



Figure 1. Heart failure (HF) begins after an index event (eg acute coronary syndrome) produces an initial decline in the heart's pumping capacity. After this initial decline, various compensatory mechanisms are activated, including the activation of adrenergic signalling, upregulation of the RAAS and activation of vasodilatory cytokines. Importantly, many of these vasodilatory peptides, including bradykinin, ANP and BNP, are degraded by neprilysin, a membrane-bound peptidase. At some point, these compensatory mechanisms fail and patients decompensate, with an increase in overt symptoms of HF and a concurrent increase in mortality. Although the exact mechanisms that are responsible for this transition are unknown, the transition to symptomatic HF is accompanied by increasing activation of neurohormonal, adrenergic and cytokine systems that lead to maladaptive changes within the myocardium collectively, referred to as left ventricular remodelling.¹⁷

ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; NO, nitric oxide; RAAS, renin-angiotensin-aldosterone system