The German CPU Registry: Comparison of troponin positive to troponin negative patients

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Chest pain is a major cause of admission to an emergency department [1,2]. Erroneous discharge from the emergency department has been reported earlier [3–5]. Since 2008, more than 130 CPUs in Germany have been certified by the German Cardiac Society [6] and the German CPU Registry was implemented. The goal is the validation of the quality of care, including benchmark reports and risk-adjusted comparisons in a prospective fashion. We compared troponin positive (Trop+) with troponin negative (Trop−) patients.

The registry prospectively enrolled 11,656 patients admitted to one of the 38 participating CPUs between December 1st 2008 and August 18th 2011. Follow-up was attained from 5313 patients. The diagnostic algorithm was based on the detection of cardiac troponin above the 99th percentile of the upper reference limit with a rise and/or fall [7]. Troponin assays used in clinical routine included 4th generation cardiac troponin T (20.3%), high sensitive (hs) troponin T (14.5%), or troponin I (65.2%) without further differentiation into different manufacturers. Baseline characteristics are shown in Table 1a. Patients that initially were Trop− but developed a troponin subsequently (n = 544) were similar to the Trop+ group with 64% male patients, 34% smokers, 30% diabetes, 80% hypertension, and 48% dyslipidemia.

Both, times from begin of symptoms until hospitalization (9 h 07 min vs. 7 h 40 min) and times from first medical contact to hospitalization (1 h 08 min vs. 51 min) were significantly longer in the Trop+ than the Trop− group (p < 0.01, respectively).

In the Trop+ group significantly more patients complained about chest pain (i.e. angina pectoris) and dyspnea (Fig. 1a). Again, patients that initially were Trop− but developed a troponin subsequently were similar to the Trop+ group with 90% having angina pectoris. A pre-hospital ECG was rarely done, i.e. in only 20% of Trop+ patients but still more often than in Trop− patients (11%, p < 0.01). In these pre-hospital ECGs, we found more frequent ST-segment elevations and depressions in the Trop+ as compared to the Trop− group. Similarly, an ECG recorded within 5 min after presentation to the CPU showed ECG changes more often in the Trop+ patients (Fig. 1b).

Among all patients admitted to the CPU an acute coronary syndrome (ACS) was the most frequent diagnosis (41%), including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UAP). In 83% of patients in the Trop+ group an ACS was the primary diagnosis as compared to only 28% in the Trop− group (p < 0.01). Other diagnoses were less frequent but more often found in the Trop− group except for peri-/myocarditis (Fig. 2a).

Coronary interventions were much more frequent in the Trop+ patients (Fig. 2b). The median time interval from hospital admittance to intervention was exactly 5 h for Trop+ patients as compared to 22 h 29 min for Trop− patients (p < 0.01). Also, the stay in the CPU was much longer in Trop+ patients than in Trop− patients (31 h 16 min vs. 7 h 26 min, p < 0.01). More patients were dismissed directly home from the CPU in the Trop− group (34.7% vs. 22.0% Trop+, p < 0.01). Of note, patients that initially were Trop− but developed troponin subsequently were similar to the Trop+ group with 84% having an angiogram and 58% treated with a PCI.

Mortality rates in the CPUs were very low. Nevertheless, more Trop+ than Trop− patients died (0.7% vs. 0.1%, p < 0.01). Of all patients considered to have suffered an ACS, MACCE (including death, myocardial infarction, and stroke) occurred more often in the Trop+

Table 1a

Baseline characteristics. Baseline characteristics of Trop+ and Trop− patients included in the German CPU Registry. All values are in %, except for age in years (median and quartile). CVD = cardiovascular disease, PCI = percutaneous coronary intervention, CABG = coronary artery bypass graft, PVD = peripheral vascular disease, and ICD = implantable cardioverter defibrillator.

