Improved outcome in acute coronary syndrome by establishing a chest pain unit

Till Keller · Felix Post · Stergios Tzikas · Astrid Schneider · Sven Arnolds · Oliver Scheiba · Stefan Blankenberg · Thomas Münzel · Sabine Genth-Zotz

Abstract

Aims Chest pain units (CPUs) have been established to optimize treatment of patients with acute coronary syndrome (ACS) and to early and accurately discharge patients with non-coronary chest pain. The aim of this analysis was to elucidate whether treatment of ACS patients in the CPU versus emergency department (ED) has prognostic implications.

Methods and results Patients presenting with suspected ACS to either the ED between August 2004 and June 2005 or the CPU between July 2005 and May 2006 were retrospectively analyzed. Of 1,796 included patients, 483 had the discharge diagnosis ACS. When compared to patients with exclusion of ACS they had more cardiovascular risk factors and higher troponin, creatinine and C-reactive protein levels \( (P < 0.001) \) at admission. Within 1 year, 37 patients of the ACS group suffered an event. Treatment in the ED compared with the CPU showed a significant increase in hazard ratio of 2.1 \( (P = 0.034) \) for the combined endpoint death, myocardial infarction and stroke, remaining unchanged after adjusting for confounders.

Event-free 1-year survival was higher in CPU patients for the combined endpoint \( (P_{\text{logrank}} = 0.02) \).

Conclusion These results demonstrate a better 1-year prognosis for ACS patients treated in the CPU instead of the ED, therefore, supporting the idea to establish CPUs in Europe.

Keywords Chest pain unit · Emergency department · Acute coronary syndrome · Prognosis · Emergency care

Introduction

One of the most frequent causes of admission to an emergency department (ED) is acute chest pain [4]. In the past, the outcome has been suboptimal for most patients with suspected acute coronary syndrome (ACS). Death and re-infarction within hospital stay in patients with unstable angina pectoris (UAP) and non-ST-segment elevation myocardial infarction (NSTEMI) was 8–12%, the 6-month mortality 12% [7]. Although chest pain patients having an ACS are within the primary clinical focus in the ED, many patients with chest pain have non-cardiac etiology, that is, in most cases benign [3]. Thus, the clinical dilemma posed by this situation has often been resolved by unnecessary admissions to avert a missed diagnosis of ACS, resulting in suboptimal patient care [12] and resource use [1].

To fight this problem, chest pain units (CPU) have been introduced to apply a systematic approach to optimize treatment of patients with ACS by affording [2]:

1. prompt identification and treatment of patients with an ischemic etiology;
2. early and accurate discharge of patients without evidence of myocardial ischemia.
CPUs have been enthusiastically embraced by many centers in the US, but also disdained as marketing ploys by critics.

In 2003, the first CPUs have been introduced in Germany for patients with chest pain to receive serial observations with respect to ECG monitoring and cardiac biomarker testing followed, if necessary, by an exercise testing.

In the US and UK, previous studies have demonstrated that CPUs located within or close to an ED are safe, effective and cost-saving [12, 13] in patients with high and intermediate risk of cardiovascular events. Whereas direct comparisons of the long-term prognosis of patients with ACS after discharge being treated in CPUs versus EDs are to our knowledge non-existing.

Here, we sought to compare the long-term outcome of patients with chest pain evaluated in an ED to those patients admitted to a newly implemented CPU.

Methods

Population

The service of the CPU, located next to the ED in Mainz, Germany was started in July 2005. From May 2004 to May 2006, we retrospectively collected data on patients treated in the ED or the CPU of the Johannes Gutenberg-University Mainz with suspected ACS.

The ED is run by physicians being in training for internal medicine including fellows from gastroenterology, nephrology, hematology and pulmonology. The ED provides up to three monitoring beds for all patients admitted. Patients with acute chest pain were treated by the physician on duty responsible for therapeutic decisions. If needed or in case of diagnosis of an acute coronary syndrome, the cardiologist on call was consulted.

