Hypertensive pulmonary oedema is due to diastolic dysfunction

Nearly half of patients hospitalized with congestive heart failure are found to have preserved systolic function (i.e. a left ventricular ejection fraction greater than 0.50)\[^1\]–\[^5\]. Thus, most cardiologists presume that the heart failure in these patients is due to isolated diastolic dysfunction\[^6\]. However, not all experts have accepted the hypothesis that a large portion of patients presenting with pulmonary congestion have isolated diastolic dysfunction\[^7\].

Is hypertensive pulmonary oedema due to diastolic dysfunction?

Acute pulmonary oedema is a dramatic presentation of heart failure and a frequent cause for hospitalization. More than 85% of patients presenting with acute pulmonary congestion are markedly hypertensive (systolic arterial pressure >160 mmHg)\[^8\]. The evaluation of left ventricular ejection fraction in such patients usually occurs after the patient's clinical status has improved and the hypertension has resolved. For example, Vasan and Levy proposed that a normal left ventricular ejection fraction (≥0.50) within 72 h of an episode of pulmonary congestion indicates that the patient has heart failure due to diastolic (not systolic) dysfunction\[^9\].

Accordingly, we hypothesized that many patients hospitalized with acute pulmonary oedema in association with hypertension have transient left ventricular systolic dysfunction, which is not present when the left ventricular ejection fraction is evaluated after the patient has been treated. To test this hypothesis, we used Doppler echocardiography to evaluate left ventricular ejection fraction, regional wall motion, and mitral regurgitation in 38 patients both during an acute episode of hypertensive pulmonary oedema and 24 to 72 h later, after treatment and resolution of the hypertension and pulmonary congestion\[^10\].

In contrast to our hypothesis, we found that left ventricular ejection fraction and regional wall motion were similar, both during the acute episode of hypertensive pulmonary oedema and after resolution of the congestion and control of the blood pressure (Fig. 1)\[^10\]. One half of the patients had an ejection fraction ≥0.50 during their presentation with acute pulmonary oedema. Eighty-eight percent of the patients with a preserved ejection fraction (≥0.50) after treatment had an ejection fraction ≥0.50 during the acute episode, and all of these patients had an ejection fraction ≥0.43. Thus, the ejection fraction obtained 1–3 days after the acute presentation of patients with hypertensive pulmonary oedema accurately identified patients with a preserved ejection fraction during the presentation whose acute heart failure was due to isolated diastolic dysfunction.

Even in the patients with systolic dysfunction (i.e. follow-up ejection fraction <0.50), the left ventricular ejection fraction was similar during the acute heart failure and after therapy. Thus, the acute pulmonary oedema in these patients was not due to a worsening of the pre-existing systolic dysfunction. This suggests that diastolic dysfunction is also an important contributor to acute hypertensive pulmonary oedema in patients with baseline systolic dysfunction.

Transient ischaemic left ventricular dysfunction can produce acute pulmonary oedema. More than half of our patients had segmental wall motion abnormalities on the echocardiogram performed after treatment, suggesting the presence of ischaemic heart disease. However, in our patients, the ejection fraction was not reduced during the acute episode, and only two patients had recognizable regional wall motion abnormalities acutely that were not present after therapy. Thus, acute ischaemic systolic left ventricular dysfunction was not the cause of acute heart failure in our patients\[^10\]. However, ischaemia may have contributed to diastolic dysfunction without producing a measurable reduction in the ejection fraction or regional wall motion\[^3\].
It is possible that many patients with pulmonary oedema due to ischaemic left ventricular systolic dysfunction or acute mitral regurgitation are not able to generate high systolic pressures\(^\text{[11]}\). However, it is important to recognize that more than 85% of patients presenting with acute pulmonary oedema have marked systolic hypertension\(^\text{[8]}\).

