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ORIGINAL PAPER

Temporal trends in incidence and outcome of acute coronary syndrome

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Abstract

Background We aimed to investigate changes of incidence, outcome and related interventions of patients with acute coronary syndrome (ACS) over the past decade in Germany.

Methods Data on the international statistical classification of diseases and procedural codes from the Federal Bureau of Statistics in Germany was used. This included all ACS cases in Germany in the years 2005–2015. Analyses were performed separately for the diagnoses of overall ACS, ST-elevation myocardial infarction (MI), non-ST-elevation MI and unstable angina pectoris. Procedures including coronary angiography and percutaneous coronary intervention and the endpoint in-hospital mortality were assessed.

Results Between 2005 and 2015 a total of 3797,546 cases of ACS were recorded. The mean age was 69 years and 36% were females. In-hospital mortality was 6.3%, 62% underwent coronary angiography and 42% received percutaneous coronary intervention. In-hospital mortality was highest for patients with ST-elevation MI (12.0%) and lowest for patients with unstable angina pectoris (0.6%). From 2005 to 2015 the incidence rates of ACS, ST-elevation MI and unstable angina pectoris decreased, while the incidence rate of non-ST-elevation MI increased. The percentages of performed coronary angiographies and percutaneous coronary interventions increased from 52 to 70% and 34 to 50%, respectively. The adjusted incidence rate of in-hospital mortality decreased from 64.9 cases per 1000 person-years to 54.8 cases.

Conclusion In a large dataset including more than 3.7 million cases, we report an increase in coronary procedures and a reduction of ACS incidence and related mortality in the past decade in Germany.

Keywords Acute coronary syndrome · Myocardial infarction · STEMI · NSTEMI · Unstable angina pectoris · Outcome · In-hospital mortality · Trend · Germany

Introduction

Patients presenting with suspected acute coronary syndrome (ACS) are an important population in emergency departments worldwide and account for more than 20 million presentations to the emergency department in Europe and North America [1]. In the past decades, diagnostic and therapeutic pathways for these patients have substantially improved [2, 3]. This includes on the one hand faster and more accurate diagnostic algorithms, which are based on high-sensitivity cardiac troponin [4]. On the other hand, therapeutic options have substantially improved, as modern drug-eluting-stents, potent P2Y12 inhibitors and lipid-lowering drugs are routinely used nowadays [5, 6]. Finally, awareness for primary prevention strategies in the general population has become more available and could reduce disease burden on a large scale [7, 8].

These changes over time had an impact on outcome, as the incidence rates of acute myocardial infarction (MI), as well as related mortality decreased in developed countries [2, 9, 10]. However, there is limited data on the temporal

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trends of ACS diagnosis within the past decade from large contemporary datasets. Therefore, we aimed to assess incidence, outcome and related interventions of patients admitted with ACS in Germany. For this purpose, we analyzed clinical data from all cases treated for ACS in Germany between 2005 and 2015.

Methods

Study population and study design

In Germany, all clinical cases treated within a hospital have to be collected within one central database by the Federal Bureau of Statistics to enable reimbursement. Within this database, all diagnoses and performed procedures are stored. The diagnoses are coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision, German modification (ICD-10-GM). All procedures are coded according to the German Procedure Classification (OPS). The guidelines for coding, as well as annual adaptations, allow a uniform documentation. For the present analyses, we used all cases of patients with the main diagnosis of ACS (ICD-codes I20.0, I21 or I22) from the years 2005–2015. All ICD and OPS codes, which were used for the present analyses, are provided in Table S1. The variables included age, sex, type of ACS-subgroup (ST-elevation MI (STEMI), non-ST-elevation MI (NSTEMI), and unstable Angina pectoris (UAP)), cardiovascular risk factors (hypertension, dyslipidemia, diabetes), prevalent comorbidities (peripheral artery disease, prior stroke, atrial fibrillation, chronic obstructive pulmonary disease (COPD), renal insufficiency, prior coronary-artery-bypass-grafting (CABG)) and performed procedures (coronary angiography, performed percutaneous coronary intervention (PCI), performed CABG), as well as in-hospital mortality.

The data export was performed on our behalf by the Research Data Center of the Federal Bureau of Statistics and Statistical Offices of the Federal States in Wiesbaden, Germany, and aggregated statistics were provided on the basis of R codes that we supplied to the Research Data Center. There was no commercial support for the study or the preparation of this manuscript. This study did not involve direct access by the investigators to data on individual patients, but only access to completely anonymized summary results provided by the Research Data Center. Therefore, approval by an ethics committee and informed consent were not required in accordance with German law.

