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Pre- and early in-hospital procedures in patients with acute coronary syndromes: first results of the "German chest pain unit registry"

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Abstract

Background In an attempt to improve the treatment of patients with acute coronary syndromes (ACS), a network of certified chest pain units (CPUs) has been recently established in Germany.

Methods Data from patients admitted between December 2008 and September 2011 for ACS in 40 certified CPUs participating in the registry were prospectively collected.

Results A total of 5,457 patients was admitted for ACS; 798 patients (14.6 %) were diagnosed with an ST-elevation myocardial infarction (STEMI), 2,244 (41.1 %) with a non-ST-elevation myocardial infarction (NSTEMI), and 2,415 (44.3 %) with unstable angina. The mean time to first medical contact was 2:08 h for STEMI patients. A pre-hospital ECG was available in 23.8 % of all ACS patients. Importantly, evidence of ST-segment elevation was present in 79.7 % of the STEMI patients already in this pre-hospital ECG. As many as 76.6 % of the patients, independently of their symptoms and final diagnosis, received an ECG within 10 min of reaching the CPU. 98.2 % of STEMI patients underwent invasive diagnostics, with an in-hospital delay as little as 31 (11–75) min.

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Conclusion The establishment of a nation-wide network of certified CPUs optimizes the medical treatment of patients with ACS while providing an ideal infrastructure to evaluate and improve, both on a nation-wide and a single center scale, the adherence to guidelines. The median delay between symptom onset and first medical contact remains high. Although performed relatively rarely, a pre-hospital ECG facilitates earlier diagnosis of a STEMI in a large majority of patients. The introduction of CPUs minimizes in-hospital delays and exploits the benefit of invasive diagnostics and treatment.

Introduction

Acute chest pain is one the most frequent complaints of patients contacting emergency services [1]. Although the differential diagnosis of chest pain may be complex, timeliness and accuracy are of paramount importance in this setting; in ST-segment elevation myocardial infarction (STEMI) patients, it has been consistently demonstrated that early reperfusion is an important determinant of patient outcome, and current guidelines emphasize the need "to make every effort to minimize all time delays, especially within the first 2 h after onset of symptoms, by the implementation of a system of care network" [2]. Conversely, inappropriate discharge of patients with acute coronary syndromes (ACS) is associated with increased mortality and morbidity [3, 4].

Despite significant improvements in diagnostic and therapeutic strategies, the outcome of patients with suspected ACS remains suboptimal. Registry studies of patients with presumed myocardial infarction or ACS report 1-month overall mortality rates as high as 50 %, and about one half of these deaths occur within the first 2 h [5]. For patients admitted to traditional emergency departments, the incidence of death and recurrent myocardial infarction within the hospital stay following a diagnosis of non-ST-elevation myocardial infarction (NSTEMI) has been reported to be in the range of 10 %, and the 1-year mortality is comprised between 15 and 25 % despite the implementation of guidelines and the systematic use of invasive strategies [6, 7]. Importantly, technological and pharmacological developments have lead to a significant decrease in in-hospital mortality, whereas pre-hospital mortality has changed little over the last years [8].

In order to address this problem, the concept of a unit dedicated to the diagnosis and treatment of acute chest pain has been introduced in countries such as the United States and United Kingdom. The mission of these specialized emergency units is to allow a more systematic approach to differential diagnosis of chest pain, thus optimizing the treatment of patients with ACS [9]. Chest pain units (CPUs) have been rapidly introduced in many centers in the US and the UK, although some argue that this process has occurred at times "in a disorganized way" [10]. Several studies comparing the outcome of patients treated in a traditional emergency ward versus settings where a CPU was available revealed that the existence of a CPU is associated with a more effective diagnosis and a improved clinical outcomes [9, 11]. In particular, the establishment of CPUs in the US reduced the percentage of patients who were discharged before receiving appropriate treatment and was also cost saving, mostly due to the prevention of complications and unnecessary admissions in this subset of patients [12].

Based on these findings, the German Cardiac Society implemented a certification process aimed at maintaining elevated and uniform standards of care in the rapidly enlarging CPU network. Between September 2008 and October 2011, a total of 132 CPUs were certified [13, 14]. Beyond improved patient care, this network provides a platform for the collection of real-world data on the diagnosis and treatment of ACS in Germany.

