Medium-term survival after primary angioplasty for myocardial infarction complicated by cardiogenic shock after the age of 75 years


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Summary
Aims of the study. — To assess mortality in people ≥75 years of age 6 months after myocardial infarction complicated by cardiogenic shock and treated by angioplasty with complete revascularisation and optimal anti-thrombotic treatment; to compare results to those of younger patients with or without shock and to analyse predictive factors for death.

Materials and methods. — The study is based on 1011 consecutive patients with myocardial infarction admitted for primary angioplasty, subdivided into four groups by age and the presence or absence of cardiogenic shock: group 1 (<75 years of age without shock, n=733), group 2 (<75 years of age with shock, n=49), group 3 (≥75 years of age without shock, n=208) and group 4 (≥75 years of age with shock, n=20). These four patient groups were compared for mortality rates and predictive factors for in-hospital and 6 month mortality.

Results. — In-hospital mortality in groups 1 to 4 was 1.7%, 30.6%, 9.1%, and 70% (p<0.0001) respectively and 6-month mortality was 3.1%, 40%, 16% and 78% (p<0.0001). By univariate analysis renal failure was a predictive factor for death at 6 months in patients without cardiogenic shock (groups 1 and 3), and left ventricular function in patients in group 2. No predictive factors were found in group 4 patients. The independent predictive factors for death at 6 months were: age >75 years of age (P<0.0003), cardiogenic shock (P<0.0001), triple vessel lesions (P<0.01) and creatinine clearance (P=0.004).

Conclusion. — Mortality after angioplasty remains high in people ≥75 years with cardiogenic shock despite all the advances in the management of myocardial infarction. These disappointing results should encourage us to assess the role of surgical revascularisation and circulatory assistance.

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Introduction

Between 5 to 10% of myocardial infarctions are complicated by cardiogenic shock, which remains the most worrying complication of myocardial infarction and is the main cause of in-hospital deaths. Most cases of cardiogenic shock develop in the first days following admission. In the SHOCK study (SHould we emergently revascularise Occluded coronaries for Cardiogenic shock) [1], 75% of the patients developed shock during the first 24 hours following their admission.

Fibrinolysis in the acute phase of the infarction reduces the risk of developing cardiogenic shock in patients without initial haemodynamic complications but does not improve patient prognosis if the infarction has already been complicated by cardiogenic shock [2]. The improvement in prognosis in patients with infarction and initial cardiogenic shock relies on early revascularisation, intra-aortic balloon pumping and optimal medical management. The mortality rate from post-infarction cardiogenic shock has fallen since the advent of revascularisation techniques, from 70 to 80% in 1975 to less than 50% now. This benefit however is seen mostly in younger patients, with the mortality rate in patients under 75 years of age falling from 55.8% in 1995 to 39.5% in 2004 in the meta analysis by Babaev [3], whereas the benefit in patients over 75 years of age is more limited (69.9% in 1995 vs 64% in 2004).

In the SHOCK study, which randomised revascularisation against medical treatment in patients with acute infarction complicated by cardiogenic shock, revascularisation reduced the risk of death at 6 months by 30% in patients under 75 years of age although increased mortality by 41% compared to medical treatment alone in patients over 75 years of age [1]. The limitations of the SHOCK study are that it included a small number of patients (only 16 patients ≥75 years of age revascularised, of which 10 underwent angioplasty), with sub-optimal anti-thrombotic treatment, and low successful revascularisation (77%), coronary stenting (33%) and complete revascularisation (23%) rates. Conversely, in the SHOCK register, in-hospital mortality of patients ≥75 years of age was lower after revascularisation (48% vs 79% in non-revascularised patients) [4]. The benefits and selection criteria for primary angioplasty in patients ≥75 years of age with infarction complicated by cardiogenic shock are therefore controversial.

The aims of this study were:

- to assess mortality in people ≥75 years of age 6 months after myocardial infarction complicated by cardiogenic shock due to predominant left ventricular dysfunction and treated according to current recommendations by angioplasty with complete revascularisation and optimal anti-thrombotic treatment;
- to compare these results to those in younger patients with or without shock.

Patients and methods

The study was conducted at the Pitié-Salpêtrière Hospital Institute of Cardiology between January 2000 and December 2005. It was based on 1011 consecutive patients admitted for myocardial infarction within 12 hours, investigated by emergency coronary angiography for revascularisation by primary angioplasty.

