International Journal of Cardiology 287 (2019) 132–138

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Sex-specific differences regarding seasonal variations of incidence and mortality in patients with myocardial infarction in Germany

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A R T I C L E I N F O

Article history:
Received 10 December 2018
Received in revised form 27 March 2019
Accepted 10 April 2019
Available online 11 April 2019

Keywords:
Season
Mortality
Myocardial infarction
Winter
Summer

A B S T R A C T

Background: Seasonal variation regarding the incidence and the short-term mortality of acute myocardial infarction (MI) was frequently reported, but data about sex-specific differences are sparse.

Methods: We analysed the impact of seasons and temperature on incidence and in-hospital mortality of patients with acute MI in Germany between 2005 and 2015.

Results: The nationwide sample comprised 3,008,188 hospitalizations of MI patients (2005–2015). The incidence was 334.7/100,000 citizens/year. Incidence inclined from 316.3 to 341.6/100,000 citizens/year (β 0.17 [0.10 to 0.24], $P < 0.001$), while in-hospital mortality rate decreased from 14.1% to 11.3% (β −0.29 [−0.30 to −0.28], $P < 0.001$). Overall, 377,028 (12.5%) patients died in-hospital.

Seasonal variation of both incidence and in-hospital mortality was of substantial magnitude. Seasonal incidence (86.1 vs. 79.0/100,000 citizens/year, $P < 0.001$) and in-hospital mortality (13.2% vs. 12.1%, $P < 0.001$) were higher in winter than in summer. Risk to die in winter was elevated (OR 1.080 (95% CI 1.069–1.091), $P < 0.001$) compared to summer season independently of sex, age and comorbidities. Reperfusion treatment with drug eluting stents and coronary artery bypass graft were more often used in summer.

We observed sex-specific differences regarding the seasonal variation of in-hospital mortality: males showed lowest mortality in summer, while females during fall. Low temperature dependency of mortality seems more pronounced in males.

Conclusion: Incidence of acute MI increased 2005–2015, while in-hospital mortality rate decreased. Seasonal variation of incidence and in-hospital mortality were of substantial magnitude with lowest incidence and lowest mortality in the summer season. Additionally, we observed sex-specific differences regarding the seasonal variation of the in-hospital mortality.

1. Introduction

Ischaemic heart disease (IHD) is the most common cause of death with an increasing frequency worldwide [1]. It accounts for approximately 20% of all deaths in Europe [1] and the United States of America [2]. Approximately 1/3 of the IHD patients present with sudden cardiac death [3]. The acute presentation of IHD, myocardial infarction (MI), is a life-threatening, serious health problem which causes substantially morbidity and mortality [1–3].

MI is frequently preceded by specific triggers, which can include common activities such as physical exertion, stressful events, alcohol consumption and heavy meals [4]. The research on MI triggers has predominantly focused on the increased risks to the individual, while population burden of MI triggers has not received comparable attention [4]. The research about environmental and other triggers of MI has been intensified in the last decades. Especially, a growing interest regarding chronobiology of acute MI has been arisen. It is well established that the onset of MI follows a circadian and seasonal periodicity [5–11]. During the daily routine, MI has a peak incidence in the morning hours (after awakening) [5,12]. A large body of evidence suggests a seasonal periodicity in MI incidence [5,6,11,13,14] and mortality [5,8,15]. Both, the incidence [5,6,11,13] as well as the short-term mortality [5,8,15] of an acute MI were in most studies higher in the cold winter months than in those of the warm summer. In addition, the role of temperature and weather has also been explored [5,6,16].

Although already several studies published results about seasonal variability of incidence and short-term mortality (for a number of different countries) [5,6,11–13,17,18], our objectives were to investigate both incidence and mortality in the German nationwide inpatients sample

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https://doi.org/10.1016/j.ijcard.2019.04.035
0167-5273/

with >3 million included MI cases and in this context to address unanswered questions regarding possible sex-specific differences. We aimed to assess whether incidence and in-hospital mortality changed during different seasons and temperatures and seasonal variation differed in males and females.

2. Methods

2.1. Data source

The German Research Data Center of the Federal Statistical Office and the Statistical Offices of the federal states (source: RDC of the Federal Statistical Office and the Statistical Offices of the federal states, DRG Statistics 2005–2015, own calculations), in Wiesbaden (Germany), performed the present analyses on our behalf; they provided the aggregated statistic results on the basis of SPSS codes (SPSS® software, version 20.0, SPSS Inc., Chicago, Illinois), which were supplied from us to the Research Data Center. For this analysis, all hospitalized patients diagnosed with acute MI (2005–2015) were selected.