Statistical analysis

Binary variables were shown as absolute numbers and percentages, whereas continuous variables were shown as mean ± standard deviation (SD). Subgroup analyses were performed for patients with STEMI, NSTEMI, UAP, according to settlement geography (urban and rural) and by month of documentation. Furthermore, age- and sex-adjusted incidence rates were calculated for overall ACS, STEMI, NSTEMI, and UAP using the age- and sex-specific distribution in Germany at the 31st of December of each year as reference. The distribution of ACS in Germany was applied as reference for incidence rates of in-hospital mortality. These were calculated in three different models: unadjusted, adjusted for age and sex, and adjusted for age, sex, diabetes, dyslipidemia, hypertension and renal failure. All statistical methods were written in R statistical software version 3.5.2 (R Foundation for Statistical Computing) and were performed at the Federal Bureau of Statistics in Germany.

Results

Characteristics of the overall population

Between 2005 and 2015 a total of 3797,546 cases of ACS were recorded (Table 1). The mean age was 68.8 years (SD 16.47) and 36.0% were females. 57.3% were diagnosed with hypertension, 43.5% with dyslipidemia, and 27.2% with diabetes. There were 1441,876 cases of UAP, 1331,514 cases of NSTEMI and 925,424 cases of STEMI in the overall dataset. Patients with NSTEMI were older compared to STEMI patients (71.7 vs. 66.2 years), were more often female and had a higher prevalence of cardiovascular risk factors.

The mean duration of the hospital stay was 7.2 days (SD 7.7) and was longer in STEMI (8.4 days, SD 8.4) and NSTEMI patients (8.6 days, SD 8.5), compared to UAP patients (5.1 days, SD 5.7). In the overall ACS population, 62.2% received a coronary angiography and 42.4% a PCI. Among STEMI patients, these rates were higher (71.6% coronary angiography and 65.3% PCI), compared to NSTEMI (60.2% and 41.0%) and UAP patients (60.8 and 30.7%). In total, 4.7% of all patients underwent coronary artery bypass grafting.

In the refining analyses according to settlement geography, no major differences in the patient characteristics were observed (Table 2). The rate of coronary angiographies was 68.5% in urban and 68.2% in rural regions. In-hospital mortality was 5.9% in urban and 6.3% in rural regions.

Table 1 Characteristics of all patients with ACS, subtypes of STEMI, NSTEMI, and UAP in Germany summarizing the years 2005–2015

	ACS	STEMI	NSTEMI	UAP
N available	3797,546	925,424	1331,514	1441,876
Age, years	68.82 ± 12.82	66.22 ± 13.6	71.65 ± 12.47	67.6 ± 12.01
Female sex	1366,045 (35.97%)	299,305 (32.34%)	501,080 (37.63%)	525,143 (36.42%)
Hypertension	2177,441 (57.34%)	487,043 (52.63%)	780,009 (58.58%)	868,198 (60.21%)
Dyslipidemia	1651,199 (43.48%)	397,288 (42.93%)	563,518 (42.32%)	669,732 (46.45%)
Diabetes	1031,660 (27.17%)	216,875 (23.44%)	429,798 (32.28%)	358,806 (24.88%)
PAD	181,713 (4.79%)	31,486 (3.4%)	83,689 (6.29%)	62,307 (4.32%)
Prior stroke	31,253 (0.82%)	10,850 (1.17%)	14,737 (1.11%)	4186 (0.29%)
Atrial fibrillation	638,165 (16.8%)	123,577 (13.35%)	298,643 (22.43%)	198,792 (13.79%)
COPD	269,854 (7.11%)	46,731 (5.05%)	122,055 (9.17%)	94,140 (6.53%)
Renal insufficiency	697,787 (18.37%)	132,728 (14.34%)	337,861 (25.37%)	208,507 (14.46%)
Prior CABG	262,781 (6.92%)	27,849 (3.01%)	100,727 (7.56%)	129,576 (8.99%)
During hospital stay				
Median hospital stay, days	7.19 ± 7.69	8.39 ± 8.37	8.61 ± 8.46	5.12 ± 5.68
Coronary angiography	2363,107 (62.23%)	662,746 (71.62%)	802,169 (60.24%)	876,373 (60.78%)
In-hospital PCI	160,8487 (42.36%)	604,679 (65.34%)	546,125 (41.02%)	442,252 (30.67%)
In-hospital CABG	179,749 (4.73%)	38,443 (4.15%)	77,865 (5.85%)	58,919 (4.09%)
In-hospital Mortality	239,958 (6.32%)	111,090 (12%)	88,305 (6.63%)	8259 (0.57%)