The patients were divided into 4 groups by age and presence or absence of cardiogenic shock: group 1 (patients <75 years of age without cardiogenic shock: 733 patients, 73%), group 2 (patients <75 years of age with cardiogenic shock: 49 patients, 5%), group 3 (patients ≥75 years of age without cardiogenic shock: 208 patients, 20%), group 4 (patients ≥75 years of age with cardiogenic shock: 20 patients, 2%). These 4 groups of patients were compared in terms of clinical, laboratory and angiographic features and by the death rates and predictive factors for death at 6 months.
All the patients underwent emergency coronary angiography. The approach for the angioplasty was usually radial, including those patients with cardiogenic shock in whom angioplasty was conducted under an intra-aortic balloon pump inserted via the femoral artery. All the angioplasties were performed under aspirin, clopidogrel, LMWH and antiGP IIb/IIIa (abciximab). The great majority of stents implanted were uncoated. The primary angioplasty was limited to the artery responsible for the infarction except for patients with cardiogenic shock in whom complete revascularisation by angioplasty was performed on all accessible lesions, consistent with ACC/AHA 2004 and ESC 2005 recommendations [5]. All the patients in cardiogenic shock were treated with intravenous positive inotropes, mechanical ventilation in cases of refractory hypoxia and all were put on an intra-aortic balloon pump. Data were collected from the patients’ medical dossiers and/or by telephone for the 6-month follow up.

The diagnosis of myocardial infarction was made on admission, based on clinical findings (typical pain) with ST segment elevation, confirmed retrospectively from a rise in the troponin. The diagnosis of cardiogenic shock was based on systolic arterial blood pressure < 90 mmHg for at least 30 minutes with clinical signs of tissue hypoperfusion and clinical signs of left heart failure and echocardiographical findings of left ventricular dysfunction, either on admission or during the hospitalisation. Left ventricular dysfunction was considered to be a predominant component of the cause of shock when none of the following causes were present: isolated right ventricular dysfunction, mechanical complication (mitral incompetence or septal rupture), cardiac tamponade or rupture, severe valve disease, excessive beta-blocker or calcium blocker treatment [1]. Renal dysfunction was defined as creatinine clearance <60 ml/min. A past history of diabetes was defined as two fasting blood glucose concentrations over 1.26 g/l distant to any acute coronary episode. Hypertension was defined by an arterial blood glucose concentrations above 140/90 mmHg or treatment with antihypertensive agents.

Statistical analysis

Results were expressed as mean +/- standard deviation or as percentages. Qualitative data were compared by the Chi2 test or Fisher’s exact test and quantitative variables by analysis of variance. The statistical significance threshold was a value of p<0.05. Predictive factors for death at 6 months were investigated using multivariate analysis with logistic regression from the predictive factors identified in the univariate analysis. Data were analysed on Statview statistics software.

Results

The clinical and angiographical features of the 1011 patients are shown in table 1. Angioplasty was not performed in 115 patients (11.4%) because of death on table, lesions inaccessible to angioplasty, emergency surgical revascularisation indicated or absence of any significant lesion. Of those patients who underwent angioplasty, 93.9% were TIMI 3 and 6.1% were TIMI 2 post-angioplasty. The comparisons of clinical, laboratory, echocardiographical and angiographical features of the four patient groups are shown in table 2.

Follow up data were available on 90% of patients at one month and on 87% at six months. Cardiogenic shock occurred in 69 patients (6.8%). The risk of developing cardiogenic shock was not influenced by age: 6.2% in patients <75 years of age versus 8.8% in older patients. The overall in-hospital death rate was 6% (61 deaths) and the 6 month death rate was 7.7% (78 deaths). In-hospital and 6 month mortality rates were very significantly different in the four groups. The in-hospital death rates for groups 1 to 4 were 1.7%, 30.6%, 9.1% and 70% (p<0.0001) and 6-month death rates were 3.1%, 40%, 16% and 78% (p<0.0001) (table 2) (figure 1).
The predictive factors for death at 6 months in the 4 groups are illustrated comparatively in table 3. In group 1 (<75 years of age without cardiogenic shock): age, triple vessel lesions and low creatinine clearance were three predictive factors for death. In group 2 (<75 years of age with cardiogenic shock), LVEF was the only predictive factor for death (27±16 versus 41±8 P=0.0002). In the third group (>75 years of age without cardiogenic shock), age (p=0.0004) and creatinine clearance (p=0.001) were both predictive factors for death and no predictive factors for death were found in group 4 (>75 years of age with cardiogenic shock).