Materials and methods

The German CPU network

The German CPU network consists of CPUs across the country which meet or exceed quality-of-care measures defined by the German Cardiac Society [14]. Certification is awarded to those CPUs which fulfill a set of minimum requirements and successfully complete the certification process by an expert committee of the German Society of Cardiology. Within this framework, CPUs plan and organize the delivery of care in a systematic manner. The introduction of additional "best practice" recommendations (for instance, the introduction of 17-lead ECG) furthers development and innovation while guaranteeing a minimum standard throughout the network. More details on the nature of the CPU network and on the procedures followed are described in [15].

Definitions

Consecutive patients admitted for chest pain to one of the CPUs throughout Germany were prospectively enrolled. The criteria for German CPUs include a minimum requirement of biomarkers assays at admission and 6–9 h thereafter; an additional ECG + biomarker assessment 3 h

after admission is considered an additional recommendation. ACS were classified as STEMI, NSTEMI, or unstable angina (UA). STEMI was diagnosed if the electrocardiogram at admission or by the emergency physician showed an ST-elevation above 0.1 mV in at least two contiguous leads or (previously unknown) left bundle branch block and typical clinic. The diagnosis of NSTEMI was made in the absence of ST elevations when at least one cTn assay exceeded the 99th percentile with a rise and or fall on subsequent samples. UA was diagnosed in the absence of a cTn elevation in a patient with suspected ACS due to clinical presentation (rest angina, severe angina, new onset or crescendo angina) with ECG evidence of myocardial ischemia (ST-segment depression >1 mm in ≥2 ECG leads without elevated troponin or CK-MB) at rest, abnormal exercise testing or in the presence of a significant coronary stenosis on coronary angiography.

Statistical analysis

The median, with lower and upper quartiles (in brackets), is used as measures of location and dispersion for metrical variables. Categorical variables are described by absolute frequencies and percentages (Tables 1, 2).

Statistical tests were performed in addition to descriptive comparisons between three subgroups of patients with the diagnosis STEMI, NSTEMI, or UA. The classical (Pearson's) Chi-square test for dichotomous variables and a Kruskal–Wallis rank test for metrically scaled variables were used. Differences were considered significant if the test for one variable rejected the null hypothesis (of no difference between the three subgroup distributions) on a significance level of 0.05. This level applies to each hypothesis (i.e., variable) individually, without adjustment for multiple testing. Resulting empirical significance levels (P values) are added to the descriptive statistics (Tables 1, 2).

All statistical computations were done using SAS®, version 9.2 (SAS Institute Inc., Cary, NC, USA.).

Results

Baseline characteristics

A total of 5,457 patients were admitted to one of the CPUs from December 2008 to September 2011 with a diagnosis of ACS. Table 1 shows the baseline characteristics of these patients. 1,832 (33.6 %) were females, median age was 68.7 (57.4–76.4) years and median body mass index was 27.2 (24.7–30.2) kg/m^2.

798 patients (14.6 %) received a final diagnosis of STEMI, 2,244 (41.1 %) were diagnosed with NSTEMI, and 2,415 (44.3 %) with UA. The prevalence of diabetes mellitus, chronic kidney failure, hyperlipidemia, arterial hypertension, and of a positive family history for coronary artery disease was significantly higher in NSTEMI and UA patients than for STEMI patients ($P < 0.0001$ for the comparison across groups; Table 1), while active smoking was significantly more prevalent in patients presenting with a STEMI ($P < 0.0001$; Table 1). Similarly, patients with NSTEMI and UA were older, more frequently female, and had a higher prevalence of prior myocardial infarction (all $P < 0.0001$), stroke or peripheral arterial disease (both $P < 0.05$). This difference in the previous cardiovascular history was also reflected in a larger prior use of aspirin in NSTEMI and UA patients ($P < 0.0001$) although only 20 % were taking aspirin versus ~60 % with history of cardiovascular disease.