ACS acute coronary syndrome, *UAP* unstable angina pectoris, *STEMI* ST-elevation myocardial infarction, *NSTEMI* non-ST-elevation myocardial infarction, *PAD* peripheral artery disease, *COPD* chronic obstructive pulmonary disease, *CABG* coronary artery bypass grafting, *PCI* percutaneous coronary intervention

Table 2 Patients with ACS in urban, suburban and rural regions

	Urban	Suburban	Rural	*p* value
N available	818,158	487,491	367,785	
Age, years	68.86 ± 13.03	69.28 ± 12.9	69.3 ± 12.78	< 0.001
Female sex	284,932 (34.83%)	168,109 (34.48%)	130,377 (35.45%)	< 0.001
Hypertension	484,058 (59.16%)	284,031 (58.26%)	208,993 (56.82%)	< 0.001
Dyslipidemia	384,412 (46.99%)	207,260 (42.52%)	172,074 (46.79%)	< 0.001
Diabetes	225,588 (27.57%)	135,823 (27.86%)	108,552 (29.52%)	< 0.001
PAD	43,778 (5.35%)	24,869 (5.1%)	19,192 (5.22%)	< 0.001
Prior stroke	6298 (0.77%)	3774 (0.77%)	2794 (0.76%)	0.898
Atrial fibrillation	146,275 (17.88%)	90,678 (18.6%)	68,702 (18.68%)	< 0.001
COPD	62,708 (7.66%)	34,880 (7.16%)	26,643 (7.24%)	< 0.001
Renal insufficiency	157,469 (19.25%)	95,261 (19.54%)	82,690 (22.48%)	< 0.001
Prior CABG	60,288 (7.37%)	33,470 (6.87%)	25,641 (6.97%)	< 0.001
During hospital stay				
Median hospital stay, days	6.9 ± 7.76	6.8 ± 7.22	6.9 ± 7.24	< 0.001
Coronary angiography	560,089 (68.46%)	323,431 (66.35%)	250,934 (68.23%)	< 0.001
In-hospital PCI	389,279 (47.58%)	224,014 (45.95%)	176,622 (48.02%)	< 0.001
In-hospital CABG	41,365 (5.06%)	23,710 (4.86%)	14,708 (4%)	< 0.001
In-hospital Mortality	47,998 (5.87%)	29,690 (6.09%)	23,279 (6.33%)	< 0.001

Temporal trends of patient characteristics, incidence and outcome from 2005 to 2015

From 2005 to 2015 we observed an increase of age (2005 mean age 68.3 years vs. 2015 69.1 years) and a decrease in female sex (37.7% vs. 34.1%) (Table 3 and S2). The presence of cardiovascular risk factors slightly increased, while the mean duration of hospital stay decreased from 7.8 days (SD 7.7) to 6.5 days (SD 6.9). Rates of coronary angiography and PCI increased from 52.4% and 33.8% to 70.5% and

Table 3 Characteristics of all ACS patients for the years 2005 and 2015, see Table S2 for results displayed per year

	2005	2015	*p* value
N available	373,199	317,438	
Age, years	68.29 ± 12.56	69.08 ± 12.96	< 0.001
Female sex	140,755 (37.72%)	108,292 (34.11%)	< 0.001
Hypertension	210,499 (56.4%)	185,529 (58.45%)	< 0.001
Dyslipidemia	151,654 (40.64%)	146,831 (46.26%)	< 0.001
Diabetes	94,613 (25.35%)	89,309 (28.13%)	< 0.001
PAD	15,975 (4.28%)	17,294 (5.45%)	< 0.001
Prior stroke	3643 (0.98%)	2470 (0.78%)	< 0.001
Atrial fibrillation	54,724 (14.66%)	59,658 (18.79%)	< 0.001
COPD	25,216 (6.76%)	23,997 (7.56%)	< 0.001
Renal insufficiency	54,808 (14.69%)	65,087 (20.5%)	< 0.001
Prior CABG	24,028 (6.44%)	22,533 (7.1%)	< 0.001
During hospital stay			
Median hospital stay, days	7.79 ± 7.71	6.53 ± 6.92	< 0.001
Coronary angiography	195,716 (52.44%)	223,736 (70.48%)	< 0.001
In-hospital PCI	126,267 (33.83%)	159,645 (50.29%)	< 0.001
In-hospital CABG	17,703 (4.74%)	14,883 (4.69%)	0.56
In-hospital Mortality	24,032 (6.44%)	18,830 (5.93%)	< 0.001