The newly established CPU is controlled by the cardiology department offering a 24 h availability of trained nurses and physicians. It provides six monitoring beds as well as the opportunity for treadmill testing from 8 a.m. to 8 p.m. and in addition bedside echocardiography. Patients with chest pain in the CPU were treated according to strict protocols. This includes serial biomarker testing and ECGs at admission, after 3 and 6 h or during any new episode of chest pain. Those with positive biomarkers, significant ECG changes or relevant risk factors were admitted to the catheterization laboratory. If myocardial necrosis was excluded by negative biomarkers and no evidence for ischemia in the ECG, a treadmill test was performed.

The collected patient data include all available information, such as patient charts, discharge summary, diagnostic reports and laboratory results from serial biomarker testing. The follow-up of all patients was achieved by telephone or a standardized letter between May 2007 and November 2007. In addition, available outpatient information was used. The local civil registry office provided information about death of a patient. Our outcome measures were major cardiovascular event rate, defined as a composite of all cause mortality, myocardial infarction and stroke within 1 year.

Discharge diagnosis

The final diagnosis at discharge was made by an expert committee of two cardiologists using all available data. The patients were characterized as having an ACS including unstable angina pectoris (UAP), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) or non-coronary chest pain (NCCP).

Acute myocardial infarction was diagnosed according to the current universal definition of myocardial infarction with STEMI based on the ECG. The diagnosis of NSTEMI was made if no ST elevation was present, the routine laboratory results, however, showed a typical kinetic with rise or fall in cardiac enzymes, such as cardiac troponin T and creatine kinase. UAP was diagnosed if serial biomarker levels were negative, but ischemia was present in treadmill test or hemodynamically relevant stenosis revealed in coronary angiography.

Statistical analysis

Between-group analysis was done in binary variables by Fisher’s exact test, in continuous variables if normally distributed by Student’s $t$ test, and otherwise by Mann-Whitney $U$ test. Hazard ratios (HR) were calculated by Cox regression analysis. Survival analyses were made by Kaplan–Meier survival curves. For the primary hypothesis of association of treatment in the chest pain unit on the event-free survival within 1 year, the significance level was set at 5%. An influence was seen to be statistically significant if $P < 0.05$. Further analyses were regarded as explorative, and the $P$ values of the corresponding tests are presented for descriptive reasons. Statistic analysis was performed using the software package SPSS V13.0 and R 2.8.0

Results

Baseline characteristics

A total of 1,827 patients was screened, in 1796 patients sufficient information on diagnosis was available and they
were included in the analysis, in 73% of these patients an ACS could be excluded.

Table 1 shows the baseline characteristics of the overall study population on admission to the CPU or the ED with an ACS \(n = 483\) as compared to patients with exclusion of an ACS \(n = 1,313\).

Patients with an ACS were older and more often male. They had more cardiovascular risk factors, including diabetes mellitus, hypertension and dyslipidemia. These patients also had more often a history of coronary artery disease and their troponin T levels on admission were higher. The biomarkers C-reactive protein, as well as baseline creatinine level were higher in ACS patients.

Patients discharged with an ACS treated in the CPU had a final diagnosis of unstable angina in 13%, of NSTEMI in 11% and of STEMI in 6%. In contrast, in the ED the diagnosis of an ACS was made less frequently with 6% STEMI, 8% NSTEMI and 3% UAP.

**Prediction of outcome**

Follow-up information was available for 1,704 (94.9%) patients; follow-up time was 542 ± 360 days (CPU 372 ± 244 days; ED 971 ± 219 days). We defined an event as composite of first occurrence of myocardial infarction, stroke or death of any cause within 1 year after initial hospitalization. We could not observe a significant effect regarding hazard ratio for this composite as well as death within 1 year in a multivariate model in the unselected overall population comparing treatment in the CPU versus the ED (data not shown). Therefore, we looked in depth into patients at risk with the initial diagnosis of ACS. In this clinically relevant group, 26 patients died, 17 patients suffered a myocardial infarction and 6 a stroke. In total, using the first occurrence of one of the three endpoints 37 patients (7.9%) experienced an event, whereas 432 patients had no event (Table 2). Interestingly, there were no significant differences between these two groups with respect to the presence of diabetes mellitus, hypertension, dyslipidemia, body mass index and known coronary artery disease. As expected, patients suffering an event were older \((P = 0.001)\) and had more often the diagnosis of NSTEMI without reaching statistically significance. Higher levels of biomarkers reflecting myocardial necrosis (troponin T, \(P \leq 0.001\)), evidence for inflammation (C-reactive protein, \(P < 0.001\)) and impaired renal function (creatinine, \(P < 0.001\)) were observed in the group suffering an event. Patients with 1-year event-free

