Critical Care

RESEARCH LETTER

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Seasonal trends of incidence and outcomes of cardiogenic shock : findings from a large, nationwide inpatients sample with 441,696 cases

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Keywords: Cardiogenic shock, Seasonal trends, Winter, Myocardial infarction, Mechanical circulatory support, Outcomes, Mortality

Research letter

An increase in the annual incidence of cardiogenic shock (CS) and a growing sub-population of patients without acute myocardial infarction (AMI) was documented in Germany [1]. However, contemporary data regarding seasonal trends of CS irrespective of the underlying cause are rare.

In this study, we aimed to analyze seasonal trends of (i) incidence; (ii) patient characteristics; and (iii) outcomes in a nation-wide sample of more than 400,000 CS cases between 2005 and 2017 in Germany.

For the present analyses, all CS cases (ICD-10-GM code R57.0) in patients ≥ 18 years between 2005 and 2017 in Germany were included. Patients were categorized based on admission in one of four groups: spring, summer, fall, and winter.

Temperature-related morbidity and mortality is a growing public health issue. Several studies outside Germany demonstrated more fatal and nonfatal cardiovascular events in the winter than in the summer [2], but contemporary data is missing. We show in our study: the highest incidence of CS was recorded during the winter, while the lowest incidence of CS was observed in the summer. The number of patients admitted with CS in the winter exceeded those in the summer by almost 10,000 (Table 1). Our study also revealed that in-hospital mortality of CS patients was higher in the winter than in the summer (winter vs. summer, n = 70,727 (61.1%) vs. n = 62,379 (58.8%), p < 0.001) (Fig. 1). Additionally, we found that patients admitted with CS in the winter were slightly older than in those admitted in the summer (winter vs. summer, mean age 71.1 (± 13.6) vs. 70.8 (± 13.8), whereas sex did not differ over the seasons (p = 0.8). Notably, incidence of AMI, pre-hospital and in-hospital cardiac arrest among CS patients varied across seasons as well (p < 0.001). This is in line with previous studies showing increased incidence of sudden cardiac death in the winter [3].

The field of temporary mechanical circulatory support (MCS) to manage patients with CS enhanced in the last decade [4]. In this study, intra-aortic balloon pump (IABP) was the most used assist device, followed by veno-arterial extracorporeal membrane oxygenation (VA-ECMO) and left ventricular assist device (LVAD) in CS patients, illustrating the perceived clinical need for MCS devices.

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Table 1 Overall seasonal trends of CS cases in Germany from 2007 to 2015

	Winter (N = 115,710; 26.2%)	Spring (N = 108,949; 24.6%)	Summer (N = 105,980; 23.9%)	Fall (N = 111,057; 25.1%)	p value
Demographics					
Age, years	71.1 ± 13.6	70.7 ± 13.7	70.8 ± 13.8	71.0 ± 13.7	< 0.001
Sex, female	44,927 (38.8%)	42,141 (38.6%)	41,191 (38.8%)	43,124 (38.8%)	0.814
Outcomes					
In-hospital mortality	70,727 (61.1%)	64,382 (59.0%)	62,379 (58.8%)	67,381 (60.6%)	< 0.001
Clinical presentation					
Acute myocardial infarction	54,780 (47.3%)	52,745 (48.4%)	50,500 (47.6%)	53,967 (48.5%)	< 0.001
Pre-hospital cardiac arrest	16,540 (14.2%)	16,272 (14.9%)	16,145 (15.2%)	16,956 (15.2%)	< 0.001
Intra-hospital cardiac arrest	44,038 (38.0%)	40,818 (37.4%)	39,705 (37.4%)	42,890 (38.6%)	< 0.001
Post cardiothoracic surgery	4060 (3.5%)	3920 (3.6%)	3842 (3.6%)	3899 (3.5%)	0.329
Severe pulmonary embolism	4629 (4.0%)	4251 (3.9%)	4374 (4.1%)	4626 (4.1%)	0.006
Acute myocarditis	452 (0.3%)	318 (0.2%)	332 (0.3%)	368 (0.3%)	< 0.001
Treatment					
Invasive ventilation	52,354 (45.2%)	48,356 (44.3%)	46,957 (44.3%)	49,505 (44.5%)	< 0.001
Non-invasive ventilation	13,979 (12.0%)	13,220 (12.1%)	13,083 (12.3%)	13,619 (12.2%)	0.271
Dialysis	19,412 (16.7%)	18,307 (16.8%)	17,634 (16.6%)	18,423 (16.5%)	0.459
IABP	11,812 (10.2%)	11,307 (10.3%)	10,689 (10.0%)	10,777 (9.7%)	< 0.001
LVAD	507 (0.4%)	494 (0.4%)	496 (0.4%)	468 (0.4%)	0.398
VA-ECMO	2374 (2.0%)	2453 (2.2%)	2430 (2.2%)	2568 (2.3%)	< 0.001