Clinical presentation

Chest pain was the most frequent symptom (92.2 % of all patients), followed by dyspnea (26.3 %). Chest pain was the predominant clinical manifestation in STEMI patients (95.5 %), and it was slightly less frequent in NSTEMI and UA patients (respectively, 87.8 and 95.1 %, $P < 0.0001$). In contrast, dyspnea was more frequent in NSTEMI and UA patients (27.7 and 26.5 %) than in STEMI patients (22.0 %, $P < 0.01$). The first medical contact was the family physician in as many as 17.4 % of the patients with STEMI, and even more frequently in NSTEMI (21.2 %) and UA patients (22.5 %, $P < 0.01$). 14.1, 19.2 and 31.1 %, respectively, of the patients reached the CPU on their own ($P < 0.01$) and only 55.2, 37.6 and 42.6 % ($P < 0.0001$) of the patients called the emergency services.

Pre-hospital and in-hospital diagnosis (Table 2)

Given the importance of early diagnosis and treatment, a pre-hospital ECG is recommended by STEMI guidelines [2]. A pre-hospital ECG (whether performed by a family physician or emergency staff) was available in 23.8 % of the overall ACS population, and in 42.9 % of STEMI patients. Confirming the (unexploited) importance of pre-hospital ECG in shortening the time delay to diagnosis and treatment, as many as 79.7 % STEMI patients showed ST-elevation in this ECG and an additional 3.1 % showed a left bundle branch pattern, while only 10.9 % showed ST-depression or T-wave inversion. Thus, ECG was diagnostic for ischemia from the very early phase in the large majority of STEMI patients. In contrast, ECGs (both pre- and in-hospital) were not diagnostic for ischemia in a large percentage of patients with NSTEMI and UA (65.0 and 77.7 %, respectively).

Upon reaching the CPU, the median time to first ECG was 5 (3–10) min, and 76.6 % of the ECGs were performed

Table 1 Baseline characteristics of the patients with diagnosis of ACS

Demographic data	STEMI (798, 14.6 %)	NSTEMI (2,244, 41.1 %)	UA (2,415, 44.3 %)	P value
Age (years)	64 (54–75)	70 (59–78)	68 (57–76)	<0.0001
Female gender	220 (27.6 %)	726 (32.4 %)	886 (36.7 %)	<0.0001
BMI	26.7 (24.3–30.1)	27.3 (24.7–30.4)	27.2 (24.8–30.1)	0.06
Previous medical history				
History of cardiovascular disease	37.2 %	58.3 %	66.6 %	<0.0001
Previous MI	13.2 %	24.6 %	25.9 %	<0.0001
Previous PCI	17.2 %	26.3 %	40.9 %	<0.0001
Previous ACB	5.6 %	14.0 %	14.6 %	<0.0001
Previous stroke	2.9 %	5.2 %	4.4 %	<0.05
PAD	5.3 %	7.5 %	5.4 %	<0.010
Heart failure	3.8 %	9.3 %	6.6 %	<0.0001
Diabetes	22.0 %	29.6 %	23.3 %	<0.0001
Chronic kidney failure	6.6 %	12.7 %	7.1 %	<0.0001
Smoking	42.3 %	33.3 %	30.8 %	<0.0001
Hyperlipidemia	43.9 %	49.9 %	53.9 %	<0.0001
Arterial hypertension	66.1 %	80.1 %	79.7 %	<0.0001
Positive family history	21.4 %	21.9 %	26.9 %	<0.0001
Previous use of aspirin	9.4 %	18.1 %	21.3 %	<0.0001
Clinical presentation				
Angina	95.5 %	87.8 %	95.1 %	<0.0001
Dyspnea	22.0 %	27.7 %	26.5 %	<0.01

P values for the comparison across groups

ACB aorto-coronary by-pass surgery, BMI body mass index, MI myocardial infarction, PAD peripheral artery disease, PCI percutaneous coronary intervention

