fixed, 95% CI
	Events	Total	Events	Total			
O'Connor <sup>6</sup>	126	3564	141	3577	93.3%	-0.00 [-0.01, 0.00]	
Miller et al. <sup>7</sup>	1	53	4	48	1.3%	-0.06 [-0.15, 0.02]	
Peacock et al. <sup>8</sup>	5	127	1	123	3.3%	-0.03 [-0.01, 0.07]	
Mills <sup>10</sup> (0,015 µg)	0	22	3	29	0.7%	-0.10 [-0.23, 0.03]	
Mills <sup>10</sup> (0,03 µg)	1	26	3	29	0.7%	-0.06 [-0.20, 0.07]	
Mills <sup>10</sup> (0,06 µg)	1	26	3	29	0.7%	-0.06 [-0.20, 0.07]	
<b>Total (95% CI)</b>		<b>3818</b>		<b>3835</b>	<b>100.0%</b>	<b>-0.01 [-0.01, -0.00]</b>	
Total events	134		155				
Heterogeneity: Chi <sup>2</sup> = 9.29; df = 5 (p < 0.010); I <sup>2</sup> = 46%							
Test for overall effect: Z = 1.20 (p = 0.23)							
*Meta-analysis of selected studies. Overall result expressed in the difference of absolute risk, with no statistically significant benefit.							

Figure 1 – Mortality.

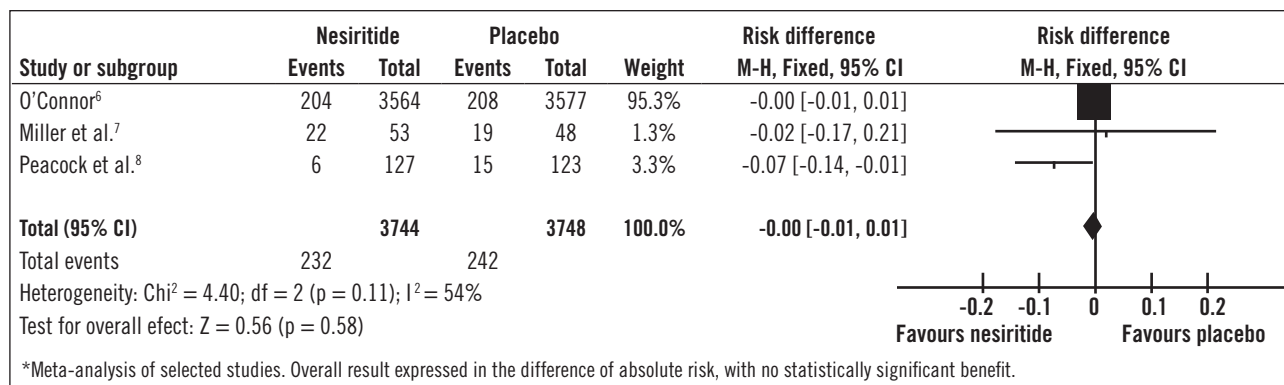


Figure 3 – Readmission.

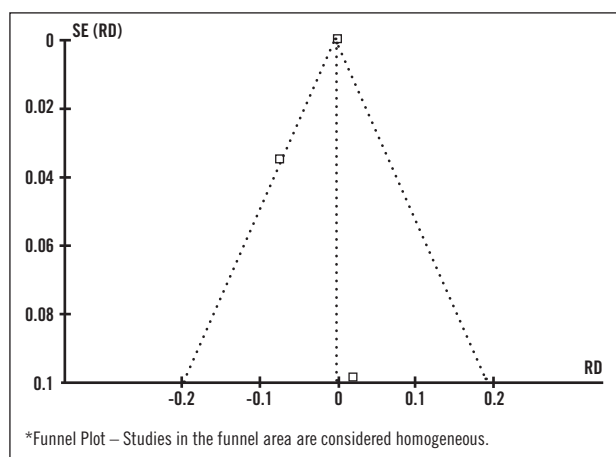


Figure 4 – Heterogeneity test.

## RESULTS

The literature review was completed in August 2011. We retrieved 411 articles, but only seven<sup>5-11</sup> met the inclusion criteria. After analysis of the selected articles, two were excluded from the final selection; one<sup>5</sup> for not having a placebo group for comparison, and the other<sup>11</sup> for not providing absolute data on the outcomes, preventing the calculation of risk difference.

In the study by Colucci et al.<sup>9</sup>, two doses of nesiritide were tested (0.015 and 0.030 µg/kg/min) and compared to placebo. Mills et al.<sup>10</sup> tested three doses (0.015, 0.03, and 0.06 µg/kg/min) compared to placebo.

## MORTALITY

Four studies<sup>6-8,10</sup> presented data on mortality (Figures 1 and 2). There was no statistically significant difference in risk for both the effect of individual studies and the overall effect.

## READMISSION

Of the three studies<sup>6-8</sup> evaluating the number of readmissions, only one study<sup>8</sup> showed a significant benefit of nesiritide. However, there was no significant difference in the overall effect (Figures 3 and 4).

## CONCLUSION

Analysis of best available evidence shows that the use of nesiritide is safe because it did not cause significant differences in mortality and readmission rates.

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