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# Guideline-adherence regarding critical time intervals in the German Chest Pain Unit registry

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#### **Abstract**

**Background:** Since 2008, the German Cardiac Society certified 256 Chest Pain Units (CPUs). Little is known about adherence to recommended performance measures in patients with suspected acute coronary syndrome (ACS) presenting to CPUs. We investigated guideline-adherence regarding critical time intervals and selected performance measures in German Chest Pain Units.

**Methods:** From 2008 to 2014, 23,804 consecutive patients with suspected ACS were prospectively enrolled in the Chest Pain Unit registry of the German Cardiac Society.

**Results:** Median time from symptom onset to first medical contact was 2 h in patients with ST-elevation myocardial infarction (STEMI) and 4 h in patients with unstable angina and non-STEMI (NSTEMI). In patients with STEMI, median time from hospital admission to percutaneous coronary intervention (PCI) was 40 min and median time from first medical contact to PCI was I h 35 min. Primary PCI was performed in 94.7% of patients with STEMI, 70.0% of patients with NSTEMI and 37.4% of patients with unstable angina. PCI was performed during the first 24 h in 79.5% of patients with NSTEMI and the first 72 h in 89.0% of patients with unstable angina. Electrocardiograms were performed in 99.5% after a median of 6 min after admission and obtained within 10 min in 71%. Interestingly, 56.1% of patients were found to have non-ACS diagnoses, underlining the importance of access to additional diagnostic modalities including echocardiography, stress testing or computed tomography. **Conclusions:** Guideline-adherence regarding critical time intervals and primary PCI rates is good in German Chest Pain Units. More than half of patients admitted with suspected ACS had non-ACS diagnoses. Improvements in pre-hospital time delays through public awareness programmes are warranted.

# **Keywords**

Acute coronary syndrome, Chest Pain Unit, guideline-adherence, time intervals

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### Introduction

The implementation of specialized Chest Pain Units (CPUs) as compared with general emergency departments (EDs) has been shown to reduce mortality, improve quality of care and reduce costs. <sup>1,2</sup> CPUs aim for a standardized, rapid and goal-oriented diagnostic work-up of patients with acute chest pain and initiation of necessary therapeutic measures with minimal delays. It has been shown in general EDs that time delays and various problems with correct diagnosis and treatment of patients with chest pain can lead to failure to hospitalize patients with acute cardiac ischaemia, which is associated with increased mortality.<sup>3</sup>

Triage systems such as the Manchester triage system prioritize patients depending on illness severity based on the main complaint using standardized questionnaires. Although most patients are correctly classified, a significant number of patients with chest pain may be classified as lower priority, leading to time delays from arrival to electrocardiogram (ECG) acquisition.<sup>4</sup>

Since 2008, 256 CPUs in Germany have received certification from the German Cardiac Society (GCS). All CPUs undergo a standardized initial certification process and subsequent regular re-certification at pre-specified intervals, ensuring adherence to standards defined by the Chest Pain Unit-Task Force of the GCS.<sup>5-7</sup> These standards include the availability of a directly accessible cardiac catheterization laboratory at all times to reduce delays in treatment of patients with acute coronary syndrome (ACS). Short time delays in patients with ST-elevation myocardial infarction (STEMI) from diagnosis to reperfusion therapy are recommended, since delays are associated with increased mortality.8,9 Patients presenting with acute myocardial infarction during off-hours have been shown to have higher mortality than patients presenting during regular hours. 10 Clearly defined critical pathways are one way of effectively improving patient care and reducing costs of care. 11,12

There are data suggesting that CPUs are associated with greater adherence to critical ACS pathways.<sup>2</sup> However, little is known about the effect which the implementation of CPUs has had regarding adherence to recommended time intervals in the real-world setting. The present study aimed to investigate these critical time intervals, analysing data from the German Chest Pain Unit Registry.