Ejection measurements of left ventricular performance such as ejection fraction are afterload dependent\(^\text{[12,13]}\). Thus, one expects the ejection fraction to decline with increasing systolic blood pressure if the left ventricular contractile state remains constant. In contrast, we found that the left ventricular ejection fraction was the same during an episode of acute hypertensive pulmonary oedema and after the blood pressure was controlled. It is possible that the inotropic stimulation produced by increased beta adrenergic tone during acute pulmonary oedema offsets the effects of increased afterload on systolic performance.

**Therapy of diastolic dysfunction**

Although isolated diastolic dysfunction is an important cause of heart failure, there are little data to guide therapy\(^\text{[14]}\). In contrast to the large number of randomized, placebo-controlled studies of patients with systolic dysfunction, no such studies have been completed in patients with isolated diastolic dysfunction (Table 1). Two such studies are underway, evaluating different methods of interfering with angiotensin II. One study is evaluating the value of an angiotensin receptor blocker\(^\text{[15]}\), and the other is testing an angiotensin converting enzyme inhibitor\(^\text{[16]}\). Other studies are being planned.

The control of hypertension appears to be a key element in the treatment and prevention of diastolic dysfunction. Uncontrolled hypertension promotes the development of left ventricular hypertrophy. This hypertrophy impairs left ventricular distensibility contributing to diastolic dysfunction\(^\text{[2]}\). Furthermore, our observations in patients with acute pulmonary oedema demonstrate the dramatic acute effects of acute elevations in systolic arterial pressure in reducing diastolic performance. Since the pulmonary congestion in our patients rapidly cleared in association with lowering of the blood pressure, hypertension may have contributed to the diastolic dysfunc-

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**Table 1** There have been many large, randomized, controlled studies of the therapy of patients with heart failure due to systolic dysfunction (a partial listing). In contrast, no large randomized studies have been completed in patients with isolated diastolic dysfunction

<table>
<thead>
<tr>
<th>Systolic dysfunction</th>
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<td>ANZ</td>
<td>Milrinone-Dig</td>
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<td>VAL-HeFT</td>
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<td>MERIT-HF</td>
<td>VHeFT I*, II*</td>
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*Included some patients with normal ejection fraction.
tion[10,17]. Normally, the left ventricle compensates for an increase in systolic load by using pre-load reserve. However, in a patient with reduced diastolic distensibility, this small increase in left ventricular end-diastolic volume results in a marked elevation in diastolic pressure. In addition, acute increases in systolic pressure slow left ventricular relaxation and reduce diastolic distensibility further[18,19]. Thus, untreated hypertension contributes to the development of diastolic dysfunction and acute elevations in systolic arterial pressure exacerbate diastolic dysfunction resulting in acute pulmonary oedema.

**Exercise intolerance due to diastolic dysfunction**

Diastolic dysfunction not only produces acute pulmonary oedema, it can also contribute to exercise intolerance[20]. Exercise intolerance due to diastolic dysfunction may be much more common than is presently recognized. Systolic hypertension may play a role here as well. Not only do elderly subjects have reduced diastolic ventricular distensibility, there is also reduced aortic compliance. This results in the frequent development of marked arterial systolic hypertension (>200 mmHg) in normal elderly subjects during exercise[21]. We recently observed that blunting this increase in arterial pressure with an angiotensin receptor blocker improved exercise tolerance in patients with diastolic dysfunction[22].

**Conclusion**

We found that left ventricular ejection fraction is similar, both during an acute episode of hypertensive pulmonary oedema and, subsequently, after treatment and control of the blood pressure[10]. Thus, a preserved left ventricular ejection fraction after treatment of a patient with hypertensive pulmonary oedema indicates that it is likely that the pulmonary congestion was due to isolated diastolic dysfunction since transient systolic dysfunction or severe acute mitral regurgitation during the acute episode is infrequent in these patients. This study helps establish that diastolic dysfunction is a frequent cause of acute pulmonary congestion and emphasizes the role of hypertension in producing and exacerbating diastolic dysfunction.

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**References**