	Trop+ (n = 2853)	Trop− (n = 8803)	p
Age (years)	70.0 (58.1–78.0)	67.5 (54.9–76.1)	<0.01
Male	67%	58%	<0.01
Smoking	32%	25%	<0.01
Diabetes	29%	20%	<0.01
Hypertension	77%	72%	<0.01
Dyslipidemia	45%	42%	<0.01
Family history	20%	24%	<0.01
Known CVD	58%	65%	<0.01
Prior PCI	27%	38%	<0.01
Prior CABG	13%	11%	<0.01
Prior stroke	6%	5%	=0.08
PVD	8%	6%	<0.01
Chronic kidney disease	13%	7%	<0.01
Heart failure	11%	9%	<0.01
ICD or pacemaker	7%	9%	<0.01

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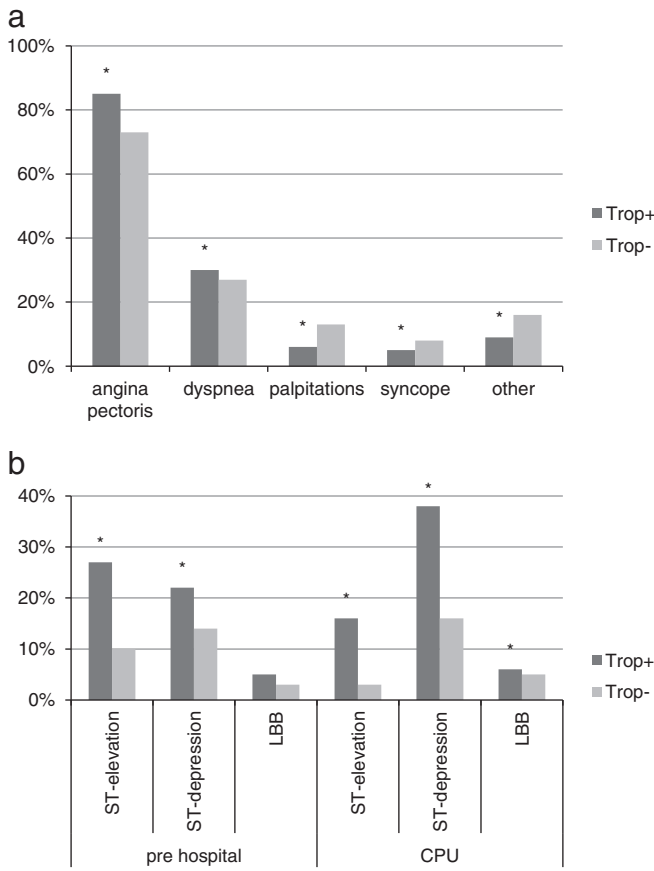*E-mail address:* lmaier@med.uni-goettingen.de (L.S. Maier).

