Clinical research

Predictors of in-hospital mortality in 1333 patients with acute myocardial infarction complicated by cardiogenic shock treated with primary percutaneous coronary intervention (PCI)

Results of the primary PCI registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK)

Uwe Zeymera*, Albrecht Vogtb, Ralf Zahn, Michael A. Weberg, Ulrich Tebed, Martin Gottwik, Tassilo Bonzelf, Jochen Sengesa, Karl-Ludwig Neuhausb, for the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK)

Medizinische Klinik B, Herzzentrum Ludwigshafen, Ludwigshafen, Germany
Medizinische Klinik II, Klinikum Kassel, Kassel, Germany
Medizinische Klinik I, Amper-Klinikum Dachau, Dachau, Germany
Medizinische Klinik II, Klinikum Lippe-Detmold, Detmold, Germany
Medizinische Klinik 8, Klinikum Nürnberg, Nürnberg, Germany
Medizinische Klinik II, Klinikum Fulda, Fulda, Germany

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Aims Acute myocardial infarction complicated by cardiogenic shock is associated with an exceedingly high mortality, even if patients are treated with early reperfusion therapy. The aim of this study was to evaluate predictors of in-hospital mortality of a large cohort of consecutive patients with cardiogenic shock treated with primary percutaneous coronary intervention (PCI).

Methods and results Between July 1994 and March 2001 all interventions performed in 80 centres in Germany were prospectively entered into the primary PCI registry of the ALKK. A total of 9422 procedures were registered, of these 1333 (14.2%) were performed in patients with cardiogenic shock. Total in-hospital mortality was 46.1% and was dependent on TIMI flow grade after PCI, with mortality rates of 78.2%, 66.1% and 37.4% in patients with TIMI 0/1, TIMI 2 and TIMI 3 flow, respectively. In a multivariate analysis left main disease, TIMI <3 flow after PCI, older age, three-vessel disease and longer time-intervals between symptom onset and PCI were significant independent predictors of mortality. The relative number of PCIs performed in patients with cardiogenic shock did not change significantly from 1995–2000. There was a significant decrease in mortality over the years (P for trend 0.02).

Conclusions In-hospital mortality in patients with acute myocardial infarction complicated by cardiogenic shock remains high, even with early interventional therapy. However, our data demonstrate that the PCI in these high-risk patients is feasible in a wide spectrum of community hospitals with acceptable success rates. Our results in connection with the results of the randomized SHOCK study advocate an early invasive approach in younger patients with cardiogenic shock, while the best strategy in elderly patients is still a matter of debate.

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KEYWORDS
Cardiogenic shock;
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Stents
Introduction

Acute myocardial infarction is complicated by cardiogenic shock in 5 to 10% of patients. The mortality rate in these patients is exceedingly high and reaches 70–80% in those treated conservatively. Most recent experiences from large thrombolytic trials demonstrate of about 60% mortality in shock patients treated with the most effective thrombolytic regimens. Non-randomized studies report encouraging mortality rates among patients undergoing early interventional therapy. However, these studies were performed in highly specialized centres and a selection bias is most likely. A randomized study comparing angioplasty with conventional therapy in 55 patients was prematurely terminated and reported no significant mortality difference between the two groups. The larger randomized SHOCK trial performed in 302 patients showed a trend towards an improved outcome after 30 days in the early invasive group, and a lower 6-month survival rate in the invasive group. In the recent guidelines of the European Society for patients with ST elevation myocardial infarction interventional therapy is recommended for cardiogenic shock.

The purpose of this study was to evaluate the in-hospital mortality rate and to determine independent predictors of mortality in a large cohort of unselected consecutive patients with acute myocardial infarction complicated by cardiogenic shock treated with percutaneous coronary intervention in 80 centres in Germany.

Methods

Structure of the ALKK Registry

The PCI registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK) contains all PCI procedures from 80 centres in Germany since October 1992. Details of the organization of the registry have been published previously. In brief all interventions were prospectively enrolled in the registry by telephone or fax to the coordinating centre in Kassel. All complications occurring in the catheter room and during the in-hospital phase were prospectively documented. In July 1994, a sub-register was opened, which includes all PCI procedures in acute myocardial infarction within 24 h after symptom onset in more detail than in the general registry. The procedures in the sub-registry from July 1994 until end of March 2001 were analysed for this report. All data were collected prospectively and analysed centrally.