Table 2 Pre-hospital and in-hospital diagnosis by ECG

	STEMI (798, 14.6 %)	NSTEMI (2,244, 41.1 %)	UA (2,415, 44.3 %)	P value
Pre-hospital ECG				
ECG available	42.9 %	22.2 %	18.1 %	<0.0001
ST-elevation	79.7 %	2.3 %	1.0 %	<0.0001
ST-depression or T-wave inversion	10.9 %	27.8 %	17.8 %	<0.0001
Not diagnostic for ischemia	9.9 %	65.0 %	77.7 %	<0.0001
Time from admission to first ECG	0:05 (0:02–0:14)	0:05 (0:03–0:10)	0:05 (0:03–0:10)	0.15
Available in less than 10 min	71.3 %	75.2 %	79.4 %	<0.0001
ST-elevation	77.8 %	2.8 %	2.3 %	<0.0001
ST-depression or T inversion	19.8 %	43.7 %	25.1 %	<0.0001
Not diagnostic for ischemia	6.0 %	51.9 %	67.2 %	<0.0001

and read within 10 min of admission. A cardiac ultrasound was available in 78.8 %, and as many as 84.5 % (98.2 % of those with STEMI) underwent cardiac catheterization.

Troponin (T, I or high-sensitive troponin T) were assayed in 4,759 patients (87.2 %). Blood was collected in 642 STEMI patients (80.5 %). Importantly, this value was negative in as many as 38.5 % of the cases.

Pre-hospital and in-hospital time delays in STEMI patients

The time to first medical contact after symptom onset was 128 (48–720) min in STEMI patients. Only 8.9 % of these patients contacted a physician within 60 min of symptom onset.

The median time between medical contact and admission to the hospital was 58 (35–118) min, and the median time between admission to the hospital and invasive diagnosis (door to needle) was 31 (11–75) min, i.e., a total "first medical contact to needle" time of 95 (60–195) min. As many as 47.8 and 61.7 %, respectively, of the patients reached a catheterization laboratory within 90 and 120 min, respectively, of symptom onset. Overall, the median time interval between symptom onset and arrival in the catheterization laboratory was 322 (149–1,338) min. STEMI were classified as "emergency" (immediate access to catheterization laboratory) in 93 % of the cases, and as "urgent" (catheterization on the next working day) in a remaining 5.7 %.

Therapy of STEMI patients

The large majority of patients received aspirin (91.4 %), heparin (82.5 % unfractionated heparin, 13.7 % low-molecular weight) and clopidogrel or prasugrel, with a larger use of these drugs in STEMI than in NSTEMI and UA patients. Since the data were collected prior to the publication of the most recent NSTEMI-ACS guidelines, clopidogrel was more frequently used than prasugrel, and ticagrelor was not yet available. The use of GpIIb/IIIa inhibitors in the CPU was relatively less common (26.7 %). Fibrinolytic therapy was administered to only 2.5 % of all STEMI patients. PCI was performed in 90 % of the patients with STEMI, 60 % of those with NSTEMI, and 33 % of those with unstable angina (Fig. 1).

Discussion

While only 10–15 % of the patients presenting to the hospital with chest pain have an ACS [3], a rapid and accurate differential diagnosis in this setting has a profound impact on their prognosis. Data from single center
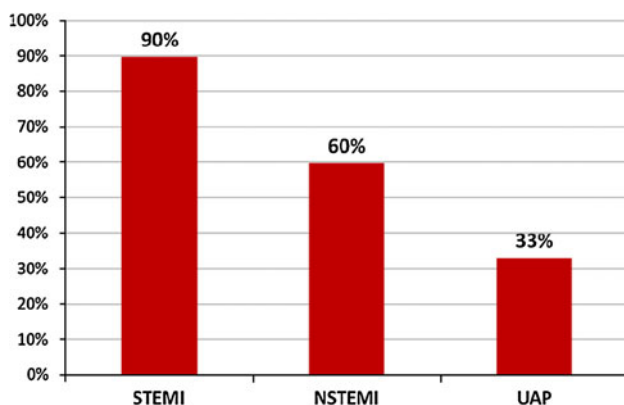
Fig. 1 Access to the catheterization laboratory based on the diagnosis performed in the CPU

experiences demonstrate that the establishment of CPUs specifically dedicated to this subset of patients is associated with improved health care [11, 16]. However, it remains less well explored how this strategy performs on a nation-wide scale. In order to provide a structured approach to this problem, the German Society of Cardiology developed in 2008 a standardized certification system for CPUs [13, 14]. Specific aims of this CPU network are to reduce pre- and in-hospital delays, limit inappropriate discharge of ACS patients and avoid unnecessary hospitalizations for non-ACS patients while reducing unnecessary costs [17]. Within the framework of this initiative, a "nation-wide German CPU Registry" was established.