2.2. Diagnoses, procedural codes, and definitions

Diagnoses are coded according to the International Classification of Diseases and Related Health Problems in its 10th Revision with German Modification (ICD-10-GM) and diagnostic, surgical or interventional procedures are coded according to the German Procedure Classification (OPS, surgery and procedures codes [Operationen- und Prozedurenschlüssel]).

We included all MI patients (ICD code I21) with an acute MI (except those MI events, which are recurrent events during the first 28 days after previous MI (ICD-code I22)), who were hospitalized in Germany (2005–2015), in this analysis. MI patients were further stratified according to seasons and patients admitted in summer and winter were compared. The seasons comprised the following months: winter included the months December to February, spring March to May, summer June to August and fall September to November. Monthly mean temperature in Germany was obtained by the German meteorological service (Deutscher Wetterdienst).

2.3. Study outcome

We analysed the seasonal incidence of MI. The primary study outcome was death of all causes during the in-hospital stay (in-hospital death). In addition, we analysed the seasonal differences in cardiopulmonary resuscitation (CPR).

2.4. Ethical aspects

Since this study did not involve direct access by the investigators to data of individual patients, approval by an ethics committee and informed consent were not required, in accordance with German law.

2.5. Statistical methods

Statistical analyses are described in the supplementary material.

3. Results

3.1. MI incidence and mortality rate between 2005 and 2015

In a time period of 11 years (2005–2015), the nationwide inpatient sample included 3,008,188 hospitalizations due to acute MI in Germany (37.7% females). The mean annual incidence of MI was 334.7 per 100,000 population in Germany in this aforementioned timeframe. Among these hospitalized MI patients, 377,028 (12.5%) died during in-hospital course.

While the incidence of MI increased slightly from 316.3 events per 100,000 citizens in 2005 to 341.6 events per 100,000 citizens in 2015 (β 0.17 (95% CI 0.10 to 0.24), $P < 0.001$) similar to the rate of CPR (β 0.05 (95% CI 0.04 to 0.07), $P < 0.001$), the in-hospital mortality rate decreased from 14.1% in 2005 to 11.3% in 2015 (β −0.29 (95% CI −0.30 to −0.28), $P < 0.001$) during the investigated period (Fig. S1 in supplementary material). Additionally, the median in-hospital stay in days declined (β −0.01 (95% CI −0.01 to −0.01), $P < 0.001$).

3.2. Patient characteristics stratified by seasons

The patient characteristics stratified by seasons revealed a significant higher incidence of acute MI events during winter and spring compared to the summer season. In parallel, highest mortality rate was found in the winter and lowest in the summer (Table 1).

MI patients hospitalized in the winter were more often older than 70 years and of female sex compared to the summer. Additionally, MI patients hospitalized in the summer presented less often with heart failure and COPD. Median time of hospitalizations were similar between winter and summer season (7 (IQR 4–12) vs. 7 (IQR 4–13)).

3.3. Seasonal variation of absolute numbers of MI, incidence and mortality

Seasonal variation regarding absolute numbers of MI as well as in-hospital mortality was of substantial magnitude (Fig. 1). For absolute numbers of MI events, summer season was significantly different from winter ($P < 0.001$), spring ($P < 0.001$) and fall ($P = 0.006$) season. Regarding in-hospital mortality, winter and summer ($P = 0.001$) and winter and fall ($P = 0.006$) were significantly different with a strong correlation between season and both absolute number of MI as well as in-hospital death (Fig. 1, Table S1 in supplementary material). The lowest absolute numbers of MI were consecutively found in the summer season in all investigated years (sex-unspecific: Fig. S2 in supplementary material, sex-specific: Fig. 2). Although we observed some annual differences regarding the peak number of MIs between the investigated years, in most years the peaks were in winter or spring. In parallel, the lowest in-hospital mortality was found in the summer season in most of the investigated years (7/11 years = 63.6%). Our seasonal data showed no annual trend over time (Fig. S2 in supplementary material). In addition, no substantial differences in the seasonal variations regarding MI incidence and MI mortality were detected with respect to the federal states of Germany in the north vs. south and west vs. east (Fig. S3 in supplementary material). The minimum incidence was in all federal states of Germany in the summer season and the lowest mortality rate in ¾ of the federal states in the summer.