| Table 1 Baseline characteristics of the population according to diagnosis |
|---------------------------------|-----------------|-----------------|------|
| Age (years)                     | non-ACS \(n = 1,313\) | ACS \(n = 483\) | \(P\) value |
| Male gender (%)                 | 60.0 ± 16.3     | 65.8 ± 11.5     | <0.001 |
| Classical risk factors          |                 |                 |      |
| Hypertension (%)                | 59.7            | 73.9            | <0.001 |
| Diabetes mellitus (%)           | 61.9            | 79.5            | <0.001 |
| Smoking (%)                     | 15.9            | 24.1            | <0.001 |
| Dyslipidemia (%)                | 41.2            | 45.0            | >0.05  |
| Body mass index (kg/m²)         | 27.6 ± 5.2      | 27.9 ± 4.8      | >0.05  |
| Known CAD (%)                   | 23.1            | 41.4            | <0.001 |
| Laboratory parameters at admission |               |                 |      |
| Troponin T (ng/mL)              | 0.01 (0.01–0.01)| 0.01 (0.01–0.17)| <0.001 |
| C-reactive protein (mg/dL)      | 2.2 (1–5.8)     | 3.50 (1.5–10)   | <0.001 |
| Creatinine (mg/dL)              | 0.94 (0.81–1.09)| 1.00 (0.85–1.18)| <0.001 |
| Diagnosis and treatment         |                 |                 |      |
| Admission to CPU (%)            | 66.9            | 81.2            | <0.001 |
| NSTEMI (%)                      | –               | 39.3            | –     |
| STEMI (%)                       | –               | 23.0            | –     |

Baseline characteristics by diagnosis of ACS or exclusion of ACS for all patients admitted either to the chest pain unit (CPU) or the emergency department (ED)

Data presented as percentage of patients with comparison between groups by Fisher’s exact test, mean ± standard deviation for even variables with comparison by Student’s \(t\) test, or median and 25th/75th interquartile range for skewed variables with comparison by Mann–Whitney \(U\) test

Admission to CPU denotes percentage of patients admitted to the chest pain unit versus emergency department of the group ‘ACS’ or ‘non-ACS’, respectively

NSTEMI percentage of patients with diagnosis non-ST-segment elevation myocardial infarction in the ACS group. STEMI accordingly denotes percentage of patients with diagnosis ST-segment elevation myocardial infarction, CAD denotes coronary artery disease
survival had been treated more frequently in the CPU \((P = 0.014)\).

The HRs for the composite endpoint death, myocardial infarction and stroke within 1 year after the initial hospitalization due to ACS are given in Table 3. Regarding the HR for treatment of ACS patients in a CPU as compared to an ED we used two models, one adjusted only for age and gender, the second additionally adjusted for hypertension, obesity, diabetes mellitus, and dyslipidemia. In the first model, we observed a HR of 2.1 \((P = 0.034)\) for treatment in the ED. For comparison, a troponin T above the cut off of the 10% coefficient of variation at admission had a HR of 3.8 \((P = 0.002)\) and C-reactive protein above the median at admission had a HR of 3.9 \((P = 0.001)\). In the second fully adjusted model, treatment in the ED still showed a significantly increased HR of 2.3 \((P = 0.018)\) as well as troponin T (HR 3.9; \(P = 0.003\)) and C-reactive protein (HR 4.4; \(P = 0.001\)) did. Owing to small number of events and limited availability of information on possible confounders, the second model was based on 5% less patients than the first model, which might explain the slight increase in HR after adjustment of all evaluated variables.