Patient selection

All patients undergoing PCI for an acute myocardial infarction within 24 h after symptom onset were considered for this analysis. Acute myocardial infarction was confirmed by the presence of symptoms of myocardial ischemia associated with ST-segment elevations, left bundle branch block, or elevation of the creatine kinase > 3 times the upper normal range. Patients receiving thrombolysis before PCI were excluded from this analysis. It was recommended to diagnose cardiogenic shock in cases with systolic blood pressure <90 mmHg or the need for catecholamines to maintain a systolic blood pressure >90 mmHg. The use of glycoprotein IIb/IIIa receptor inhibitors was evaluated only in the years 1999 until 2001, and is therefore available only in the minority of the patients and not reported here.

Statistical analysis

All data shown are observed data except for the odds ratios given in Table 4. Continuous variables were summarized as means±SD and categorical variables as percentages. Univariate analysis was performed with Chi-square tests. Multivariate analysis was done with logistic regression. Tests for trends were performed with the Cochran–Armitage test for trends. We performed a multivariate analysis with age, left main disease, three intervals between symptom onset and treatment, TIMI <3 flow after PCI, 3 vessel-disease, female gender, year of intervention (1995, 1996, 1997, 1998, 1999, 2000) and stent implantation, all parameters which were significantly related to mortality in a univariate analysis. All statistical calculations were made with the CSS STATISTICA software package by STATSOFT.

Results

Patients

Between July 1994 and April 2001 a total of 9422 patients from 80 hospitals were entered into the primary-PCI registry of the ALKK. Of these 1333 (14.2%) patients were in cardiogenic shock as diagnosed by the local investigator and had not received thrombolysis before PCI. The baseline characteristics of these 1333 patients are shown in Table 1.

Angiographic findings and outcome of PCI

Before the intervention an occluded infarct-related artery (TIMI 0/1 flow) was observed in 1160 (87.0%), a TIMI 2 flow in 120 (9.0%) and a TIMI 3 flow in 53 (4.0%) of the patients. The infarct related artery was the left main in 6.0%, the left anterior descending in 39.5%, the circumflex in 14.8%, the right coronary artery in 37.1% and a bypass graft in 2.0% of the patients. Single, double and triple vessel coronary artery disease was observed in 32.2%, 27.6% and 37.3% of the patients, respectively. The mean time from catheter insertion until achievement of the final TIMI flow was 27.6±20.1 min. The mean total fluoroscopy time was 12.0±8.8 min. The intervention resulted in a TIMI 3 flow in 76.2% and a TIMI 2 flow in 12.0% and a TIMI 3 flow in 53.4% of the patients, while 15.1% had a TIMI 0/1 flow in the infarct-vessel after PCI.

A stent was implanted in 741 (55.6%) patients. In patients with stent implantation the incidence of TIMI 3 flow post PCI was significantly higher than in patients with plain balloon angioplasty (85.2% vs 65.0%, P<0.001). Accordingly the rate of patients with a final TIMI 0/1 flow was significantly lower with stent implantation (3.2% vs 26.8%, P<0.001) (Table 2).
Mechanical support with an intra-aortic balloon pump was used in only 151 (11.4%) patients, 99 (65.6%) of these died. Urgent coronary artery bypass surgery was performed in 46 (4%) patients. Of the latter 21 (41.3%) died. A re-infarction occurred in 43 (3%) of the patients. The mean creatine kinase value increased to 1699±1809 U/l.

In-hospital mortality

The total in-hospital mortality rate was 46.1% (614/1333 patients). The impact of TIMI patency after PCI on mortality is given in Table 2, indicating the lowest mortality in patients with TIMI 3 flow. There were no significant differences in mortality in patients within the different TIMI flow grades between balloon angioplasty and stenting (Table 2). Because of the significantly higher incidence of TIMI 3 flow after stenting the total mortality was significant lower compared to balloon angioplasty (39.1% vs 54.7%, P=0.02). The influence of the infarct-related artery on mortality is given in Table 3, revealing the highest mortality in patients with left main disease. Mortality in patients with three-, double- and single-vessel disease was 58.2%, 45.1% and 32.8%, respectively. The mortality in different age groups is shown in Fig. 1 with the highest mortality in the patients >75 years. In Fig. 2 the impact of the time-interval between symptom-onset and admission is depicted, which shows an increase of mortality with the increasing time-interval.