Similarly, for CPR a winter peak was observed, while lowest CPR rate was found in the summer season (6.4% vs. 6.2%, $P < 0.001$) (Fig. S4 in supplementary material); this result was confirmed in the logistic regressions (Table 2).

In the sex-specific analyses, absolute numbers of MI in men revealed comparable results to the sex-unspecific analyses (significant differences between summer and winter ($P < 0.001$), summer and spring ($P < 0.001$) and between summer and fall ($P = 0.031$)). In contrast, women (difference between summer and winter ($P < 0.001$), summer and spring ($P < 0.001$) and between summer and fall ($P = 0.001$)) showed an additional significant difference between winter and fall ($P = 0.041$) (Figs. 1+2). Figs. 1+2 visualize the sex-specific differences regarding the seasonal variation of the in-hospital mortality rate between male and female patients with acute MI. While in men the lowest in-hospital mortality rate was observed in the summer season with a distinct decrease of the in-hospital mortality rate from winter over spring to summer and an increase from summer to fall, the in-hospital mortality rate in females decreased from winter continuously over spring and summer to fall (Fig. 1).

In the sex-specific analyses regarding the in-hospital mortality, men and women demonstrated a significant difference between summer

Table 1
Baseline characteristics of 3,008,188 hospitalizations due to acute MI stratified by seasons.

	Winter	Spring	Summer	Fall	*P* for difference between summer and winter
Median temperature (°C)	1.1 (−0.5–3.6)	8.7 (5.7–12.4)	17.2 (16.1–18.2)	9.1 (6.8–12.8)	<0.001
Seasonal (3-month) incidence of MI per 100,000 citizens	86.1	86.2	79.0	83.4	<0.001
Number of MI events	773,461 (25.7%)	774,785 (25.8%)	710,283 (23.6%)	749,659 (24.9%)	<0.001
Age >70 years	443,762 (57.4%)	438,086 (56.5%)	397,009 (55.9%)	428,523 (57.2%)	<0.001
Female gender[a]	294,304 (38.1%)	291,325 (37.6%)	267,242 (37.6%)	283,375 (37.8%)	<0.001
Obesity	71,661 (9.3%)	73,454 (9.5%)	67,958 (9.6%)	69,555 (9.3%)	<0.001
Diabetes mellitus	236,190 (30.5%)	235,647 (30.4%)	213,015 (30.0%)	229,617 (30.6%)	<0.001
Hyperlipidemia	290,669 (37.6%)	293,864 (37.9%)	274,013 (38.6%)	290,499 (38.8%)	<0.001
Essential arterial hypertension	421,468 (54.5%)	424,918 (54.8%)	389,372 (54.8%)	412,883 (55.1%)	<0.001
Heart failure	281,876 (36.4%)	279,882 (36.1%)	253,578 (35.7%)	272,090 (36.3%)	<0.001
Atrial fibrillation/flutter	168,410 (21.8%)	164,975 (21.3%)	150,202 (21.1%)	163,085 (21.8%)	<0.001
Cancer	27,846 (3.6%)	28,250 (3.6%)	28,119 (4.0%)	28,447 (3.8%)	<0.001
COPD	71,899 (9.3%)	70,085 (9,0%)	60,155 (8,5%)	65,035 (8.7%)	<0.001
Stroke	21,908 (2.8%)	22,221 (2.9%)	20,881 (2.9%)	21,853 (2.9%)	<0.001
Renal insufficiency	208,664 (27.0%)	206,724 (26.7%)	189,953 (26.7%)	204,479 (27.3%)	0.001
Anterior myocardial infarction	124,352 (16.1%)	127,008 (16.4%)	1115,803 (16.3%)	118,367 (15.8%)	<0.001
Posterior myocardial infarction	114,329 (14.8%)	117,281 (15.1%)	107,641 (15.2%)	110,271 (14.7%)	<0.001
NSTEMI	464,675 (60.1%)	461,317 (59.5%)	424,583 (59.8%)	456,583 (60.9%)	<0.001
BMS	146,552 (18.9%)	151,734 (19.6%)	136,569 (19.2%)	137,825 (18.4%)	<0.001
DES	148,186 (19.2%)	150,712 (19.5%)	145,864 (20.5%)	159,859 (21.3%)	<0.001
BVS	1539 (0.2%)	1643 (0.2%)	1736 (0.2%)	1972 (0.3%)	<0.001
CABG	34,393 (4.4%)	35,988 (4.6%)	33,329 (4.7%)	35,739 (4.8%)	<0.001
Deep vein thrombosis or thrombophlebitis	4946 (0.6%)	4862 (0.6%)	4906 (0.7%)	5110 (0.7%)	<0.001
Pulmonary embolism	5348 (0.7%)	5048 (0.7%)	4793 (0.7%)	5203 (0.7%)	0.219
Shock	51,915 (6.7%)	52,494 (6.8%)	48,544 (6.8%)	50,904 (6.8%)	0.003
CPR	49,200 (6.4%)	48,136 (6.2%)	43,694 (6.2%)	46,804 (6.2%)	<0.001
In-hospital death	102,074 (13.2%)	97,283 (12.6%)	85,927 (12.1%)	91,744 (12.2%)	<0.001