### **Methods**

From 1 December 2008 until 14 May 2014, a total of 23,804 patients in 38 CPUs were enrolled into the prospective CPU registry endorsed by the GCS. The centres were asked to include all consecutive patients admitted to one of the certified CPUs with a documented CPU diagnosis, of which no patients were excluded.

Alist of all participating centres is available (Supplementary Material online, Supplement 1). The Stiftung Institut für Herzinfarktforschung (IHF), Ludwigshafen, was responsible

for project management, maintenance of the database and central follow-up of patients. Electronic case report forms were used for documentation of all patient data. Patient data were transferred for statistical analysis as anonymized data records. Recorded data included patient symptoms, demographics, risk factors, medical history, critical time intervals (onset of symptoms-first medical contact-hospital admission-percutaneous coronary intervention (PCI)), ECG and blood tests at admission, other diagnostic measures as well as medical, interventional and surgical treatment. Intra-CPU complications were documented in all patients with diagnosis of ACS. The main diagnosis, recommended treatment and modalities were recorded at time of discharge from CPU. All patients consenting to be contacted for follow-up in their consent form were contacted three months after discharge. No formal monitoring was performed.

# Statistical analysis

The patient population is described by absolute numbers and percentages. Medians and quartiles were used as descriptive statistics for continuous variables. Differences between entities were assessed by Chi-squared test with regard to categorical variables or by Kruskal–Wallis test with regard to metrical variables. Descriptive statistics are based on available cases, the number of which is shown as denominator for binary variables. The Global Registry of Acute Coronary Events (GRACE) score for in-hospital death was calculated according to formulas from Granger et al.  $^{13}$  p-values  $\leq 0.05$  were considered significant without adjustment for multiple testing. All p-values are results of two-tailed tests. Statistical analyses were performed at the biometrics department of the IHF using SAS software release 9.3 (SAS Institute Inc., Cary, NC, USA)

# Results

# Baseline and clinical characteristics

Baseline characteristics of different subgroups of patients including STEMI, non-ST-elevation myocardial infarction (NSTEMI), unstable angina and non-ACS diagnoses are listed in Table 1. Of 23,804 included patients, the majority (56.1%) had non-ACS diagnoses. The most frequent ACS-diagnosis was NSTEMI (19.2%), followed by unstable angina (17.0%) and STEMI (7.7%). In the entire cohort, median age was 68.1 years and 29.7% of all patients were ≥ 75 years old. In 60.6% of all patients, a history of cardio-vascular disease was known. Interestingly, 63.7% of patients with non-ACS diagnoses as compared with 33.4% of patients with STEMI had a history of cardiovascular disease.

Arterial hypertension was the most common risk factor in the overall group (73.6%) and in all subgroups. Chronic renal failure was most frequently observed in patients with NSTEMI (12.1%), as compared with patients with STEMI

Table 1. Baseline characteristics.