Predictors of in-hospital mortality

We performed a multivariate analysis with all parameters which were significantly related to mortality in a univariate analysis. The odds ratios for these different parameters for the prediction of in-hospital mortality are shown in Table 4.

Temporal trends

The relative number of PCIs performed in patients with cardiogenic shock did not change significantly from 1995–2000. There was a significant decrease in mortality

| Table 1 | Baseline characteristics of 1333 patients with acute myocardial infarction complicated by cardiogenic shock and treated with primary PCI |
|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Characteristic         | n=1333                 | Mean age (years) 63.9±12.6 | Male gender 923 69.2%  | Previous percutaneous coronary intervention 128 9.6% | Previous coronary-artery bypass grafting 58 4.4% |
|                       |                        |                         |                         | Transfer patient 358 26.9% | Mean time between symptom onset and start of PCI (min) 272±267 |
|                       |                        |                         |                         | Mean creatinine kinase before PCI (U/l) 285±559 | ECG before PCI              |
|                       |                        |                         |                         |                             | ST elevation 1173 88.0%    |
|                       |                        |                         |                         |                             | ST depression 60 4.5%      |
|                       |                        |                         |                         |                             | Bundle branch block 75 5.6% |
|                       |                        |                         |                         |                             | Other 18 1.4%              |

| Table 2 | Incidence of TIMI flow grades and in-hospital mortality related to TIMI flow grade after PCI in patients treated with balloon angioplasty alone or additional stent implantationa |
|------------------------|------------------------|------------------------|------------------------|------------------------|
| TIMI flow            | Total n (%)           | Mortality n (%)        | PTCA alone n (%)       | Mortality n (%)        | Stent n (%)          | Mortality n (%)     |
|                       |                       |                       |                       |                       |                       |
| TIMI 3               | 1016 (75.2%)          | 380 (37.4%)           | 385 (65.2%)           | 160 (41.6%)           | 631 (85.2%)          | 220 (34.9%)         |
| TIMI 2               | 115 (9.3%)            | 76 (66.1%)            | 48 (7.9%)             | 35 (72.9%)            | 67 (9.2%)           | 41 (61.2%)          |
| TIMI 0/1             | 202 (15.5%)           | 158 (78.2%)           | 159 (26.9%)           | 129 (81.1%)           | 43 (5.6%)           | 29 (67.4%)          |
| Total                | 1333                  | 614 (46.1%)           | 592                   | 324 (54.7%)           | 741                  | 290 (39.1%)         |

*The differences in mortality in patients with balloon angioplasty versus stenting in the three TIMI flow groups were statistically not significant.

| Table 3 | In-hospital mortality related to the infarct-related artery |
|------------------------|------------------------|------------------------|
| Infarct-related artery | n  | Mortality |
| Left main stem         | 80 | 81.3%     |
| Coronary artery bypass graft | 27 | 59.3%     |
| Circumflex artery      | 201| 48.7%     |
| Left anterior descending | 528| 46.2%     |
| Right coronary artery  | 497| 38.6%     |
over the years (\(P\) for trend 0.02) (Fig. 3) in the univariate analysis, which was not significant in the multivariate analysis any more. The use of stents increased from to 24% to over 70%. However, the rate of final TIMI grade 3 flow did not change over time (Fig. 4).

Discussion

Cardiogenic shock remains the leading cause of death in patients admitted to a hospital with acute myocardial infarction. The results of the SHOCK trial indicate that an early invasive strategy with revascularization may improve outcome in these high risk patients.\(^9\) We report about the outcome of a large cohort of consecutive patients treated with primary PCI in 80 German community hospitals for acute myocardial infarction complicated by cardiogenic shock. Therefore this result represents the ‘real world’ experience of PCI in this high risk subgroup.