Abbreviations: MI = myocardial infarction; COPD = chronic obstructive pulmonary disease; NSTEMI = non-ST-segment elevation myocardial infarction; BMS = bare-metal stent; DES = drug eluting stent; BVS = drug eluting bioresorbable stent; CABG = coronary artery bypass graft; CPR = cardio-pulmonary resuscitation.
[a] Information about sex available for n = 3,008,060 hospitalized patients.

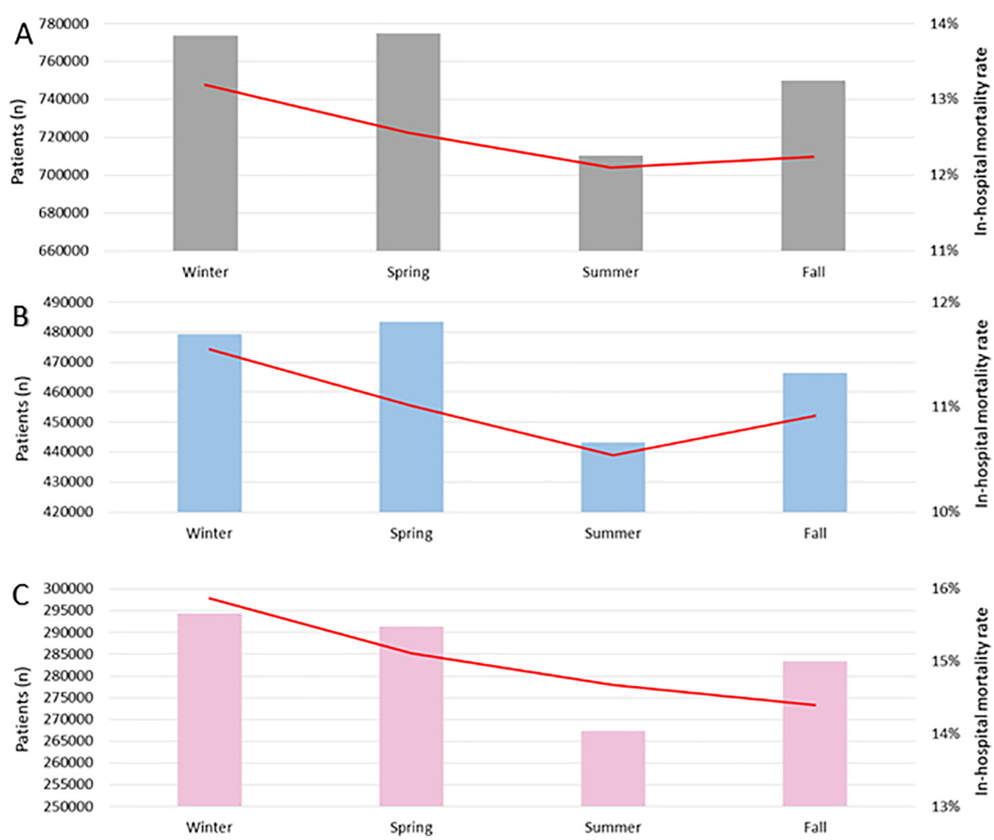

Fig. 1. A - Absolute numbers of MI patients (grey bars) and in-hospital mortality (red line) stratified for seasons. B- Absolute numbers of MI patients (blue bars) and in-hospital mortality (red line) stratified for seasons in males. C- Absolute numbers of MI patients (pink bars) and in-hospital mortality (red line) stratified for seasons in females.