The first results of the CPU registry

Clinical presentation, diagnostic and therapeutic procedures

In contrast with earlier publications reporting a larger proportion of ST-elevation infarctions [18–21], NSTEMI and UA were by far the most frequent diagnoses in our population. This might in part be explained by the fact that reference values for troponin levels have been progressively lowered within the last years (resulting in a higher number of patients being classified as NSTEMI). Further, many STEMI patients by-pass the CPU and are transported to the catheterization laboratory resulting in the underreporting of these patients in a CPU registry. A third explanation should, however, be considered. Patients diagnosed with NSTEMI and UA presented significantly more often with atypical symptoms (dyspnea rather than angina), and had a non-diagnostic ECG in more than two-thirds of the cases. In contrast to STEMI, repeated ECGs and systematic laboratory investigations are thus necessary for these diagnoses, and without a structured diagnostic algorithm (comprehensive of stress ECG, cardiac ultrasound, laboratory markers and, when indicated, coronary angiography), a significant proportion of NSTEMI and UA patients is systematically missed, with negative prognostic implications [22, 23]. Thus, the difference in the distributions of STEMI, NSTEMI and UA as compared to previous reports might partially reflect the diagnostic accuracy of the CPU model, in which ECG (within 10 min of admission), cardiac ultrasound and cardiac catheterization were performed in >75 % of the patients. Finally, the systematic inclusion of 17-lead ECGs might further change these relationships. 17-lead ECGs have been introduced in the CPU certification as "additional recommendations" since recently. It is possible that the systematic implementation of this method might increase the proportion of STEMIs otherwise undiagnosed.

Early availability of an ECG accelerates decision-making, limits in-hospital delays and increases the success rate

of reperfusion therapies [24–27]. Only 23.8 % of our patients received a pre-hospital ECG. These data emphasize the importance of pre-hospital diagnosis and transfer strategies and identifies a weakness in our system, and an issue to be addressed in the future. In contrast, demonstrating the efficacy of the CPU as a tool to implement guidelines, an ECG was available within 10 min of admission to the CPU in as many as 76.6 % of the patients, regardless of their final diagnosis and clinical presentation. This figure represents a significant improvement compared to "standard" emergency room treatment [28]. The advantage of early ECG recordings is evident when one considers the proportion of patients who can be diagnosed in this early stage. Notably, as many as 80 % of the patients with STEMI showed evidence of ST-elevation in the ECG recorded by ambulance staff: while being performed in less than a quarter of all ACS patients, a pre-hospital ECG allows early diagnosis in the large majority of the cases. The present data also confirm the concept that "one should not wait for the results (of cardiac blood markers) to initiate reperfusion treatment" [2]. Indeed, as many as 38.5 % of the patients with STEMI had normal troponin levels at admission. While markers of necrosis may be helpful in deciding between an early invasive or a more conservative strategy in selected cases, reliance on these biomarkers in the early diagnosis of ACS carries a substantial risk of false negative results (and causes an unnecessary time delay).

Our data also confirm the concept that the availability of a CPU allows early and effective treatment of ACS and the exploitation of invasive strategies. Overall, the median time from first medical contact to catheterization was 95 min in STEMI patients, which is in line with guidelines for optimal treatment [2] and well below the maximum acceptable percutaneous revascularization-related time delay as compared to fibrinolytic therapy [29–32]; the timeliness of first in-hospital ECG and the availability of PCI facilities thus partially compensated for the low rate of pre-hospital ECGs. Several other reasons explain the very low use of fibrinolytic therapy in the German CPU network [33, 34]. First, since the major time delay was between symptom onset and first medical contact, given the availability of 24-h PCI facilities, a more systematic use of fibrinolysis would have not shortened the time to effective reperfusion. Further, as described above, patients with STEMI generally by-pass the CPU and are directed to the catheterization laboratory. Therefore, STEMI patients included in the present registry generally received a first diagnosis while already in-hospital (e.g., no pre-hospital ECG available, false negative diagnosis by the emergency physician, new ST-elevation, self referrals to the CPU, etc.) and could therefore be directly transferred to the catheterization laboratory with no extra delay.