### Survival analysis

The Kaplan–Meier survival analysis could not detect a significant difference in 1-year mortality for ACS patients comparing treatment in the ED and the CPU (data not shown). In contrast, with a combined endpoint of death, myocardial infarction and stroke the event-free survival after 1 year was significantly higher \((P_{\text{logrank}} = 0.02)\) in patients treated in the chest pain unit as compared to the ED (Fig. 1).

### Discussion

Chest pain is one of the most common symptoms in ED comprising about 5–20% ED visits, yet only 10–15% of patients with chest pain indeed have an ACS [16]. To manage these patients, traditionally seen in the coronary care unit, CPUs have been introduced. The aim of CPUs is to reduce pre-hospital delay of chest pain patients, to reduce in-hospital delay in identifying and treating patients with an ACS, to prevent inappropriate discharge of ACS.
patients, to reduce unnecessary hospitalization for non-ACS patients and to reduce costs in the assessment of chest pain patients [2]. So far, the impact of introducing a CPU on the long-term outcome of patients with an ACS is not well characterized.

The CPU in Mainz was established in 2005 as the second CPU located at a university hospital in Germany. In 2008, Mainz was one of the first four German CPUs getting certified by the German Society of Cardiology. This CPU provides emergency services for the 200,000 inhabitants of the city of Mainz including 24-h PTCA availability for around 500,000 residents of the region of Rhenish Hesse.

In the year 2006, the ED of the university hospital Mainz treated nearly 9,000 patients, of which 1,631 were transferred to the nearby-located CPU.

To address whether treatment of patients with chest pain evaluated in the CPU as compared to patients seen in the ED may improve outcome, we retrospectively analyzed a total of 1,796 patients.

When comparing the amount of patients with chest pain admitted to the ED or to the CPU, after implementation in 2005, the CPU shows a higher rate of patients with the discharge diagnosis ACS of 30 versus 17% in the ED.

A certain preselection of patients presenting with chest pain to a highly specialized CPU may account for this high percentage. The observed difference may also reflect more frequently performed ergometry, resulting in a higher discharge diagnosis of ACS due to a higher rate of UAP.

In 1,313 patients of the 1,796 evaluated patients an ACS could be excluded, while 483 patients had the discharge diagnosis ACS. Concerning cardiovascular risk factors we found that, as expected, patients with the discharge diagnosis ACS had more often hypertension, diabetes mellitus, dyslipidemia and known CAD, although the incidence of risk factors in the group of patients with NCCP was also quite high.

With respect to laboratory values on admission, patients with an ACS had higher troponin T, C-reactive protein and creatinine levels. In addition, the hazard ratio for C-reactive protein and troponin T each in an adjusted model to suffer one of the endpoints, such as stroke, AMI and death within 1 year was significantly increased. These findings are in line with previous observations where increased levels of troponin [14], markers of inflammation [17] as well as kidney function [11] have been shown to have prognostic impact in patients with a chest pain suggestive of an ACS.

CPU treatment of patients with chest pain improves long-term outcome

The present analysis demonstrates that treatment of ACS patients in a CPU correlates with better outcome as compared to treatment of these patients in an ED, whereas we could not show such an effect in the overall population of patients admitted with acute chest pain.

The treatment of ACS patients in an ED was identified as a predictor for future events, such as death, stroke and myocardial infarction, which remained significant after adjusting for classical covariates (Table 3).

Kaplan–Meier survival analysis revealed that, with respect to the chosen combined endpoint, patients getting CPU diagnostics and treatment had a significantly better prognosis within a follow-up period of 1 year as compared to patients where an ACS was diagnosed and treated in the

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<th>Model 2</th>
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<td>HR (95% CI)</td>
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<td>P value</td>
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<tr>
<td>ED</td>
<td>2.1 (1.1–4.1)</td>
<td>2.3 (1.16–4.7)</td>
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<td>Troponin T</td>
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<td>C-reactive protein</td>
<td>3.9 (1.7–9.1)</td>
<td>4.4 (1.8–10.9)</td>
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Model 1: adjusted for age and gender
Model 2: adjusted for age, gender, hypertension, obesity, diabetes mellitus, and dyslipidemia

Due to available data, Model 1 includes n=469 patients, Model 2 includes n=448 patients

ED treatment in the emergency department compared with treatment in the chest pain unit, Troponin T: troponin T at admission above 10% coefficient of variation (0.03 ng/mL). C-reactive protein: C-reactive protein at admission above median of 3.5 mg/dL. HR: hazard ratio, CI: confidence interval

Fig. 1 Survival analysis. Kaplan–Meier survival curves in patients with acute coronary syndrome for the composite endpoint of death, myocardial infarction and stroke within 1 year. CPU: patients treated in the chest pain unit, ED: patients treated in the emergency department.
ED. This beneficial effect on prognosis cannot be attributed to a reduction in death, because this endpoint did not differ between the ED and CPU group.