	All	STEMI	NSTEMI	NA	Non-ACS	p-value
Number of patients Age in years, median (IOR)	23,804 (100.0%) 68.1 (55.7; 76.6)	1832 (7.7%) 63.2 (53.7; 74.2)	4561 (19.2%) 70.5 (59.2; 78.0)	4056 (17.0%) 68.2 (57.1; 75.6)	13,355 (56.1%)	<0.0001
Age $\geq$ 75 years	29.7% (7056/23,736)	23.1% (422/1826)	34.9% (1588/4547)	26.7% (1078/4035)	29.8% (3968/13,328)	<0.0001
Male gender	62.0% (14.745/23.798)	72.7% (1331/1832)	69.5% (3167/4559)	64.6% (2617/4053)	57.1% (7630/13.354)	<0.0001
History of cardiovascular disease	60.6% (14,377/23,735)	33.4% (605/1813)	57.2% (2601/4545)	66.4% (2682/4042)	63.7% (8489/13,335)	<0.0001
Prior MI	19.3% (4589/73 735)	12.4%	24.0% (1093/4545)	26.0% (1052/4042)	16.6%	<0.0001
Prior CABG	10.8% (2569/23,735)	4.5% (82/1813)	13.2% (602/4545)	14.0% (566/4042)	9.9% (1319/13,335)	<0.0001
Prior PCI	31.3% (7431/23,735)	15.7% (285/1813)	26.9% (1222/4545)	40.9% (1655/4042)	32.0% (4269/13,335)	<0.0001
Prior stroke	4.8% (1143/23,735)	2.8% (50/1813)	5.5% (251/4545)	4.6% (185/4042)	4.9% (657/13,335)	<0.0001
PAD	6.1% (1446/23,735)	4.2% (76/1813)	8.1% (369/4545)	5.5% (222/4042)	5.8% (779/13,335)	<0.0001
ICD or PM	7.7% (1837/23,735)	1.2% (22/1813)	5.2% (236/4545)	5.4% (218/4042)	10.2% (1361/13,335)	<0.0001
Risk factors						
Diabetes	22.1% (5250/23,726)	21.1% (384/1824)	28.9% (1312/4546)	24.0% (969/4044)	19.4% (2585/13,312)	<0.0001
Chronic renal failure	8.8% (2091/23,726)	5.6% (102/1824)	12.1% (550/4546)	7.4% (299/4044)	8.6% (1140/13,312)	<0.0001
Smoker	28.1% (6667/23,726)	44.9% (819/1824)	33.8% (1536/4546)	30.9% (1250/4044)	23.0% (3062/13,312)	<0.0001
Hyperlipidaemia	44.8% (10623/23,726)	47.0% (857/1824)	53.1% (2413/4546)	54.8% (2215/4044)	38.6% (5138/13,312)	<0.0001
Arterial hypertension	73.6%	67.8%	80.2%	80.2%	70.2%	<0.0001
Family history of CAD	(1/4/2/23,/29) 23.3% (5521/23,726)	(1236/1624) 21.6% (394/1824)	(3047/4340) 22.9% (1041/4546)	(3243/4044) 27.7% (1121/4044)	(7346/13,312) 22.3% (2965/13,312)	<0.0001

Percentage (%) and number of cases.
ACS: acute coronary syndrome; CABG: coronary artery disease; ICD: implantable cardioverter-defibrillator; IQR: interquartile range; MI: myocardial infarction; ACS: acute coronary syndrome; CABG: coronary artery disease; PCI: percutaneous coronary intervention; PN: pacemaker; STeMI: ST-elevation myocardial infarction; UA: unstable angina.

Table 2. Clinical characteristics.

	All	STEMI	NSTEMI	UA	Non-ACS	p-value
Symptoms at admission						
Chest pain	76.9% (18,286/23,785)	95.7% (1750/1829)	87.1% (3964/4553)	95.3% (3862/4053)	65.2% (8710/13,350)	<0.0001
Dyspnoea	27.1% (6441/23,785)	17.4% (318/1829)	28.6% (1300/4553)	24.5% (995/4053)	28.7% (3828/13,350)	<0.0001
Heart failure, Killip II+	9.7% (2310/23,720)	8.4% (153/1816)	12.7% (578/4547)	6.1% (245/4040)	10.0% (1334/13,317)	<0.0001
Heart rate, beats/min	75 (65; 87)	75 (65; 86)	75 (65; 87)	71 (63; 82)	75 (65; 89)	<0.0001
GRACE score for in-hospital mortality	118.5 (96.2; 142.8)	128.8 (107.0; 150.9)	127.0 (103.6; 151.3)	105.5 (85.4; 127.6)	-	<0.0001
GRACE score >140	27.4% (2820/10,236)	36.0% (638/1770)	35.5% (1587/4471)	14.4% (577/3995)	-	<0.0001

Median and interquartile range or percentage (%) and number of patients.

ACS: acute coronary syndrome; GRACE: Global Registry of Acute Coronary Events; NSTEMI: non-ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction; UA: unstable angina.

(5.6%), unstable angina (7.4%) or non-ACS diagnoses (8.6%).