Fig. 1. a: Symptoms on admission to CPU. Percentage of symptoms in Trop + (n = 2853) and Trop − (n = 8,803) patients admitted to CPU. *p < 0.01 for Trop + vs. Trop − patients. Multiple symptoms were possible. b: ECG in CPU patients. ECG findings in pre-hospital and CPU ECGs stratified for Trop + (n = 2853) and Trop − (n = 8803) patients. *p < 0.01 for Trop + vs. Trop − patients.
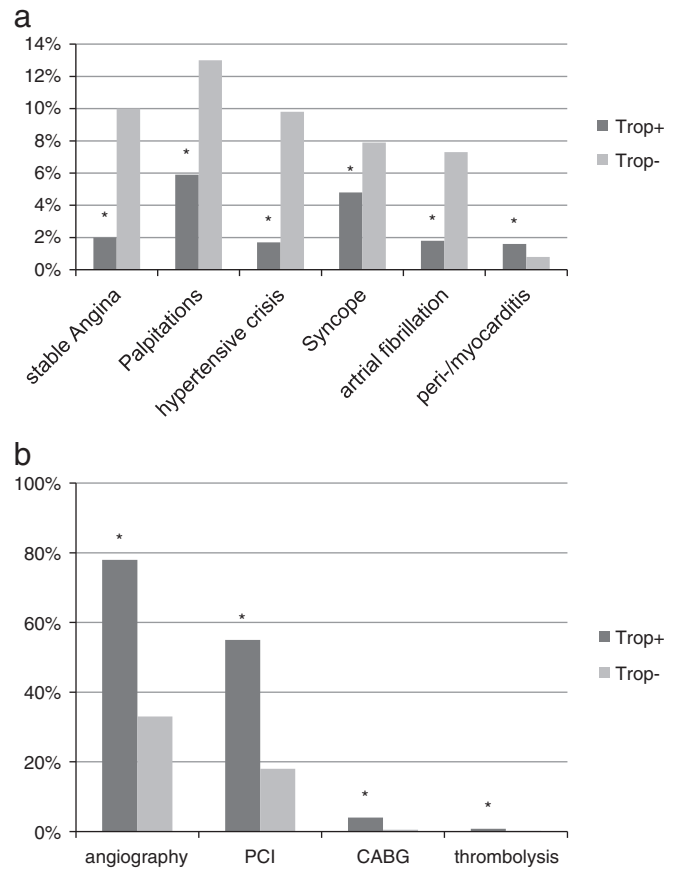
Fig. 2. a: Distribution of minor chest emergencies. Except for PM = Peri/myocarditis all other minor chest emergencies were found more frequently in the Trop − patients. *p < 0.01. b: Interventions in the CPU. Percentage of Trop + and Trop − patients receiving an intervention in the CPU. *p < 0.01 between Trop + vs. Trop − patients.

than in the Trop − group (9.5% vs. 1.4%; p < 0.01). Of note, patients that initially were Trop − but developed troponin subsequently were similar to the Trop + group with 0.6% died in the CPU with a MACCE rate of 8.1%. Interestingly, no difference between severe (0.6% vs. 0.2%, p = 0.09) and moderate (0.9% vs. 0.5%, p = 0.18) bleedings were found between Trop + and Trop − patients.

Follow-up was attained from 46% of all patients almost half of whom were previously diagnosed with ACS during index admission (n = 2519). The percentage of Trop + patients reached at follow-up was somewhat higher with 52% of whom 86% had a previous ACS. In contrast, follow-up was less successful in Trop − patients with 44% of whom only 32% had an ACS. At follow-up after 3 months, independently of ACS 7.6% of Trop + patients (n = 112) had died vs. 3.1% (n = 118) of Trop − patients (p < 0.01). Interestingly, those patients who were dismissed directly home from the CPU had a much smaller incidence of death with 1.4% for Trop + patients and 0.6% for Trop − patients. Death occurred after 26 days (8–77 days) in the Trop + group compared to 38 days (11–110 days) in the Trop − group (p < 0.05). The cause of death was not different between Trop + vs. Trop − patients, including sudden death (13% vs. 22%, p = 0.17), cardiovascular death (46% vs. 36%, p = 0.27), non-cardiovascular (33% vs. 38%, p = 0.53), or unknown (8.2% vs. 3.6%, p = 0.28).

However, it is interesting to know that Trop + patients that had died during the 3 month follow-up had more often a history of cardiovascular disease (87%) as compared to Trop + survivors (53%, p < 0.01), a clearly higher GRACE risk score for intrahospital mortality of 5.2% vs. 1.6% (and at 6 month of 9.1% vs. 2.9%, respectively), were less often interventionally treated with 36% vs. 71% (PCI or bypass), and thus treated more often only with medication (56% vs. 24%, p < 0.01). Of note, Trop − patients that had

died during the 3 month follow-up only had a GRACE risk score of 2.1% for intrahospital mortality (and 3.7% for 6 month mortality, respectively). There was no difference in the percentage of patients that was interventionally treated or treated only with medication as compared to the Trop − survivors.