IABP intra-aortic balloon pump, *LVAD* left ventricular assist device, *VA-ECMO* veno-arterial extracorporeal membrane oxygenation

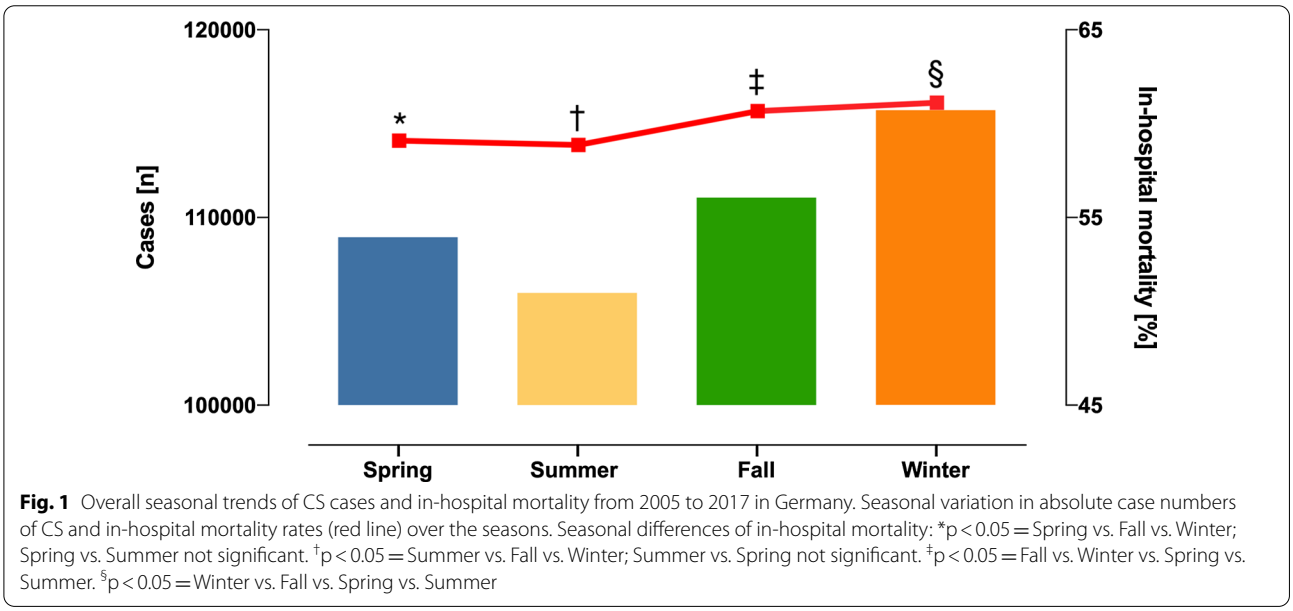

Fig. 1 Overall seasonal trends of CS cases and in-hospital mortality from 2005 to 2017 in Germany. Seasonal variation in absolute case numbers of CS and in-hospital mortality rates (red line) over the seasons. Seasonal differences of in-hospital mortality: *$p < 0.05$ = Spring vs. Fall vs. Winter; Spring vs. Summer not significant. †$p < 0.05$ = Summer vs. Fall vs. Winter; Summer vs. Spring not significant. ‡$p < 0.05$ = Fall vs. Winter vs. Spring vs. Summer. §$p < 0.05$ = Winter vs. Fall vs. Spring vs. Summer

The multidisciplinary shock team approach utilizing protocol-driven care appears to be feasible and to reduce mortality in patients with refractory CS [5, 6]. However, the extent to which the shock team approach and associated outcomes are affected by seasonal variations remains unclear. Further studies have to elucidate whether prolonged transport time due to adverse weather conditions, atherosclerotic/thrombotic incidences in terms of AMI, and time-dependent care processes are influenced by seasonal variations and/or lower temperatures.