Clinical characteristics of the entire ACS spectrum and non-ACS are listed in Table 2. In patients with STEMI and unstable angina, chest pain was a more frequently reported symptom (95.7% and 95.3%, respectively) than in patients with NSTEMI (87.1%). In patients with non-ACS diagnoses, only 65.2% of patients reported chest pain. Dyspnoea was reported in only 27.1% of all patients. Median heart rate was 75 beats/min. A GRACE risk score above 140 indicating high risk for in-hospital death was observed in less than one-third of patients (28.9%).

In 27.1% of patients, chronic aspirin therapy was documented at presentation. Patients were taking oral anticoagulation in 8.8%, with the highest percentage in patients with non-ACS (11.9%), followed by NSTEMI (5.8%), unstable angina (5.6%) and STEMI (2.5%).

### Main diagnosis and treatment strategy

The main diagnosis was ACS, in 43.9% of all patients. The most common non-ACS diagnoses were stable angina (13.8%), arrhythmia (11.5%), hypertensive crisis (11.5%) and heart failure (4.2%). A non-cardiovascular diagnosis was established in 42.7% of non-ACS patients (Supplementary Material online, Supplement 2).

Of all patients with STEMI, cardiac catheterization was performed in 95.6% and 94.7% were treated with primary PCI (Table 3). In patients with non-ACS conditions, cardiac catheterization was performed in 20.2% and 10.7% were treated with PCI. Surgical management was necessary in 2.2% of all patients, most frequently in patients with NSTEMI (5.1%). In patients with unstable angina, cardiac catheterization was performed in 40.3% with a PCI rate of 37.4%.

# Critical time intervals and other performance measures

Patients with STEMI. The shortest median time from beginning of symptoms to first medical contact was observed in patients with STEMI (2 h, interquartile range (IQR): 1; 22) (Table 4<sup>14,15</sup>). The median time interval from hospital admission to PCI ('door-to-balloon time') was 40 min (IQR: 19; 80) and door-to-balloon time was less than 120 min in 82.4% and less than 24 h in 98.1% of patients. Furthermore, the median time interval from first medical contact to PCI was 95 min (IQR: 61; 187). The majority of patients with STEMI (57.9%) arrived with emergency medical services as compared with 14.1% self-comers (Table 3). The remainder of STEMI patients were referred either from a general practitioner or from another hospital or department. In each of the participating centres, there were some STEMI patients admitted to the CPU.

Patients with non-ST-elevation ACS (NSTE-ACS). Baseline characteristics of patients with NSTE-ACS differed significantly in regard to most aspects from those in patients with STEMI. Patients with NSTE-ACS were older, presented more often with dyspnoea, had more comorbidities and more often a history of previous cardiovascular disease (Tables 1 and 2).

Critical time intervals and performance measures that were analysed include rates of performed initial ECG, time from admission to initial ECG and time from admission to receipt of the first blood sample at the laboratory for troponin measurement. All performance measures suggested adherence to guideline recommendations. <sup>14</sup> In patients with NSTE-ACS, an ECG was performed in 99.6% after a median time of 5 min (IQR: 3; 10) after admission. Receipt of the first blood sample at the laboratory within 45 min

Table 3. Way of referral, stay in CPU and treatment.