At 3 months follow-up, MACCE had occurred in 11% of Trop + patients (n = 150) vs. 5% of Trop − patients (n = 171) (p < 0.01). Interestingly, those patients who were dismissed directly home from the CPU had a much lower MACCE rate of 4.4% for Trop + patients and 1.3% for Trop − patients. Revascularization was needed in 14% of Trop + patients vs. 7% of Trop − patients (p < 0.01). 29% of Trop + patients and 23% of Trop − patients were rehospitalized within 3 months (p < 0.01). Readmission was higher in the Trop + vs. Trop − group (Table 1b).

Comparing Trop + to Trop − patients diagnosed with an ACS, the medical therapy consisted of aspirin (93% vs. 84%, p < 0.01), clopidogrel (63% vs. 53%, p < 0.01), prasugrel (13% vs. 3%, p < 0.01), ß-blocker (81% vs.

Table 1b
Readmission characteristics at 3 month follow up. Characteristics of readmitted Trop + and Trop − patients included in the German CPU Registry. Day of readmission is presented with median and quartile. Number and length of readmission is presented as mean and standard deviation.

	Trop +	Trop −	P
Readmission rate	28.9%	23.3	<0.01
Day of readmission	32 (4–61)	32 (8–67)	0.45
Cardiovascular reason	80.7%	70.0%	<0.05
Number of readmissions	1.3 ± 0.6	1.2 ± 0.6	0.46
Length of readmission	9.8 ± 10.4	8.2 ± 10.4	<0.01
MACCE (revascularization or rehospitalization)	37.8%	27.5%	<0.01

66%, p < 0.01), ACE inhibitor (68% vs. 56%, p < 0.01), AT receptor blocker (9% vs. 7%, p = 0.07), and statins (74% vs. 58%, p < 0.01).

Comparing Trop + to Trop − patients after 3 months follow-up, the medical therapy consisted of aspirin (83% vs. 55%, p < 0.01), clopidogrel (53% vs. 19%, p < 0.01), prasugrel (10% vs. 2%, p < 0.01), ß-blocker (83% vs. 65%, p < 0.01), ACE inhibitor (62% vs. 45%, p < 0.01), AT receptor blocker (18% vs. 18%, p = 0.82), and statin (76% vs. 48%, p < 0.01).

We have collected prospective data from a number of clinics with a CPU in Germany. Patients with chest pain apparently seem to benefit from the introduction of a chest pain unit because Trop + patients identified in the CPU were i) faster treated with PCI and ii) to a higher percentage as compared to Trop − patients. iii) This lead to a low death rate in the CPU as well as at 3 month follow up, also when compared to data from the current guidelines [8] as well as from other CPUs [9].

An ECG in the preclinical setting is assessed rarely but may by assessed faster with novel ECG techniques in the future [10] and if a STEMI in a patient is assessed, this patient should be transported directly to the catheter lab, as urgently recommended by international guidelines, instead of being transported to the CPU (or an emergency department) before revascularization thereby saving important time [11].

More than half of the Trop + patients underwent revascularization by PCI, underlining the importance of a specialized CPU to identify patients at risk for myocardial necrosis. In contrast, only a small percentage of Trop − patients had PCI (18%). Time from hospital admittance to invasive treatment was much shorter in Trop + patients underlining the importance of preparing the ground for specific reperfusion therapy in a specialized CPU.

Nevertheless, Trop + patients in the CPU were at a higher danger for immediate and intermediate risk of death and MACCE than Trop − patients. Trop + patients had more cardiovascular risk factors and most of them underwent a PCI. Therefore, a CPU may help to identify patients at risk factors and facilitate optimized reperfusion therapy. Despite care by cardiologists not all patients receive medical therapy following ESC guidelines, and the rate of rehospitalization remains high. In summary, quality improvement initiatives should identify reasons and correct the causes of low adherence to the standard of care.

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