Age and cardiogenic shock were both highly significant predictive factors for in-hospital death and at 6 months by univariate analysis in the overall population (p=0.00001). Similarly, initial left ventricular ejection fraction was significantly lower in patients who had died at 6 months (41±19 versus 51±11 p<0.001). Renal failure was a predictive factor for death both in hospital (11.5% versus 4.2%, p=0.0001), and at six months (18.9% versus 5.7%, p<0.0001). Initial creatinine clearance was 53.3±39.5 ml/min in patients who died and 83.6±34.8 ml/min in patients who were alive at 6 months (p<0.0001). Female sex was a predictive factor for death at 6 months (12% in women versus 6% in men, p=0.03), although the risk of in-hospital death was identical for both sexes (p=0.16).

By multivariate analysis in the overall population, the independent predictive factors for in-hospital and 6-month death were over 75 years of age, cardiogenic shock, triple vessel disease and renal failure (table 4). Conversely, diabetes, site of the infarction, LVEF, and sex were not independent predictive factors for in-hospital or 6-month death (table 4).

**Discussion**

The 6-month death rate after primary angioplasty was 78% in patients over 75 years of age with cardiogenic shock in our study. Despite optimal management following the most recent recommendations [5], the mortality rate in patients with cardiogenic shock is still twice as high in patients over 75 years of age compared to younger patients. In contrast...
to patients without cardiogenic shock or to patients <75 years of age, no predictive factors for survival at 6 months were found in the elderly group of patients with cardiogenic shock.

In the randomised SHOCK study of 302 patients with myocardial infarction complicated by cardiogenic shock, revascularisation in >75 year old patients was associated with increased mortality compared to medical treatment [1]. The very high mortality rate seen in our study in >75 years old patients with cardiogenic shock is similar to the 80% 1 year mortality rate in >75 years old patients treated with angioplasty in the randomised SHOCK study. In contrast to our study, the patients randomised to revascularisation in the SHOCK study could undergo either angioplasty or coronary artery bypass grafting. Patients revascularised surgically had higher co-morbidities than those revascularised by angioplasty (diabetes was more common, more widespread lesions). The revascularisation method impacted on the survival when age was taken into account. One year survival in patients <75 years of age was 56% after angioplasty and 46% after bypass whereas one year survival in >75 years old patients was only 20% after angioplasty (vs 50% after bypass). The superiority of bypass over angioplasty in >75 years old patients with cardiogenic shock was attributed to more complete revascularisation from surgery [6]. The 6 month survival in this patient group in our study was only 22% despite complete revascularisation by angioplasty in multi-vessel disease, consistent with ESC recommendations 2005 [5].

In the German, ALKK, register, of 1333 patients in cardiogenic shock treated by primary angioplasty, age was a predictive factor for death, with an in-hospital mortality rate of 30% under 55 years of age, 36% for 55 to 65 years of age, 54% from 65 to 75 years of age and 63% over 75 years of age [7]. The authors concluded that an invasive emergency strategy was useful in young patients in cardiogenic shock whereas the benefit of revascularisation over 75 years of age remained to be proven.

Dzavik examined the influence of age on prognosis in patients with cardiogenic shock in the SHOCK register [4]. Of the 277 >75 year old patients, 20 died within the first 3 hours. Of the 257 patients who had not died by hour 3, the in-hospital mortality was 48% in the 56 revascularised patients (6% by bypass, 16% by angioplasty), vs 79% in non-revascularised patients. The benefit of revascularisation over conservative treatment was similar in <75 year old patients (42% in-hospital mortality after bypass for angioplasty vs 57% with conservative treatment). More >75 year old patients treated with revascularisation had a past history of hypertension, inferior infarction or past history of angioplasty than medically treated patients. After adjusting for these variables and excluding deaths within the first 3 hours, revascularisation after 75 year of age was still associated with a reduction in risk of mortality (RR 0.46, p=0.002) [4]. Unlike the randomised SHOCK study, this register therefore supported revascularisation in >75 year old patients with cardiogenic shock. This discrepancy may be explained by appropriate patient selection using clinical and angiographical criteria, as revascularisation was only performed in 22% of >75 year old patients in the SHOCK register.