The strengths of this study are the large sample size and the well-validated database. Clinical variables such

as laboratory values, physiological markers and follow-up data beyond the hospital stay were unfortunately not available in this administrative dataset. The exact time course of the different diagnoses e.g. being prevalent at admission or incident during the hospital stay was not possible to assess in this administrative dataset. This potential bias/confounding has to be taken under consideration when interpreting our results. Finally, validation of our results outside of Germany is needed.

In this nation-wide cohort of more than 400,000 CS patients, incidence and in-hospital mortality of CS varied substantially by season, with lowest incidence/mortality during the summer and highest incidence/mortality during the winter. A better understanding of these seasonal trends, and especially if these can be attributed to temperature changes or factors related to quality of care, needs to be evaluated in future research. This might have important implications for the care of CS patients and could help to improve outcomes.

Acknowledgements
Collaboration Study Group: Alexander M. Bernhardt[3], Hermann Reichenspurner[3], Paulus Kirchhof[1,2], Stefan Blankenberg[1,2].

Authors' contributions
PMB, AG take responsibility for the integrity of the data and the accuracy of the data analysis. All persons have provided the corresponding author with permission to be named in the manuscript. *Study concept and design:* PMB, AG, BS. *Acquisition, analysis, or interpretation of data:* PMB, AG, DW. *Drafting of the manuscript:* PMB, AG. *Critical revision of the manuscript for important intellectual content:* PMB, AG, BS, NF, MS, DW, AMB, HR, PK, SB. *Statistical analysis:* AG, PMB, *Administrative, technical, or material support:* PMB, AG, BS, NF, MS, DW. All authors read and approved ther final manuscript.

Funding
The study itself was funded by the University Heart and Vascular Center Hamburg. PMB and BS are currently funded by the German Research Foundation. This work was partially supported by European Union BigData@Heart (Grant Agreement EU IMI 116074), British Heart Foundation (PG/17/30/32961 to PK; AA/18/2/34218 to PK), German Centre for Cardiovascular Research supported by the German Ministry of Education and Research (DZHK, via a grant to AFNET to PK), and Leducq Foundation to PK.

Availability of data and materials
Data and material are available.

Code availability
Software codes are available.

Declarations

Ethics approval
Not applicable.

Consent to participate
Informed consent was obtained from legal guardians.

Consent to publication
Not applicable.

Competing interests
The authors designed the study, analyzed the data, vouch for the data, wrote the paper, and decided to publish. Analysis provided by the Research Data Center of the Federal Bureau of Statistics, Wiesbaden, Germany. All authors have read and approved the manuscript. The manuscript and its contents have not been published previously and are not being considered for publications elsewhere in whole or in part in any language, including publicly accessible web sites or e-print servers. BS has received speakers fee from AstraZeneca and Abiomed (unrelated to the submitted work). DW has received speakers fee from AstraZeneca, Bayer, Novartis and Abiomed (unrelated to the submitted work). PK receives research support for basic, translational, and clinical research projects from European Union, British Heart Foundation, Leducq Foundation, Medical Research Council (UK), and German Centre for Cardiovascular Research, from several drug and device companies active in atrial fibrillation, and has received honoraria from several such companies in the past, but not in the last three years (unrelated to the submitted work). PK is listed as inventor on two patents held by University of Birmingham (Atrial Fibrillation Therapy WO 2015140571, Markers for Atrial Fibrillation WO 2016012783). SB has received speakers fee from Medtronic, Pfizer, Roche, Novartis, SiemensDiagnostics (unrelated to the submitted work). MS reports personal fees from Abbott, Biotronik, Boston Scientific, Edwards Lifesciences and from Medtronic (unrelated to the submitted work). RSP has received honoraria from Abiomed and Medtronic (unrelated to the submitted work). AMB reports personal fees from Abbott, Abiomed, AstraZeneca, BerlinHeart, Medtronic, Novartis (unrelated to the submitted work). The following authors had nothing to declare: PMB, NF, AG.

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Received: 28 April 2021 Accepted: 25 June 2021
Published online: 06 September 2021

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