

# Chapter 1

## The Role of Natriuretic Peptides in the Pathophysiology and Treatment of Heart Failure

**Jennifer L. Mathews**  
St. John Fisher College, USA

**Anne Schweighardt**  
St. John Fisher College, USA

### ABSTRACT

*The pathophysiology of heart failure is due in part to compensatory mechanisms utilized to maintain cardiac output. Neurohormonal responses include activation of the renin-angiotensin-aldosterone and sympathetic nervous systems leading to vasoconstriction, increased blood volume through reabsorption of sodium and water, and increased myocardial contractility and heart rate. Prolonged activation of these systems often results in a maladaptive response and a further reduction in cardiac output (Colucci, 2015). Natriuretic peptides counterbalance the neurohormonal systems by antagonizing the actions of renin-angiotensin-aldosterone, promoting vasodilation and natriuresis. In hypervolemic states atrial myocytes are stretched resulting in the release of atrial natriuretic peptide (ANP). Ventricular cells secrete brain-type natriuretic peptide (BNP) in response to the high ventricular filling pressures (de Sa, 2008). The natriuretic peptides are degraded enzymatically by neprilysin. Plasma concentrations of ANP and BNP can be used as markers for the diagnosis of heart failure (Grewal, 2004). The kidneys also produce a natriuretic peptide, urodilatin, and new studies suggest a role for this peptide in the pathophysiology and treatment of heart failure (Anker, 2015). The natriuretic peptides can be targeted therapeutically for the treatment of heart failure. Nesiritide, a recombinant preparation of human B-type natriuretic peptide (BNP), is FDA approved and has been available for several years for treatment of acute decompensations of heart failure, but has received limited use due to cost and adverse effect profile. Ularitide, a synthetic analog of urodilatin, is currently in phase three clinical trials. In addition, the FDA has recently approved an angiotensin receptor blocker-neprilysin inhibitor that has shown mortality benefit.*

DOI: 10.4018/978-1-5225-2092-4.ch001

## **INTRODUCTION**

The pathophysiology of heart failure is due in part to compensatory mechanisms aimed at maintaining cardiac output (Colucci, 2015). Prolonged activation of these systems often results in a maladaptive response and a further reduction in cardiac output (Colucci, 2015). Natriuretic peptides counterbalance the neurohormonal systems by antagonizing the actions of renin-angiotensin-aldosterone and promoting vasodilation and natriuresis (de Sa, 2008). The natriuretic peptides can be targeted for the treatment of heart failure and current clinical trials aim to introduce novel compounds with therapeutic benefits over medications currently on the market.

## **BACKGROUND**

Heart failure (HF) is a complex condition which effects 5.7 million people in the United States, or approximately 10 out of every 1,000 individuals over the age of 65 (Lloyd-Jones, 2002). Newly diagnosed cases of HF are expected to increase 46% by 2030 (Heidenreich, 2013). Heart failure occurs equally in men and women and is more prevalent in African Americans and Hispanics followed by Caucasians and Asian Americans (Lloyd-Jones, 2002; Bahrami, 2008).

Risk factors for HF include: cigarette smoking, hypertension, obesity, diabetes and dietary sodium intake (He 2001; 2002). Seventy-five percent of patients with HF have pre-existing hypertension and the lifetime risk for people with blood pressure (BP) >160/90 mmHg is double that of those with BP <140/90 mmHg (Lloyd-Jones, 2002).

Significant healthcare dollars are spent on the diagnosis and treatment of HF. Total cost for HF has been estimated to be over \$30 billion and projections show that by 2030 the total cost of HF will increase to \$69.7 billion or \$244 for every US adult (Heidenreich, 2013). On average, patients with HF take 6 medications and 78% have at least two hospital admissions per year (English, 1995). Heart failure is the most common hospital discharge diagnosis among individuals served by Medicare and more Medicare dollars are spent for the diagnosis and treatment of heart failure than for any other diagnosis (Massie, 1997).

The cardiac dysfunction that underlies HF is often chronic and irreversible, interspersed with episodes of acute decompensation. Current drug therapies aim to manage symptoms associated with the syndrome. Despite advances in treatment the 5-year mortality rate for HF has remained high at 50% (Roger, 2004).

## **PATHOPHYSIOLOGY OF HEART FAILURE**

Heart failure begins with myocardial damage which can often be attributed to ischemic heart disease, hypertension or diabetes (Mozaffarian, 2016). The impaired myocardial fibers may be unable to contract (systolic HF) or relax (diastolic HF).

### **Cardiovascular Parameters**

With each heartbeat, a volume of blood from the left ventricle is ejected into the aorta and the same happens from the right ventricle into the pulmonary artery. The amount of blood pumped out of the

14 more pages are available in the full version of this document, which may be purchased using the "Add to Cart" button on the publisher's webpage:

[www.igi-global.com/chapter/the-role-of-natriuretic-peptides-in-the-pathophysiology-and-treatment-of-heart-failure/176206](http://www.igi-global.com/chapter/the-role-of-natriuretic-peptides-in-the-pathophysiology-and-treatment-of-heart-failure/176206)

## Related Content

---

### Valvular Heart Disease

Christine M. Lennon, Alexander C. P. Fortand Shawn Hansberry (2015). *Modern Concepts and Practices in Cardiothoracic Critical Care* (pp. 168-215).

[www.irma-international.org/chapter/valvular-heart-disease/136909](http://www.irma-international.org/chapter/valvular-heart-disease/136909)

### A New Approach for Coronary Artery Diseases Diagnosis Based on Genetic Algorithm

Sidahmed Mokeddem, Baghdad Atmaniand Mostéfa Mokaddem (2019). *Coronary and Cardiothoracic Critical Care: Breakthroughs in Research and Practice* (pp. 44-59).

[www.irma-international.org/chapter/a-new-approach-for-coronary-artery-diseases-diagnosis-based-on-genetic-algorithm/225354](http://www.irma-international.org/chapter/a-new-approach-for-coronary-artery-diseases-diagnosis-based-on-genetic-algorithm/225354)

### Recent Innovations in Coronary Stents

Poulomi Sengupta (2017). *Emerging Applications, Perspectives, and Discoveries in Cardiovascular Research* (pp. 233-244).

[www.irma-international.org/chapter/recent-innovations-in-coronary-stents/176220](http://www.irma-international.org/chapter/recent-innovations-in-coronary-stents/176220)

### Surgical Management of Mitral Valve Disease

Robin Varghese (2015). *Modern Concepts and Practices in Cardiothoracic Critical Care* (pp. 713-727).

[www.irma-international.org/chapter/surgical-management-of-mitral-valve-disease/136928](http://www.irma-international.org/chapter/surgical-management-of-mitral-valve-disease/136928)

### Assessment of Cardiac Dynamics and Risk Factor Analysis Using Deep Neural Nets

Jayanthi G., Purushothaman R., Sivant Moduguru, Harshini Senthil Kumaran, Siva Kumar Reddy C. H. V., Aparna Shankar, Anbu Ezhilmathi Nambiand Anantha Narayanan Sampath Varadharajan (2022). *Leveraging AI Technologies for Preventing and Detecting Sudden Cardiac Arrest and Death* (pp. 138-165).

[www.irma-international.org/chapter/assessment-of-cardiac-dynamics-and-risk-factor-analysis-using-deep-neural-nets/308839](http://www.irma-international.org/chapter/assessment-of-cardiac-dynamics-and-risk-factor-analysis-using-deep-neural-nets/308839)