Explanation for improvement of prognosis in patients with ACS being diagnosed and treated in the CPU as compared to the ED?

The CPU analyzed in this study is situated adjacent to the general ED. The staff of the CPU, both physicians and nurses, has been specifically trained to treat patients with suspected ACS. Hence, integrated patient care upon arrival in this specialized emergency facility allows rapid and efficient patient evaluation, early ACS identification, high-quality care and cost-effectiveness.

One of the key issues explaining the observed improvement of patient outcome may be the use of systematic algorithms and specific management protocols in the CPU as indicated in Fig. 2, whereas evaluation and treatment of chest pain patients in the compared ED was the responsibility of the physician on duty. In our CPU, patients with an ST elevation myocardial infarction directly go to the catheterization laboratory, a fact that has been shown to substantially reduce the coronary reperfusion time and improve patient outcome [5]. Patients with ECG changes and risk factors such as elevated biomarkers are getting transferred to the catheterization laboratory within 72 h, as do patients with no risk factors, but being troponin positive within 3–6 h after admission. Patients with no troponin change and no evidence for ischemia are getting an exercise test. In case exercise testing is positive, patients are admitted to the catheterization laboratory, in case it is negative, patients are discharged. These strict protocols guarantee a precise identification of patients at risk and a fast initiation of an adequate therapy.

Development of CPUs in Germany

In 2005, a task force was founded by the German Society of Cardiology to define criteria for the certification of a CPU [9]. So far, 42 CPUs are certified; Mainz was the second CPU to be certified. The common basis is a protocol-driven patient evaluation by an accelerated diagnostic strategy, including clinical observations, sequential ECGs and serial cardiac biomarkers.

The next step is the introduction of a structured register including all CPUs in Germany, which has been established recently.

In a recent article, Miro et al. raised the question whether European EDs are unenthusiastic about CPUs [15]. Indeed, Cross et al. recently described that the development of CPUs in the UK has been limited and mostly restricted to the research setting [10]. They also mentioned that the development of CPUs in the UK is progressing in a disorganized way [10]. In Spain, where EDs are chronically overcrowded, the Spanish Society of Cardiology recommended 2002 that CPUs should be set up in all EDs to provide fast and efficient care for patients with chest pain [6]. Since then, only four centers have followed this advice. Interestingly, in one setting, the cardiology department is running the CPU [18], while elsewhere ED is running the CPU [8]. Thus, the poor development of CPUs in Europe greatly contrasts with their expansion in the US where more than 1,500 CPUs are currently available.

To build up CPUs in an organized way and to avoid the disdain of CPUs as marketing ploys, a certification process has been established in Germany. The results of the present evaluation will further encourage the establishment of CPUs for the entire country. To completely cover Germany, about 300 CPUs are needed.

Limitations

Our analysis involved a single center with a retrospective approach, which may limit its generalizability. The number of observed events was rather small. Subgroup analysis according to diagnosis UAP, NSTEMI and STEMI were statistically underpowered and, therefore, evaluation of interesting subgroups was not feasible. We also did not discriminate cardiac and non-cardiac deaths.

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**Fig. 2** Flow sheet for evaluation and treatment of patients presenting with suspected acute coronary syndrome to the chest pain unit. ECG electrocardiogram, AP angina pectoris
Conclusion

Implementing a chest pain unit improves long-term outcome in patients with an acute coronary syndrome. Therefore, the concept of certified CPUs should be widely adopted to optimize patient care.

Acknowledgments We are indebted to Monia Passalacqua for help with data acquisition.

Conflict of interest statement None.

References