The approximate 14% rate of patients with cardiogenic shock in our registry is higher compared to reports in other acute myocardial infarction registries, this is certainly due to a selection bias, since an invasive approach is recommended by the current guidelines and not all centres performed primary PCI in all patients with acute myocardial infarction. In addition a quarter of our patients were transferred from hospitals without catheter laboratories.

Earlier retrospective reports in highly specialized centres showed very low mortality rates of around 30% with PCI in cardiogenic shock. The very encouraging results might be explained at least in part by selection bias.\(^7\) The 30-day mortality in the early invasive arm of the prospective SHOCK trial was 46.7%,\(^9\) which is comparable to our in-hospital mortality of 46.1%. Still, these mortality rates are lower compared to patients treated conservatively or with thrombolytic therapy only. Therefore an invasive strategy in patients with cardiogenic shock is recommended in the current guidelines of the European Society of Cardiology for patients with ST elevation myocardial infarction.\(^10\)

Procedural success

The mortality of our patients was strongly related to the procedural success of PCI, with an improved mortality observed only in patients with TIMI 3 flow after the intervention. Therefore the achievement of TIMI 3 flow is crucial in this situation. In our registry the rate of final TIMI 3 flow of the infarct-related coronary artery was 76%. This is certainly lower compared to the over 90% TIMI 3 flow rates reported from PCI in patients with AMI without cardiogenic shock.\(^13,14\) However, in the SHOCK trial the success rate of PCI, defined as TIMI 3 or 2 flow and a residual stenosis of <50%, in the early invasive group was 77%.\(^9\) This rate was achieved in highly specialized centres, experienced in the care of patients with cardiogenic shock. Therefore our results demonstrate that PCI in this high risk subgroup of patients is feasible and associated with an acceptable success rate in a wide range of community hospitals.

The rate of stenting increased from below 25% to over 70% over the years. However, there was no increase in the rate of TIMI 3 flow with the increased use of stents. Patients receiving a stent had a higher TIMI 3 flow rate and this was associated with a lower mortality. However, selection bias is very probable, since primary failure of the procedure by inability to cross the lesion will certainly preclude from attempting a stent. In addition, difficult anatomical features might have prohibited the use of stents in some patients treated with balloon angioplasty alone. In addition, in randomized trials stenting in patients with acute myocardial infarction did not result in higher TIMI 3 flow rates.\(^13,14\) Therefore the impact of stenting on the procedural success and clinical outcome in our patients remains uncertain.

In recent reports the adjunctive use of abciximab was associated with an improved TIMI 3 flow rate and an improved myocardial reperfusion rate in patients with PCI for cardiogenic shock.\(^15,16\) Since we do not have complete data of the use of abciximab in our registry we cannot comment on the influence of this therapy on procedural success. In the prospective REO-SHOCK study of the ALKK the TIMI 3 flow rate was 80% with PCI and abciximab.\(^17\) Considering the positive effect of this treatment in lower risk patients with unstable angina or ST-STEMI...
without shock in the CADILAC and EPISTENT trials,\textsuperscript{14,18} abciximab should be strongly considered in the high risk group with cardiogenic shock. Mechanical support with an intra-aortic balloon pump was used in only 151 (11%) patients, 99 (65.6%) of these died. This high mortality rate in patients with intra-aortic balloon pump might indicate a negative selection bias. The low use of this device reflects the current clinical practice in Germany and is different from the higher use of the intra-aortic balloon pump in United States.\textsuperscript{19}

### Predictors of in-hospital mortality

The total in-hospital mortality in our large series was 46.1%. This is higher compared to most recent reports from single centre experiences, but comparable to a report about the mortality in 200 patients.\textsuperscript{20} The highest mortality was observed in patients with occlusion of the left main stem as the infarct-related artery. Since this anatomic feature is usually not predictable from the admission ECG, these results do not impact the recommendation for an invasive approach. A similar high mortality was observed in patients with PCI failure, that means TIMI <3 flow after the intervention, which underscores the importance of TIMI 3 flow in this setting. Therefore all efforts should be undertaken to restore normal flow in the infarct related artery. The increase in the time-interval between symptom-onset and start of PCI was associated with an increase in mortality, advocating a rapid invasive strategy in shock patients.