	All	STEMI	NSTEMI	Υn	Non-ACS	p-value
Way of referral Emergency medical services	42.5% (10.090/23.751)	57.9% (1057/1827)	38.8% (1762/4547)	41.3% (1666/4035)	42.0% (5605/13.342)	<0.0001
Self-referral	29.7% (7048/23.751)	(4.1%) (257/1827)	18.8% (856/4547)	30.6% (1234/4035)	35.2% (4701/13.342)	<0.0001
General practitioner	20.0% (4758/23,751)	16.3% (297/1827)	22.0% (999/4547)	23.6% (954/4035)	(8.8% (2508/13,342)	<0.0001
Laboratory						
Troponin measurement	98.1% 23,355/23,804)	94.0% (1722/1832)	98.5% (4493/4561)	98.8% (4008/4056)	98.3% (13,132/13,355)	<0.0001
High-sensitivity	%0.91	23.6%	23.5%	%9.91	11.3%	<0.0001
troponin	(940/5881)	(97/411)	(318/1351)	(183/1102)	(342/3017)	
Treatment						
PCI	35.3%	94.7%	70.0%	37.4%	10.7%	<0.0001
-	(6525/18,470)	(159//168/)	(2696/3851)	(118//31/8)	(1045/9/54)	000
Surgical	2.2% (409/18,470)	1.5% (26/1687)	5.1% (197/3851)	1.7% (54/3178)	l.4% (132/9754)	-0000 -0000 -0000
Only pharmacological	56.1%	2.9% (49/1687)	21.5% (828/3851)	58.0% (1844/3178)	78.4% (7648/9754)	<0.0001
Discharge from CPU						
Home	31.5%	15.2%	25.9%	39.8%	32.2%	<0.0001
Stay in CPU, h:min	(4007/12,733) 14:03 (1:10; 40:35)	(120/72) 37:59 (2:38; 62:58)	(377724,323) 40:34 (17:28; 61:41)	(737/2412) 22:03 (7:25; 44:11)	(533)(277) 5:52 (0:50; 20:30)	<0.0001

Median and interquartile range or percentage (%) and number of patients.
ACS: acute coronary syndrome; CPU: Chest Pain Unit; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction; UA: unstable angina.

Table 4. Critical time intervals.

	All	STEMI	NSTEMI	NA	Non-ACS	p-value
Onset of symptoms → first medical contact, h:min	4:00 (1:00; 22:00)	2:00 (0:45; 11:05)	4:00 (1:00; 23:00)	4:00 (1:03; 20:00)	4:30 (1:00; 24:30)	<0.0001
First medical contact →hospital admission, h:min	0:56 (0:36; 2:06)	0:55 (0:34; 1:55)	1:27 (0:40; 5:00)	0:57 (0:37; 2:10)	0:52 (0:35; 1:32)	<0.0001
ECG performed	99.5% (23,656/23,784)	98.0% (1792/1828)	99.5% (4529/4553)	99.7% (4039/4050)	99.6% (13,296/13,353)	<0.0001
Admission → 1st ECG, h:min	0:06 (0:03; 0:13)	0:05 (0:02; 0:16)	0:05 (0:03; 0:11)	0:05 (0:03; 0:10)	0:06 (0:03; 0:14)	<0.0001
Duration ≤10 min	71.0% (13,259/18,684)	68.3% (852/1248)	74.6% (2435/3265)	77.8% (2545/3272)	68.1% (7427/10,899)	<0.0001
GCS and ESC goal: ≤10 min		•			•	
Admission $\rightarrow$ lab time <sup>a</sup> , h:min	0:18 (0:09; 0:32)	0:18 (0:08; 0:34)	0:16 (0:06; 0:31)	0:15 (0:05; 0:29)	0:20 (0:10; 0:34)	<0.0001
Duration ≤45 min	86.4% (17,369/200,096)	81.6% (1117/1369)	86.6% (2930/3383)	88.9% (3070/3455)	86.2% (10,252/11,889)	<0.0001
DTB <sup>b</sup> , h:min	7:27 (1:12; 23:28)	0:40 (0:19; 1:20)	10:42 (3:06; 21:54)	22:54 (9:57; 44:58)	29:09 <sup>b</sup> (14:57; 65:05)	<0.0001
ESC goal for STEMI: ≤60 min	22.7% (956/4207)	67.8% (726/1071)	7.9% (160/2017)	6.6% (47/709)	5.6% (23/410)	<0.0001
DTB ≤120 min	31.5%	82.4%	17.0%	9.2%	8.0% <sup>b</sup>	<0.0001
	(1324/4207)	(883/1071)	(343/2017)	(62/208)	(33/410)	
DTB ≤24 h	76.0% (3199/4207)	98.1% (1051/1071)	79.5% (1603/2017)	53.7% (381/709)	40.0% (164/410)	<0.0001
ESC goal for high risk NSTE-ACS: <24 h						
Duration ≤72 h	94.4% (3973/4207)	99.2% (1062/1071)	97.0% (1956/2017)	89.0% (631/709)	79.0% (324/410)	<0.0001
ESC goal for low-risk NSTE-ACS: <72 h		•				
First medical contact → PCI, h:min	11:00 (2:45; 27:00)	1:35 (1:01; 3:07)	15:29 (5:55; 26:30)	25:40 (12:46; 48:58)	34:07 <sup>b</sup> (19:00; 70:15)	<0.0001
ESC goal for STEMI: ≤90 min						

