the importance of treating patients with chronic heart failure with ACE inhibitors. All patients with left ventricular dysfunction and chronic heart failure should be evaluated for ACE-inhibitor therapy. Practising physicians should be reassured about the good tolerability of ACE inhibitors, and of lisinopril in particular. Treatment should be initiated by slow forced titration to a target dose. Based on ATLAS and other trials it is not clear what the optimal dose level is but my interpretations are:

- Higher dose levels of documented ACE inhibitors are better than low dose levels.
- Forced titration to a dose level of at least 20 mg daily of lisinopril or enalapril, captopril 50 mg three times daily, ramipril 10 mg daily or trandolapril 4 mg four times daily should be performed in all patients.
- There is still uncertainty over whether 35 mg of lisinopril is better than 20 mg, but better neuroendocrine protection is obtained by the higher dose levels.
- Patients at higher risk (e.g. diabetics) and tolerating the initiation of an ACE inhibitor, will also benefit more from the high dose strategy. As their relative risk reduction is similar to the reduction seen in patients at lower risk, even more patients will be saved by this improved management in these patients at higher risk.

By disseminating the experience now well documented to all physicians managing patients with chronic heart failure, cardiologists will help these patients to obtain the benefits from modern pharmacological therapy, in particular with ACE inhibitors.

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References


Cardiogenic shock: a call for aggressiveness

See page 1928 for the article to which this Editorial refers

Since it has become possible to detect and treat life-threatening arrhythmias effectively, cardiogenic shock has become the main cause of in-hospital death after acute myocardial infarction.

The incidence of cardiogenic shock has remained stable over the last years with reported in-hospital frequencies ranging from 5% to 15% depending on the definition used[1].

In this issue, Menon and colleagues[2] evaluated the outcome of patients with cardiogenic shock in two large trials of thrombolytic therapy. In the Global
Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO)-I study\(^3\) (as in the Worcester Registry\(^4\)) the incidence of cardiogenic shock was 7% to 8%. In the later performed Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO)-III trial\(^5\) only 5-5% of the patients had cardiogenic shock. This difference in incidence between GUSTO-I and GUSTO-III is mainly due to selection. At the time of enrolment in GUSTO-III, more haemodynamically unstable patients underwent primary angioplasty or bypass surgery, especially in the U.S., and therefore were not included in the trial.

In spite of a uniform definition of cardiogenic shock throughout the duration of the two studies, the GUSTO-I and GUSTO-III shock populations were not similar. Shock patients in GUSTO-III were at much higher risk than in GUSTO-I (more elderly, more co-morbidities such as diabetes and hypertension, more anterior infarctions, higher Killip class on admission). These differences can be explained by the much larger proportion of non-U.S. patients in GUSTO-III and by the clear preference in the U.S. to offer high-risk patients immediate mechanical reperfusion instead of enrolment in a trial of thrombolytic therapy.

The difference in the two populations of thrombolytic therapy also explains the higher 30-day mortality rates observed in GUSTO-III, compared with GUSTO-I: 62% vs 54%.

Even when enrolled in a thrombolysis trial, U.S. patients are more often treated with angioplasty/stenting or bypass surgery. The infrequent use of these procedures outside the U.S. is mainly related to the type of centres participating in the trial, the non-availability of a catheterization laboratory and the reluctance to transfer a moribund patient to a tertiary care centre.

The mortality rates in the revascularized group in the SHOCK trial\(^6,7\) are lower than the overall rates observed in the GUSTO-I and GUSTO-III studies, in spite of the fact that revascularization was performed rather late. Indeed, in the SHOCK trial, patients could be randomized up to 36 h after onset of infarction. One can assume that if the same aggressive treatment had been offered earlier, a much greater benefit would have been obtained. Mortality rates of \(\pm 30\%\) after revascularization observed in the U.S. population of the two GUSTO trials indirectly support this hypothesis.

The new data provided by the present analysis add to the already existing evidence from the SHOCK trial and from other non-randomized studies that an aggressive treatment approach is beneficial in patients with cardiogenic shock after acute myocardial infarction. Optimal treatment nowadays should include early angiography, intra-aortic balloon pumping, primary angioplasty/stenting or bypass surgery, depending on the anatomy of the coronary lesions. In smaller hospitals, pharmacological reperfusion should be given as soon as possible, followed by rapid transfer to a tertiary care centre, if possible after insertion of a balloon pump. This aggressive strategy may be particularly beneficial in patients up to the age of 75 years. It is in this age category that revascularization yielded the largest survival benefit in the SHOCK trial\(^6,7\).

It is likely that, with a rapid and aggressive approach in shock patients after acute myocardial infarction, 30-day mortality rates of around 30% are obtainable, which contrast with the much more than 60% fatality rates observed with conservative strategies.

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