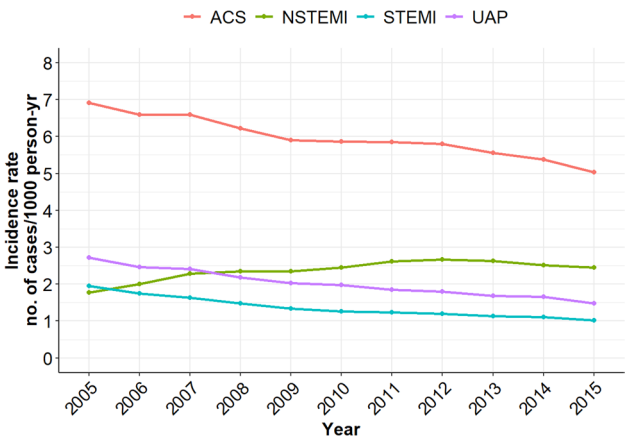

Fig. 1 Age- and sex-adjusted incidence rates of ACS, NSTEMI, STEMI and UAP cases per 1000 person-years ranging from 2005 to 2015

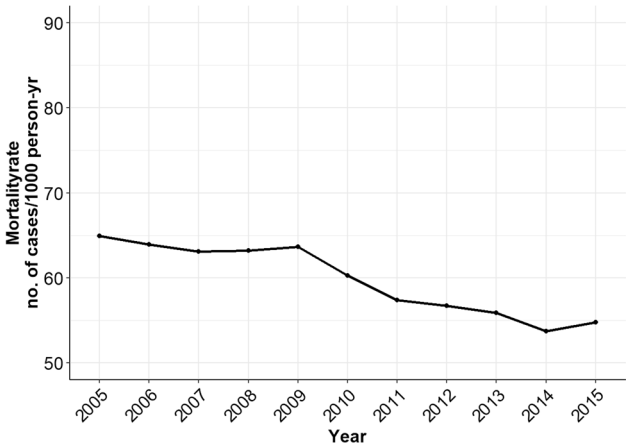

Fig. 2 Incidence rates of in-hospital mortality cases per 1000 person-years ranging from 2005 to 2015, adjusted for age and sex

50.3%, respectively. In-hospital mortality decreased from 6.4 to 5.9%. The results for each subgroup of ACS diagnosis are presented in Table S3. In subgroup analyses according to the month of documentation, the rate of ACS cases was lower in the summer months, compared to the winter months (Table S4).

The age- and sex-adjusted incidence rate of ACS decreased from 6.9 cases/1000 person-years to 5.0 cases/1000 person-years (Fig. 1a and Table S5). In subgroup analyses, the incidence rate of UAP and STEMI decreased as well, while the incidence rate of NSTEMI increased from 1.8 cases/1000 person-years to 2.5 cases/1000 person-years (Fig. 1 and Table S5).

In total, 6.3% died during the in-hospital stay. The mortality rate was substantially higher in STEMI patients (12.0% vs. 6.6% in NSTEMI and 0.6% in UAP). The unadjusted incidence rates of in-hospital mortality were reduced from 64.4 cases/1000 person-years in 2005 to 59.3 cases/1000 person-years in 2015, while the age- and sex-adjusted incidence rates of in-hospital mortality was reduced from 64.9 cases/1000 person-years in 2005 to 54.8 cases/1000 person-years in 2015 (Fig. 2 and Table S6). After additional adjustment for diabetes, dyslipidemia, hypertension and renal failure the incidence rates of in-hospital mortality was reduced from 65.1 cases/1000

person-years in 2005 to 62.3 cases/1000 person-years in 2015.

Discussion

In a large population of more than 3.7 million cases, we report a decreasing incidence of acute coronary syndrome in Germany within the past decade. While the rate of performed coronary angiographies and coronary interventions increased, the in-hospital mortality and the duration of hospital stay decreased.