Median and interquartile range or percentage (%) and number of patients.  $^{\rm a}$ Receipt of blood sample at laboratory.

<sup>b</sup>DTB refers to patients who underwent percutaneous coronary intervention.

ACS: acute coronary syndrome; DTB: door-to-balloon time (hospital admission →PCI); ECG: electrocardiogram; ESC: recommended time interval by the European Society of Cardiology for patients with NSTE-ACS¹ and STEMI;¹ऽ GCS: recommended time interval by the German Cardiac Society; NSTE-ACS: non-ST-elevation ACS; NSTEMI: non-ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction; UA: unstable angina.

after admission was accomplished in 85.7% of patients with NSTEMI and 88.8% of patients with unstable angina.

Regarding revascularization, a PCI was performed in most patients with NSTEMI (70%) and in 37.4% of patients with unstable angina. Timing of angiography in patients with NSTEMI was heterogenous (17% within 120 min, 80% within 24 h and 97% within 72 h). Only 21% of patients with NSTEMI and 58% of patients with unstable angina received only pharmacologic treatment.

# **Discussion**

The German CPU registry provides valuable information on more than 20,000 patients admitted to these certified institutions. The database provides information not only on demographic variables, on the entire spectrum of ACS and important differential diagnoses, diagnostic strategies, adjunctive treatment and outcomes but also on critical time intervals and other performance measures that may serve as quality indicators of medical care.

The main finding of this study is that guideline-adherence regarding critical time intervals and selected performance measures is very high in German CPUs. The high level of guideline-adherence in patients with STEMI, NSTEMI and unstable angina can be attributed to the successful implementation of specialized CPUs in Germany.

# Critical time intervals — guideline-adherence in patients with STEMI

Pre-hospital time delay is defined by the time period that patients determine themselves by waiting after the onset of symptoms before calling an ambulance, as well as by the time until arrival of emergency services and transportation to the hospital. In the German CPU registry, time intervals from onset of symptoms to first medical contact (2 h, IQR: 1; 22) and mean time interval from onset of symptoms until PCI (5 h 2 min, IQR: 2 h 25 min; 18 h 40 min) are quite long, mainly due to patient-borne delays. Naturally, this time interval cannot be improved by CPUs. This delay is especially crucial in patients with STEMI, where a median of 2 h passed from onset of symptoms until first medical contact. Public health initiatives of medical societies and media campaigns must aim to raise public awareness in this respect. Interestingly, the median time interval from first medical contact to PCI was 1 h 35 min in patients with STEMI, which is only slightly above the then valid ESCguideline-recommendation for primary PCI (≤90 min), which was also embraced by the GCS.15 The median doorto-balloon time was 40 min, which is excellent, since guidelines recommend a door-to-balloon time of  $\leq 60$  min. Patients who are directed to a primary PCI centre via a CPU represent a particular subset, as the recommended pathway is a direct transfer to the catheterization laboratory to avoid further time delays. Accordingly, initial management of most STEMI patients is not within the scope of CPUs, although CPUs may be involved in the alarm system and organizing process. Given that many STEMI patients were initially not admitted via a CPU, the critical time intervals may have been overestimated and do not necessarily reflect the real world setting. <sup>16</sup> Fourteen per cent of patients with STEMI were self-comers.

