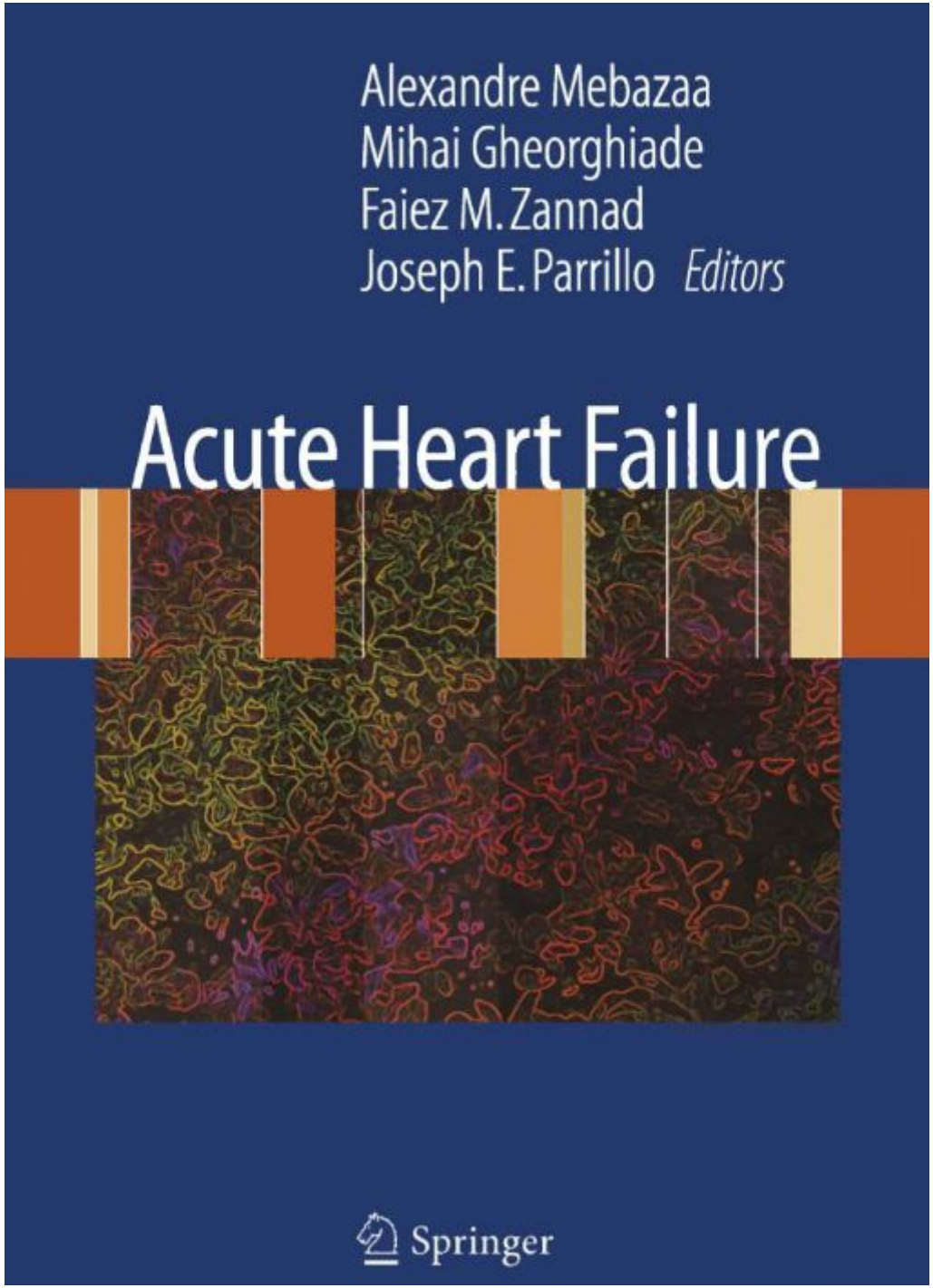
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Acute Heart Failure
Springer

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British Library Cataloguing in Publication Data
Acute heart failure
1. Heart failure – Treatment 2. Heart failure
I. Mebazaa, Alexandre
616.1´2906
ISBN-13: 9781846287817

Library of Congress Control Number: 2007929111

ISBN: 978-1-84628-781-7 e-ISBN: 978-1-84628-782-4

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enhances TNF-α expression. Although less well characterized, catecholamines appear to increase IL-10 expression via a β_2-receptor mediated pathway (25). The antiinflammatory activity of IL-10 would be consistent with the previously described effects of adrenergic action on the immune system.

In a preliminary clinical study, a reduction in norepinephrine's ability to counterregulate inflammatory cytokine production in symptomatic heart failure was observed (32). In monocytes isolated from heart failure patients, attenuation of

C-Reactive Protein in Acute Heart Failure

There is growing evidence that multiple aspects of the inflammatory response are upregulated in acute heart failure. C-reactive protein (CRP) is an inflammatory protein synthesized in the liver that activates the complement cascade and contributes to opsonization by immune cells. Serum CRP levels have also been shown to help predict the development of heart failure in patients at risk. Increased circulating levels of CRP have been

demonstrated in both acute and chronic heart failure (37–41). Despite the involvement of CRP with ischemic heart disease, there are conflicting data on whether levels differ based on heart failure etiology.

The exact role of CRP in heart failure remains to be fully defined. However, studies consistently demonstrate that elevated serum levels of CRP are independently predictive of poor clinical outcome (38, 40, 41). In the largest study to date, post-hoc analysis of the Valsartan Heart Failure Trial demonstrated approximately a 50% increase in mortality among study patients with serum CRP levels in the highest quartile (≥7.32 mg/L) versus the lowest quartile (≤1.42 mg/L) with a hazard ratio of 1.51 (95% confidence interval, 1.2–1.9) (41). A single admission CRP level was found to be predictive of progression to heart failure in acute myocardial infarction patients (42). Higher serial levels were also predictive of hypertrophy and heart failure development in patients on hemodialysis or those with cerebrovascular disease (43, 44). A potential causative role for CRP is also supported by the observation that CRP levels show a strong inversion correlation with left ventricular ejection fraction and correlated directly with left ventricular end-diastolic pressure (42, 45).

One study confirmed that levels increase in acute decompensation and decrease with symp- in CRP from these therapies results in improved outcomes is unknown.

Potential Pathogenic Role Inflammatory Response in Acute Heart Failure

Recent findings of inflammatory activation in acute heart failure have led Felker and Cotter (48) to speculate that this systemic response may contribute to the pathophysiology of decompensation leading to hospitalization in this syndrome. Experimental studies have documented that acute administration of cytokines can induce a pathophysiologic picture typical of acute heart failure with ventricular dysfunction, increased diastolic stiffness, and pulmonary edema (49, 50). The recent demonstration in humans that vaccination with *Salmonella typhi* may be associated with acute increases in IL-6 and the induction of abnormal arterial stiffness further supports the potential role of the inflammatory response in acute heart failure (51).

Other Humoral Mediators Related to Inflammatory Response

Nitric Oxide

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