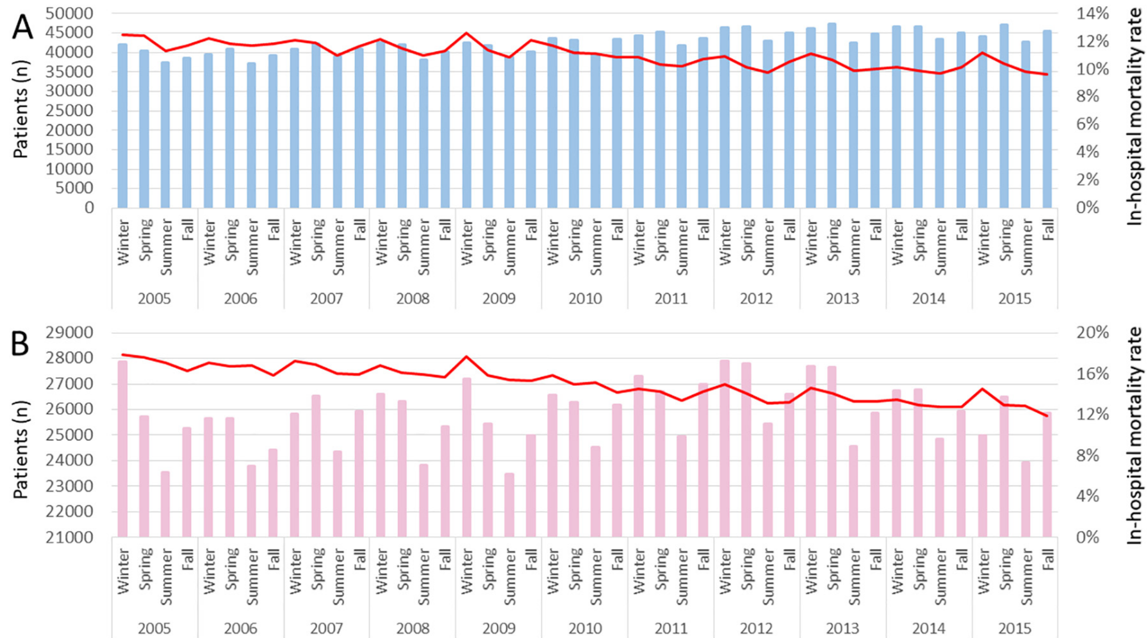

Fig. 2. Absolute numbers (blue bars in men and pink bars in women) and in-hospital mortality (red line) of male (A) and female (B) MI patients stratified for seasons.

and winter (men: $P < 0.001$; women: $P = 0.022$) as well as between winter and fall (men: $P = 0.022$; women: $P = 0.002$) (Figs. 1+2).

MI patients' risk to die during the in-hospital stay was with an OR of 1.08 independently elevated of important comorbidities, sex and age during winter vs. summer season (Table 2).

3.4. Association between mean temperature and both absolute numbers of MI events as well as in-hospital mortality

These results are presented in the supplementary material (with Figs. S5 and S6 as well as Tables S1 and S2 in the supplementary material).

3.5. Seasonal treatment differences

While the seasonal subgroups of MI patients did not differ regarding NSTEMI/STEMI events, patients in the summer season had more often circumscribed MI events (such as singular anterior or singular posterior MI events) and were more often treated with DES as well as CABG than patients in the winter (Table 1, Fig. S7 in supplementary material).

The multivariate logistic regression models confirmed a lower reperfusion treatment rate regarding implantation of DES as well as CABG surgeries in the winter compared to the summer season independently of sex, age and comorbidities (Table 2).

Table 2
Impact of winter season on different clinical parameters and outcomes in comparison to summer season.