It has previously been reported that patients with self-referral are younger, less severely ill and more frequently present with non-coronary problems as compared with patients calling emergency medical services.<sup>17</sup>

It is interesting to note that aggressive protocols with the aim of reducing door-to-balloon-time even further may lead to a higher incidence of false-positive diagnoses of STEMI with a significantly higher in-hospital mortality of this subgroup. However, an effective and beneficial method to reduce treatment times for patients with STEMI is systematic data analysis and formalized data feedback on treatment times and outcomes using quarterly interactive feedback, as shown across several regional STEMI networks in the prospective multicentre Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction (FITT-STEMI) trial. 19

# Critical time intervals — guideline-adherence in patients with NSTE-ACS

In patients with NSTE-ACS, minimizing door-to-balloon-time is not as crucial as in patients with STEMI. In this population, recommended time intervals for interventional management strongly depend on individual risk stratification, varying from no coronary angiography in very low-risk patients to urgent coronary angiography in high-risk patients.<sup>14</sup>

When CPUs were established, one of the main goals was to implement PCI as the primary revascularization strategy in patients with ACS. Our data suggest that the current rate of primary PCI among patients with NSTE-ACS (58.4%) is higher than in the Swedish SWEDEHEART registry in the period 2005–2007 (37.4%) and comparable to the rate in the second Euro Heart Survey on ACS (63%), which included 190 medical centres in Europe and the Mediterranean basin in 2004.<sup>20,21</sup>

In patients with NSTEMI, PCI was performed during the first 24 h in 79.5%. One explanation of why not even more patients were treated with PCI in this time interval may be that in some patients with type 2 myocardial infarction with an imbalance of oxygen demand and supply due to a non-coronary cause such as prolonged tachycardia or in the setting of severe acute heart failure, treatment strategies have to be individualized.

# CPU versus pre-CPU

A comparison with the situation in Germany before the introduction of CPUs may be possible by comparison with findings from the Acute COronary Syndromes (ACOS)

registry, which was conducted by the Institut für Herzinfarktforschung between 2000 and 2002 and included 16,805 patients (Anselm Gitt, 18 February 2016, personal communication). Before implementation of CPUs, patients with suspected ACS were mainly treated in coronary care units of heart centres. However, a valid comparison can only be performed for patients with STEMI. A direct comparison of patients with NSTE-ACS is problematic since, due to the development of more sensitive troponin assays and changes in the definition of myocardial infarction, more patients are diagnosed with NSTEMI who would have previously been classified as having unstable angina. Furthermore, the ACOS registry only included patients with unstable angina who also had ischaemic ECG-changes.

A comparison between the data of this study and the ACOS registry shows that among patients with ACS, the percentage of STEMI in ACOS was much higher (49.4%) than in the present registry (17.6%). This can be attributed to the fact that the recommended STEMI-pathway leads directly to the cardiac catheterization laboratory to minimize door-to-balloon-time, reflecting that STEMI patients are not the primary scope of a CPU, as compared with patients without ST-segment elevations on pre-hospital ECG. Interestingly, in the ACOS registry, the number of primary PCI in patients with STEMI was only 41.8% as compared with 94.7% in the present registry.

### ECG recommendations

According to ESC guidelines, the time from first medical contact until an ECG is recorded and immediately presented to a qualified physician should not exceed 10 min, since potentially any patient presenting to the CPU may present with STEMI. Although an ECG was recorded in nearly all patients (99.5%), only 71% received an ECG during the first 10 min. One potential explanation is that the pre-hospital ECG may have already been diagnostic and may have triggered immediate cardiac catheterization and primary PCI, obviating the need for a subsequent ECG. This assumption may be supported by the fact that the percentage of patients in whom an ECG was recorded during the first 10 min was lower in patients with STEMI (68.3%) than in patients with NSTEMI (74.6%) and unstable angina (77.8%). However, a true guideline violation to register an ECG in all patients during the first 10 min cannot be excluded. We hypothesize that overcrowding of a CPU may be one reason for underperformance. Systematic issues including lack of a dedicated room for ECG registration when monitoring beds are occupied should be identified and corrected. A study in a general ED population showed that their average door-to-ECG time of more than 20 min could be improved significantly by optimization of patient prioritization triage processes, assignment of specific personnel for ECG obtainment, feedback by review of cases falling outside the 10-min goal and staff education regarding symptoms other than chest pain suggestive of myocardial infarction.<sup>22</sup>