The in-hospital mortality rate in >75 year old patients in cardiogenic shock in our series was 70% despite the systematic use of intra-aortic balloon pump, assisted ventilation in cases of refractory hypoxia [8], triple anti-aggregant treatment and LMWH, IV positive inotropes and complete angioplasty revascularisation of all accessible lesions in accordance with current recommendations. This very high mortality rate does not support generalising revascularisation to patients >75 years age in cardiogenic shock and the decision to use an invasive approach in these patients must be made on an individual case basis. The clinical selection criteria for elderly patients remain to be identified as most of the predictive factors for death in the literature are angiographic and are therefore available after the coronary angiography has been performed: the predictive factors for 1 year death in the SHOCK study were the lesion responsible, multi-vessel disease and end of procedure TIMI grade [9]. Reduced left ventricular ejection fraction was a predictive factor for death in patients <75 years of age with cardiogenic shock in our study, consistent with what has been reported in the literature [10-12], but was not found in patients over 75 years of age. The same applies to renal failure and, in some studies, female sex and diabetes [13-16], which were predictive factors for death under 75 years of age, but not in older patients with cardiogenic shock.

The benefit of and selection criteria for primary angioplasty in patients over 75 years of age with myocardial infarction complicated by cardiogenic shock are therefore debatable. According to ACC/AHA 2004 recommendations, patients with a myocardial infarction complicated by cardiogenic shock should undergo early revascularisation if they are under 75 years of age (recommendation IA) but this is only considered to be reasonable in some >75 year old patients selected according to their prior functional status (recommendation IIa B).

The improvement in prognosis in patients with cardiogenic shock may be due to advances in circulatory assistance. Whilst the intra-aortic balloon pump is now systematically implanted, the indications for percutaneous circulatory assistance with Impella (2.5 l/min flow rate in 12F, 5 l/min in 21F) or with Tandemheart (3 to 4 l/min) are still being assessed (common vascular complications, haemorrhage, haemolysis). This also applies to surgical circulatory assistance (ECMO, artificial heart) which is currently indicated for patients in whom percutaneous methods are ineffective and patients who cannot be weaned off percutaneous methods. In the experience of the Rouen University Hospi-

### Table 4 Independent predictive factors for death by multivariate analysis.

<table>
<thead>
<tr>
<th>Predictive factors for death</th>
<th>in-hospital deaths (p)</th>
<th>1 month deaths (p)</th>
<th>6 month deaths (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥75 years</td>
<td>0.014</td>
<td>0.02</td>
<td>0.0003</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Triple vessel disease</td>
<td>0.01</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>0.007</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.3</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Site of infarction</td>
<td>0.5</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Sex</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
</tr>
</tbody>
</table>
Limitations of the study

Few patients ≥75 years of age with myocardial infarction complicated by cardiogenic shock were treated by angioplasty. It is not possible from the relatively small number of patients to identify independent predictive factors for survival at 6 months. The same limitations apply to the randomised SHOCK study (16 patients ≥75 years of age revascularised, 10 of whom by angioplasty), and the SHOCK register (56 patients ≥75 years of age revascularised, 41 of whom by angioplasty). We can only conclude from our study that prognosis in these patients is not improved despite complete revascularisation, the systematic use of stents and optimal anti-thrombotic treatment.

During the inclusion period, surgical revascularisation of patients with cardiogenic shock was reserved for patients with mechanical complications (septal rupture, mitral incompetence) who were excluded from the study. Our study only therefore considers results of coronary angioplasty and cannot be used to assess the results of surgical revascularisation in cardiogenic shock associated with predominant left ventricular dysfunction.

Conclusions

Despite advances in coronary angioplasty, complete revascularisation and optimal medical management, the mortality rate in elderly patients with myocardial infarction complicated by cardiogenic shock is still very high and the benefit of systematic angioplasty in these patients has not been proven. The disappointing results of angioplasty in these high risk patients should encourage us to assess the benefit of surgical revascularisation and circulatory assistance.

References