	Univariate OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Sex-unspecific				
NSTEMI	1.013 (1.006–1.019)	<0.001	0.996 (0.990–1.003)	0.283
DES	0.917 (0.910–0.924)	<0.001	0.933 (0.925–0.941)	<0.001
BVS	0.814 (0.760–0.872)	<0.001	0.846 (0.790–0.906)	<0.001
CABG	0.945 (0.931–0.960)	<0.001	0.955 (0.940–0.970)	<0.001
CPR	1.036 (1.023–1.050)	<0.001	1.029 (1.015–1.043)	<0.001
In-hospital death	1.105 (1.094–1.115)	<0.001	1.080 (1.069–1.091)	<0.001
Men				
NSTEMI	1.023 (1.015–1.032)	<0.001	1.002 (0.994–1.011)	0.618
DES	0.920 (0.9121–0.929)	<0.001	0.935 (0.926–0.945)	<0.001
BVS	0.823 (0.761–0.890)	<0.001	0.855 (0.790–0.924)	<0.001
CABG	0.949 (0.932–0.966)	<0.001	0.952 (0.935–0.970)	<0.001
CPR	1.033 (1.016–1.050)	<0.001	1.022 (1.005–1.039)	0.013
In-hospital death	1.109 (1.094–1.123)	<0.001	1.081 (1.066–1.096)	<0.001
Women				
NSTEMI	0.992 (0.982–1.003)	0.161	0.985 (0.975–0.996)	0.009
DES	0.913 (0.900–0.927)	<0.001	0.927 (0.913–0.941)	<0.001
BVS	0.792 (0.686–0.914)	<0.001	0.816 (0.707–0.942)	0.006
CABG	0.944 (0.915–0.973)	<0.001	0.958 (0.929–0.988)	0.007
CPR	1.044 (1.021–1.068)	<0.001	1.039 (1.016–1.063)	0.001
In-hospital death	1.096 (1.081–1.113)	<0.001	1.079 (1.062–1.095)	<0.001

Abbreviations: MI = myocardial infarction; COPD = chronic obstructive pulmonary disease; NSTEMI = non-ST-segment elevation myocardial infarction; BMS = bare-metal stent; DES = drug eluting stent; BVS = drug eluting bioresorbable stent; CABG = coronary artery bypass graft; CPR = cardio-pulmonary resuscitation.

4. Discussion

Acute MI is a dynamic and life-threatening event resulting from rupture of an atherosclerotic plaque and development of an occlusive intracoronary thrombus [5]. An identification of specific seasonal patterns in the timing of acute MI events and the in-hospital mortality after acute MI is of importance, because such patterns as seasonal variation imply that there are specific triggers of acute MI external to the atherosclerotic plaque in the coronary arteries [18]. Although the impact of season with an increase of incidence as well as short-term mortality of IHD and its acute manifestation MI in the winter season has reported previously in several published studies for different countries [5,6,12,17,18], our study results add some important key findings. The main findings of our study analysing >3 million hospitalized patients with acute MI in the German nationwide sample could be summarized as follows:

I) The incidence of MI increased between 2005 and 2015, while the in-hospital mortality rate decreased from 14.1% to 11.3%.
II) Lowest incidence and in-hospital mortality of MI were observed in the summer season, while the incidence peak was in winter/spring months and highest in-hospital mortality in winter.
III) Male MI patients showed the lowest in-hospital mortality in the summer season, whereas female patients during fall.
IV) Elevated risk to die in the winter season was independent of age, sex and important comorbidities.
V) Low temperature dependency of in-hospital mortality seems more intensive in male than in female MI patients.

4.1. Incidence of acute MI

This is one of the largest samples ever to analyse seasonal patterns regarding incidence, in-hospital mortality and sex-specific differences in patients with acute MI.

In accordance with other studies about western populations, we recognized a slight increase in the incidence from 2005 to 2015 (Fig. S1 in supplementary material) [19,20], whereas other studies reported a decrease [21–24] or no change of the MI incidence over time [23,25]. The incidence of 334.7 MI events per 100,000 citizens in mean in Germany over the eleven year period was slightly higher than in Denmark (297/100,000 in males and 156/100,000 in females in 2012) [22] and the United States (287 per 100,000 citizens in 2008) [20].

In Germany, the lowest incidence of MI was observed in the summer season, while the incidence peak was in the winter and spring months. A winter increase in IHD and MI has been noted for several countries such as Canada [15], United States [5,7,18], Japan [11], Great Britain [6], Italy [13,26], Korea [27] and Germany [12]. We identified similar seasonal incidence variations between male and female MI patients (Fig. 1).

Germany is localized in the temperate climate zone of western Europe with annual mean temperatures between 8 and 9 °C, lowest mean temperatures in January (winter, approximately −0.5 to 0.5 °C) and highest in July (summer, approximately 17 to 18 °C). As expected, beside the seasonal patterns, temperatures were also directly correlated with MI incidence.