# Patients with non-ACS diagnoses

More than half (56.1%) of the patients presenting to a CPU with suspected ACS were found to have non-ACS diagnoses. This underlines the importance of CPUs to have access to additional diagnostic modalities such as echocardiography and computed tomography for competent diagnostic work-up of this large subgroup of patients.

Of all patients with non-ACS diagnoses, 13.8% had a main diagnosis of stable angina and PCI was performed in 10.7% of patients with non-ACS diagnoses, suggesting that stable coronary artery disease is prevalent in this population.

### Limitations

In this observational study, no formal test hypotheses were specified a priori and no power calculations were made. Therefore, inferential statistics should be interpreted in a descriptive rather than in a confirmatory sense. Moreover, the reported time intervals may refer to different subpopulations. Furthermore, completion of all follow-up data was not possible in more than 20,000 patients due to financial limitations. All comparisons with the ACOS registry should be interpreted with caution, since different guidelines were in effect in the two time ranges (2000–2002 in ACOS, 2008–2014 in CPU registry).

A selection bias cannot be excluded do to the fact that not all certified CPU centres (208 centres in January 2015) participated in this registry and there were varying numbers of patients included in the different centres (Supplement 1 in Supplementary Material). There are efforts to render participation in this CPU registry obligatory for all certified CPUs in Germany, the implementation of which is still ongoing.

This paper refers to time interval recommendations in ESC guidelines valid at the time of the registry.<sup>14,15</sup> It is important to note that guideline updates have been published for both NSTE-ACS and STEMI after the inclusion period. Although eliminated from the 2017 STEMI guidelines, the door-to-balloon time was deliberately analysed, being an important target time interval in the guideline valid during the inclusion period of this study.<sup>23</sup>

# **Conclusion**

In summary, guideline-adherence regarding critical time intervals and primary PCI rates is good in German CPUs. The fact that more than half of patients admitted with suspected ACS had non-ACS diagnoses underlines the importance of further diagnostic modalities such as echocardiography, exercise testing and computed tomography. Initial certification

and recertification at regular intervals by the GCS are important safeguarding mechanisms to uphold the high standard of care utilizing standardized logistical, diagnostic and therapeutic algorithms. Additionally, continuous efforts to minimize pre-hospital time delays through public awareness programmes are warranted.

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#### **Conflict of interest**

MV has received financial support for clinical trials from Bayer Healthcare Germany and Daiichi Sankyo and has been reimbursed for travel expenses and fees associated with attending seminars and conferences by Bayer Vital, Daiichi Sankyo, Teva, Octapharma, Lilly Germany, GlaxoSmithKline, Roche Diagnostics, Brahms, Leo Pharma and Abbott. HAK has developed the cTnT assay and holds a patent jointly with Roche Diagnostics. He has received grants and research support from several companies, and has received honoraria for lectures from Roche Diagnostics. EG has received financial support for clinical trials from Roche Diagnostics Ltd, Switzerland, Mitsubishi Chemicals, Germany, Siemens Healthcare, BRAHMS Biomarkers, Clinical Diagnostics Division, Thermo Fisher Scientific, Germany. He is consultant to Roche Diagnostics and BRAHMS Biomarkers and has received speaker's honoraria from Roche Diagnostics, Siemens Healthcare, BRAHMS Biomarkers, and Mitsubishi Chemicals.

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