### Elderly patients

Mortality in patients with cardiogenic shock and an age >75 years is extremely high even with the early interventional approach. In the SHOCK trial the 6-month mortality in the early invasive group was even higher compared to the conservative group (79% vs 56%). In our registry 63% of the patients older than 75 years patients died. In contrast in the SHOCK registry there was a better outcome in patients >75 years treated with early revascularization therapy.\textsuperscript{21} Therefore the decision for interventional therapy should be carefully weighted in these elderly patients. A strategy of initial medical stabilization and subsequent PCI should be considered and the decision for an early invasive strategy should be carefully weighted on the biological age and the co-morbidity of the individual patient.\textsuperscript{22}

### Temporal trends

There was a significant decrease in mortality over time. This has been reported from other registries as well. There are several possible explanations for this positive trend. First with the growing experience in primary PCI over the last years the technical skills of the operators may have increased. Secondly there was an increase in the use of stents. Although this was not associated with an increase in the rate of TIMI 3 flow, there might be a decrease in the rate of fatal re-infarctions after primarily successful PCI. Thirdly the use of abciximab increased to

### Table 4  Multivariate independent predictors of in-hospital mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% confidence limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main stem as infarct-related artery</td>
<td>8.8</td>
<td>4.4–17.6</td>
</tr>
<tr>
<td>TIMI 0/1/2 flow after PCI</td>
<td>3.4</td>
<td>2.4–4.8</td>
</tr>
<tr>
<td>Three vessel disease</td>
<td>1.8</td>
<td>1.4–2.4</td>
</tr>
<tr>
<td>Age per year</td>
<td>1.04</td>
<td>1.02–1.06</td>
</tr>
<tr>
<td>Longer interval between symptom-onset and PCI per hour</td>
<td>1.04</td>
<td>1.01–1.07</td>
</tr>
<tr>
<td>Year of PCI</td>
<td>0.96</td>
<td>0.6–1.6</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.9</td>
<td>0.5–1.5</td>
</tr>
<tr>
<td>Stent implantation</td>
<td>0.7</td>
<td>0.5–0.9</td>
</tr>
</tbody>
</table>

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**Fig. 3** Temporal trend in in-hospital mortality in patients with cardiogenic shock and the rate of cardiogenic shock in the primary PCI registry of the ALKK. There was a trend towards a decrease of mortality over the years ($P$ for trend 0.02) in the univariate analysis.

**Fig. 4** Incidence of TIMI 3 flow and use of stents between 1995 and 2000 in patients with cardiogenic shock treated with primary PCI.
over 60%. Since we have data only from the last 2 years we were not able to determine the positive impact of the use of abciximab on mortality, which was reported in recently published series.\textsuperscript{15,16}

Limitations

The diagnosis of cardiogenic shock was made by the local investigator by clinical judgement, there were no strictly pre-specified criteria for the diagnosis of cardiogenic shock. However the high mortality rate and the stable rate of shock patients over the years makes it unlikely that the results were significantly influenced by the inclusion of patients, who would not fulfil the haemodynamic criteria for cardiogenic shock. In addition there were no exclusion criteria with respect to concomitant diseases, therefore this patient population represents the real world experience of cardiogenic shock.

Conclusions

PCI in patients with acute myocardial infarction complicated by cardiogenic shock is feasible in a wide spectrum of community hospitals. Despite early PCI the mortality in these patients remains high. Therefore all efforts should be undertaken to prevent the occurrence cardiogenic shock. One strategy seems very early initiation of reperfusion therapy with pre-hospital thrombolysis, which was associated with a reduced rate of cardiogenic shock in the CAPTIM trial.\textsuperscript{23} Once cardiogenic shock has developed in a patient with an acute myocardial infarction an early invasive therapy should be applied. In our large series TIMI 3 flow could be established in over 75% of the patients and mortality in these patients was 37%.

Younger age, absence of three-vessel disease, shorter time between symptom-onset and PCI, and the achievement of TIMI 3 flow were the best predictors of an improved in-hospital mortality. Therefore all efforts should be made to bring younger patients with cardiogenic shock as early as possible in the catheter laboratory and to restore patency and normal flow of the infarct related coronary artery. The decision for interventional therapy in the elderly (\textgtr 75 years) patients should be carefully weighted on the biological age and the co-morbidity of the individual patient.

References