Previously published studies reported that the admissions rates for acute MI on days in which the minimum temperature fell below 3 °C was nearly doubled that found on days with a of ≥15 °C [6]; additionally, others described that a 10 °C decrease in temperature was associated with a 13% increase in MI event rates [16] and an increase in air temperature of 7.4 °C was associated with a 2.8% reduction in risk of MI [28].

Potential aetiologies for seasonal patterns are not well understood [5,11]. It has been proposed that temperature and the resulting variation in biological factors mediate the seasonal differences [11]. Environmental temperature has an important impact on the onset of acute MI, but seasonal variation is most likely caused multi-factorially [5,11]. Colder weather influences a large number of parameters and is accompanied by an increase in sympathetic tone, heart rate, blood pressure, frequency of atrial spasm, myocardial oxygen consumption, haematocrit, granulocyte count, cortisol level, serum cholesterol and triglyceride levels, red blood cell and platelet count, plasma beta-thromboglobulin, platelet factor 4, activated factor VII and plasma fibrinogen, whereas anti-thrombin III decreased with colder temperatures [5,6,11,18]. Especially, elevated lipid levels and the presence of active inflammation may contribute that arterial plaques are more vulnerable to rupture [6]. Additionally, stressors like air pollution, pneumonia and influence epidemics might contribute to a higher incidence of MI in the winter [11,29]. Air pollution is predominantly high in the winter months [29,30] and associated with both an increased incidence of pulmonary diseases [29,31] as well as acute MI [29,32]. Furthermore, patients with acute MI were found to have lower 25-hydroxy vitamin D3 levels and it is well known that duration of light per day influences several parameters including 25-hydroxy vitamin D3 levels [5]. Other physiological systems of the human body, which have shown a seasonal periodicity comprise fibrinolytic activity, plasma cortisol levels, serum lipids and platelet serotonin levels [5]. In addition, physical activity is dramatically reduced due to colder temperatures especially in older individuals, which favours prothrombotic changes [33–38]. Germany is one of the countries with high numbers of annual holiday travels. In total, 69.6 million holiday travels longer than 4 days of individuals older than 14 years were recorded in Germany (2017); the majority of travels in the summer season [39]. Thus, more individuals were in summer holidays far from Germany. This might also contribute to lower incidence of MI in the summer season in Germany.

4.2. In-hospital mortality rate

Our results confirm a decrease of the in-hospital mortality from 2005 to 2015 in accordance with a large body of evidence [19,20,22,24,40,41]. The in-hospital mortality rate due to acute MI in Germany was 14.1% in 2005 and 11.3% in 2015 and thus higher than the reported 30-day mortality rate in the United States (10.5% in 1999 and 7.8% in 2008) [20]. It is a limitation of our study, that we analysed in-hospital outcomes only. In this context, it is well-known that a high proportion of sudden cardiac deaths are caused by MI. It is well described for Germany, that sudden cardiac death occurred in 81 cases per 100,000 population and in 12.5% of these cases, patients did not reach a hospital [42].

In parallel with the sex-unspecific MI incidence, the lowest mortality was found in the summer season, while the highest in-hospital mortality rate was seen in the winter season. The sex-unspecific peak of the in-hospital mortality was during winter and lowest mortality rate in the summer, which is in accordance with the majority of studies [8,11,13,43,44]. In contrast, one study demonstrated highest mortality rate in the winter and lowest in spring [5], respectively another study the lowest mortality rate in fall [15] and one further study was not able to show any seasonal variation regarding the in-hospital mortality rate of patients with MI [7]; but it has to be kept in mind that these studies were performed in different climate zones.

It was presumed that the higher mortality rate during the winter was attributed to a higher number of comorbidities [5,11] as well as an increased age of the MI patients during winter months [15]. Sheth et al. [15]. confirmed that the seasonal mortality variation in acute MI deaths (winter vs. summer) increased with growing age and the authors hypothesised that older MI patients had a decreased physiological reserve, which might be in part an explanation for the higher mortality rate in the winter [15]. Our study demonstrated a higher proportion of MI patients with an age >70 years during the winter in comparison to summer season (Table 1). However, the multivariate logistic regression analyses showed that the seasonal variation regarding the in-hospital mortality was independent of age, sex and important comorbidities. Thus, we could reject the presumed explanations of the seasonal mortality-variation regarding age and the investigated comorbidities. One clinical pathology study reported a significant difference in conditions, which could potentially contribute to the seasonal mortality variation in MI. Haemopericardium as an important complication of acute MI caused by full thickness ventricular wall infarction and subsequent rupture into the pericardium was more often observed in the winter season than in the summer season in the post-mortem pathological examinations of patients with acute MI [8].