In this manuscript, we present novel findings. First, we were able to collect all ACS cases in Germany over the past decade, which resulted in a dataset allowing for the accurate description of ACS incidence and its changes in the last 10 years. We found a decrease in ACS and STEMI diagnosis, which is in line with earlier observations. In 2010, Yeh et al. [9] for the first time reported a strong decrease of STEMI incidence in 45,000 US patients. These changes most likely mirrored recent improvements in preventive, diagnostic, and therapeutic strategies for patients with coronary artery disease [5]. In contrast, the incidence of NSTEMI diagnosis showed an increase from 2005 to 2012 and a decrease thereafter in our study. These findings might be related to the changes in troponin assays over the past years. Troponin-testing was introduced in clinical routine at the end of the last century and was first included in the definition of MI in 2000 [11]. Since that time, troponin assays became much more widely used, but also more sensitive, allowing detection of already mild troponin elevation [12]. In Germany, high-sensitivity troponin assays became widely established after their introduction in 2009 and are today used in most hospitals [13, 14]. This may explain the continuous increase of NSTEMI diagnosis up to 2012. The fact, that NSTEMI rates did not further increase after 2012 [15] might then be a result of improved prevention strategies. In the large SWEDEHEART registry, a similar trend was observed [16]. Here, the proportion of NSTEMI diagnosis was also highest in 2012, while the rate of STEMI diagnosis showed a continuous decrease over time. This Swedish population had a similar median age and a comparable distribution of cardiovascular risk factors.

The second salient finding is, that rates of invasive procedures, such as coronary angiography and PCI, were rapidly increasing in the past decade. In addition, the duration of hospital stay was reduced by more than 1 day, and in-hospital mortality decreased. These findings confirm prior reports from the SWEDEHEART registry [2, 16]. In their cohort, the authors described a decrease of in-hospital mortality from 12.4% in 1995 to 3.7% in 2014. The authors related this improvement to the uptake of evidence-based treatments, including statins and coronary interventions in the past years. During this period, the rate of primary PCI showed a strong increase and reached up to 80% for patients diagnosed with STEMI in the year 2018, which is similar to our cohort. Furthermore, we could extend these findings about a decrease in mortality to an overall ACS patients' cohort. Here, we observed a decline not only in NSTEMI but also in STEMI patients. Interestingly, this effect was less attenuated, when the in-hospital mortality was additionally adjusted for cardiovascular risk factors. However, there might be a reporting bias in the documentation of risk factors, as the incidence of dyslipidemia in ACS patients is unlikely to show a strong increase of more than 6% within 10 years. Therefore, adjustment for age and sex might be the most valid analysis.

More recently, a steady reduction of 30-days mortality had also been reported in a large US cohort study including more than 4 million Medicare beneficiaries with MI [10]. In contrast, results from the German Quality Assurance database, which compared the outcome of STEMI patients in Germany in 2008 and 2013, showed a slight increase of the in-hospital mortality in unadjusted analyses [17]. These differences might be explained by an increasing age, as well as an increasing risk profile. This would be supported by our analyses, as the trend of the unadjusted in-hospital mortality was less prominent.

In subgroup analyses, we found no substantial differences in patients treated in urban or rural regions. Germany is a densely populated country, with a good coverage of emergency facilities not only near the bigger cities, which might explain the lack of regional distinctions. Finally, we investigated the rate of ACS cases per month and observed a lower rate in the summer months, compared to the winter months. These results are supported by prior evidence, that cold weather might impact the incidence of cardiovascular events [18–20].

Our analyses have strengths, but also limitations. A major strength is, that we collected a very large dataset including all ACS cases in Germany from the past decade. Furthermore, the information on in-hospital procedures and mortality were available for all patients. A limitation is, that there might be a reporting bias for diagnoses and procedures, as these were done by each hospital locally, without a central adjudication. This could lead to an under- or over-reporting of certain diagnoses. However, due to the large sample size, this effect is unlikely to have impact on the overall results. Furthermore, there is no information on biomarkers, prescribed drugs and follow-up diagnostics in this population. Finally, due to the central organization of the Federal Bureau of Statistics, we cannot provide more detailed information about the type and volume of hospitals performing the procedures.

In conclusion, in a large dataset including 3.7 million cases from the past decade in Germany, we reported a

reduction of ACS incidence and related mortality. Whether these findings are a consequence of improved primary and secondary prevention strategies or a higher usage of invasive coronary procedures needs to be shown.

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Compliance with ethical standards

Conflict of interest JN has received honoraria from Abbott Diagnostics, Siemens and Prevencio; SB has received honoraria from Abbott Diagnostics, Siemens, Thermo Fisher, and Roche Diagnostics and is a consultant for Thermo Fisher. DW reports personal fees from Bayer, Boehringer-Ingelheim, Berlin Chemie, Astra Zeneca, Biotronik and Novartis.

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