Similar to large registries [18, 21, 35–38], the use of aspirin and heparins was in the range of 90 %, while that of clopidogrel and IIb/IIIa inhibitors remained low [39]. The introduction of new medications and new lines of evidence regarding the importance of antiplatelet therapy will probably lead to a broader use of these drugs in the future [40].

Time delay in STEMI

The time between symptom onset and reperfusion is a central determinant of patients' prognosis in the setting of STEMI [29, 41, 42]. In the present dataset, the median time between symptom onset and admission to the CPU in STEMI patients was approximately 4 h. Notably, the largest component of this delay was the interval between symptom onset and first medical contact, data that is in line with recent reports showing a worryingly trend towards an increase, rather than decrease, in this time interval [17]. In contrast, in-hospital time delays demonstrate the efficiency of the CPU system and compare favorably with those of other studies such as the EHS-ACS-I and II registry (angiography rate of 56.3 and 70.2 % respectively, door-to-balloon time of 93 and 70 min, respectively) [18, 35].

While in-hospital protocols appear to be effective, more efforts have to be invested in reducing the time interval between symptom onset and hospital admission. Recent data from regional and supra-regional networks demonstrate that this can partially be addressed by establishing a formalized data feedback on the treatment times and patient outcome between hospitals and emergency services [43].

Conclusions

The present data provide a nationwide perspective on the current treatment of ACS in Germany. Our data reinforce the importance of structured and time-efficient strategies for the early (pre-hospital) diagnosis of STEMI and to avoid under-reporting of NSTEMI and UA. Further, they emphasize the existence of significant issues, principally a time delay between symptom onset and first medical contact. Taken together, the data on the performance of medical procedures in the CPU are encouraging and demonstrate, along with the introduction of more sensitive markers [44–46], the effectiveness of CPUs as a strategy to achieve several crucially important goals; early diagnosis of STEMI, thorough evaluation of NSTEMI and UA, facilitated access to interventional therapy, and identification of weaknesses to be addressed.

Appendix: Participants of the CPU registry

Institution	Town
Ostalb Klinikum Aalen	Aalen
St. Elisabeth Krankenhaus GmbH	Bad Kissingen
Kerckhoff-Klinik	Bad Nauheim
Herz- und Gefäßklinik GmbH	Bad Neustadt
Vivantes Klinikum Neukölln	Berlin
Charité Campus Virchow	Berlin
Charité Campus Mitte	Berlin
Vivantes Klinikum Am Urban	Berlin
Herzzentrum Brandenburg in Bernau	Bernau
Städtisches Klinikum Brandenburg GmbH	Brandenburg an der Havel
MVZ am Küchwald	Chemnitz
Klinikum Lippe- Detmold	Detmold
Universitätsklinikum Erlangen	Erlangen
Universitätsklinikum Essen	Essen
Philippusstift Essen	Essen
Elisabethkrankenhaus	Essen
Elisabethkrankenhaus	Essen
Klinikum Frankfurt-Höchst	Frankfurt am Main
Markus Krankenhaus	Frankfurt am Main
Bethanien Krankenhaus	Frankfurt am Main
Helios Kreiskrankenhaus Gotha GmbH	Gotha
Universitätsmedizin Göttingen	Göttingen
Krankenhaus Neu Bethlehem	Göttingen
Vinzenzkrankenhaus Hannover	Hannover
Ev. KH Hamm	Hamm
Universitätsklinikum Heidelberg	Heidelberg
Kliniken Heilbronn GmbH	Heilbronn
Westpfalz Klinikum	Kaiserslautern
St. Vincentius Krankenhaus	Karlsruhe
Städt. Klinikum	Karlsruhe
Asklepios Kliniken Langen-Seligenstadt	Langen
Klinikum Ludwigsburg	Ludwigsburg
Klinikum der Johannes Gutenberg Universität	Mainz
Kliniken Maria-Hilf	Mönchengladbach
Klinikum Neuperlach	Munich
Städt. Klinikum München Klinik Bogenhausen	Munich
Klinik Augustinum München	Munich
Lukaskrankenhaus	Neuss
Christliches KH	Quakenbrück
Klinikum Saarbrücken gGmbH	Saarbrücken
Herzklinik Ulm	Ulm
Katharinenhospital Unna	Unna

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