Nagarajan et al. [7] identified some seasonal treatment variations between patients admitted for acute MI in summer and winter seasons. Patients admitted in summer revealed a significant shorter door to balloon time than those admitted in the winter. Accordingly, the proportion of MI patients with a door to balloon time >90 min was significantly higher in winter than in summer. In addition, some differences in administered medications were detected [7].

In accordance with these mentioned seasonal treatment differences by Nagarajan et al. [7], we observed a higher rate of DES implantation and CABG surgeries in the summer compared to winter season. These reperfusion treatments are currently the recommended treatment for the majority of patients with acute MI with significant coronary artery stenosis [1,45,46]. While the rates of BMS and DES were approximately similar in winter and spring, the implantations of DES outweighs the number of BMS implantations in summer and fall during the obeserved study period. The proportion of MI patients treated with CABG, BMS and DES in Germany was comparable with numbers of the United States of America (revascularizations within 30 days after MI: 40.7% in 1999 and 47.2% in 2008) [20], but was higher than in England, where only 19% of the MI patients received a percutaneous transluminal coronary angioplasty and only 0.8% a CABG [47]. Thus, we identified some potential factors which might contribute to the seasonal variation of the in-hospital mortality rates, but we were not able to explain the underlying causes of the increased hospital case-fatality rate in the winter season at all.

Remarkable, our results identified a sex-specific difference regarding the seasonal variation of in-hospital mortality rate due to acute MI. In females, lowest mortality rate was observed in fall and not during summer. In contrast, male MI patients had their lowest in-hospital mortality rate in the summer season. Also Gebhard et al. [48] identified that the impact of environmental parameters on the outcomes of acute MI were sex-dependent. Winter season was found to be a predictor of cardiogenic shock in female MI patients, but not in male. The proportion of women suffering from MI and arriving in cardiogenic shock was in winter higher than in summer and if outside temperatures were lower, significantly more young women presented with KILLIP class IV ST-segment-elevation MI [48].

Additionally, studies suggested an increase regarding acute MI deaths related to higher levels of air pollution [49], which is higher in the winter months [30].

5. Limitations

There are certain limitations of our study that require consideration. A study limitation is that the study results are based on ICD discharge codes, which might lead to incomplete data due to under-reporting/under-coding. Important clinical data such as information about cardiac Troponins, echocardiographic examination or concomitant medications are missing. In addition, we analysed a long time span between 2005 and 2015 with a change in treatment modalities (shift from thrombolysis to angioplasty and introduction of new antiplatelet medications and treatment regimens) and classification/definition of MI. Despite these changes over time, we observed a seasonal variation in all of the annual analyses (Fig. S2 of the supplementary material). The focus of our study was on the clear endpoints in-hospital death and CPR. A further major limitation of our study is that the investigators had no direct access to the data of individual patients, but only access to aggregated data provided by the Federal Statistical Office of Germany.

6. Conclusions

The incidence of MI increased from 2005 to 2015, whereas the in-hospital mortality rate decreased from 14.1% to 11.3%. Seasonal variation of both incidence and in-hospital mortality of patients with acute MI were of substantial magnitude with lowest incidence and lowest mortality during the summer season, while the incidence peak was in winter/spring months and highest in-hospital mortality in the winter season. We observed sex-specific differences regarding the seasonal variation of the in-hospital mortality: while male MI patients showed the lowest in-hospital mortality in the summer season, female patients revealed the minimal in-hospital mortality during fall. Temperature dependency of in-hospital mortality regarding low temperature seems more intensive in male than in female MI patients.

Acknowledgements

We thank the Federal Statistical Office of Germany (Statistisches Bundesamt, DEStatis) for providing the data and the kind permission to publish these data/results.

Funding

This study was supported by the German Federal Ministry of Education and Research (BMBF 01EO1003 and BMBF 01EO1503). The authors are responsible for the contents of this publication.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.04.035.

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