

ORIGINAL PAPER

Seasonal variation in the management and outcomes of cardiac arrest complicating acute myocardial infarction

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Summary

Background: There are limited data on the influence of seasons on the outcomes of acute myocardial infarction-cardiac arrest (AMI-CA).

Aim: To evaluate the outcomes of AMI-CA by seasons in the United States

Design: Retrospective cohort study

Methods: Using the National Inpatient Sample from 2000 to 2017, adult (>18 years) admissions with AMI-CA were identified. Seasons were defined by the month of admission as spring, summer, fall and winter. The outcomes of interest were prevalence of AMI-CA, in-hospital mortality, use of coronary angiography, percutaneous coronary intervention (PCI), hospital length of stay, hospitalization costs and discharge disposition.

Results: Of the 10 880 856 AMI admissions, 546 334 (5.0%) were complicated by CA, with a higher prevalence in fall and winter (5.1% each) compared to summer (5.0%) and spring (4.9%). Baseline characteristics of AMI-CA admissions admitted in various seasons were largely similar. Compared to AMI-CA admissions in spring, summer and fall, AMI-CA admissions in winter had slightly lower rates of coronary angiography (63.3–64.3% vs. 61.4%) and PCI (47.2–48.4% vs. 45.6%). Compared to those admitted in the spring, adjusted in-hospital mortality was higher for winter {46.8% vs. 44.2%; odds ratio (OR) 1.08 [95% confidence interval (CI) 1.06–1.10]; $P < 0.001$ }, lower for summer [43% vs. 44.2%; OR 0.97 (95% CI 0.95–0.98); $P < 0.001$]

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and comparable for fall [44.4% vs. 44.2%; OR 1.01 (95% CI 0.99–1.03); $P = 0.31$] AMI-CA admissions. Length of hospital stay, total hospitalization charges and discharge dispositions for AMI-CA admissions were comparable across the seasons.

Conclusions: AMI-CA admissions in the winter were associated with lower rates of coronary angiography and PCI, and higher rates of in-hospital mortality compared to the other seasons.

Introduction

Seasonal variation in the incidence and outcomes among patients presenting with acute myocardial infarction (AMI) has been previously reported.^{1,2} Most studies confirm a higher incidence of AMI during the winter months as compared to other seasons. Furthermore, contemporary data on the seasonal variation among patients with AMI stratified by the type of AMI [ST-segment-elevation myocardial infarction (STEMI) and non-ST-segment-elevation myocardial infarction (NSTEMI)] report worse outcomes during the winter months.^{1,2} Studies evaluating the chronobiology of AMI have not only reported a circadian and seasonal periodicity but also elucidated the potential role of environmental factors, such as air pollution and infections, such as influenza, common in winter months.^{3–5}

Our group has previously studied the impact of seasons and concomitant respiratory infections on the management and outcomes of AMI.^{2,3} However, the impact of seasons on cardiac arrest (CA) rates has been infrequently studied.^{5–8} CA rates have varied depending on the location of the country, the exposure to extremes of temperature and the presence of risk factors, such as viral infections and environmental pollution. However, the contemporary national data on CA complicating AMI and their relationship with the seasons in the USA are incompletely understood. Therefore, through this study, we sought to assess the seasonal variations in clinical outcomes of AMI complicated by CA. Using a nationally representative database, we sought to assess the seasonal variations in clinical outcomes of acute myocardial infarction-cardiac arrest (AMI-CA) while evaluating the characteristics and management of these patients. We hypothesized that winter admissions would be associated with higher rates of CA and worse outcomes due to the changes in the pathobiology of cardiac disease with seasonal variation.

Materials and methods

Study population, variables and outcomes

The National (Nationwide) Inpatient Sample (NIS) is the largest all-payer database of hospital inpatient stays in the USA. NIS contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Quality and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.⁹ Information regarding each discharge includes patient demographics, primary payer, hospital characteristics, principal diagnosis, up to 24 secondary diagnoses and procedural diagnoses. The HCUP-NIS does not capture individual patients but captures all information for a given admission. Institutional Review Board approval was not sought due to the publicly available nature of this de-identified database. These data are available to other authors via the HCUP-NIS database with the Agency for Healthcare Research and Quality.⁹

Using the HCUP-NIS data from 2000 to 2017, a retrospective cohort study of adult admissions (>18 years) with AMI in the primary diagnosis field [International Classification of Diseases

9.0 Clinical Modification (ICD-9CM) 410.x and ICD-10CM I21.x–22.x] were identified.^{10,11} A concomitant diagnosis of CA in any of the secondary diagnosis fields was identified using ICD-9CM 427.5, 427.41, 99.60 and 99.63; ICD-10CM I46.x, I49.01 and I49.02; and ICD-10PCS 5A12012.^{11–13} These administrative codes have a high positive predictive value for the presence of CA, but they show poor discrimination between in-hospital and out-of-hospital CA, therefore all CA admissions were grouped together for main analyses.^{11,12} However, in-hospital cardiac arrest (IHCA) can be identified with a high positive predictive value of 83% using the procedural code for cardiopulmonary resuscitation (CPR) (ICD-9CM 99.60, 99.63),¹² we performed subgroup analyses for IHCA and non-IHCA groups. Similar to prior literature, we defined the seasons based on the meteorological classification of the Northern Hemisphere as—spring (March–May), summer (June–August), fall (September–November) and winter (December–February).^{1,2} Admissions that did not have information on admission month were excluded [$n = 741\,672$ (6.4%)]. The Deyo's modification of the Charlson Comorbidity Index was used to identify the burden of co-morbid diseases (Supplementary Table S1).¹⁴ Demographic characteristics, hospital characteristics, acute organ failure, mechanical circulatory support, cardiac procedures and non-cardiac organ support use were identified for all admissions using previously used methodologies from our group.^{2,10,11,15–18} Similar to prior literature, we defined early coronary angiography as that performed on the day of hospital admission (day 0).^{17,19}

The primary outcome was the seasonal variation in the prevalence of CA among AMI admissions and the in-hospital mortality in admissions with AMI-CA. The secondary outcomes included receipt of coronary angiography (overall and early), percutaneous coronary intervention (PCI) and mechanical circulatory support, hospital length of stay, hospitalization costs and discharge disposition. Stratified analyses were performed for type of AMI (STEMI vs. NSTEMI) and type of CA (IHCA vs. non-IHCA). Seasonal variation in outcomes of AMI-CA was also evaluated in subgroups of hospital regions.

Statistical analysis

As recommended by HCUP-NIS, survey procedures using discharge weights provided with HCUP-NIS database were used to generate national estimates.²⁰ Using the trend weights provided by the HCUP-NIS, samples from 2000 to 2011 were re-weighted to adjust for the 2012 HCUP-NIS re-design.²⁰ Chi-square and t-tests were used to compare categorical and continuous variables, respectively. Multivariable logistic regression was used to analyze trends over time (referent year 2000). Univariable analysis for trends and outcomes was performed and was represented as odds ratio (OR) with 95% confidence interval (CI). Multivariable logistic regression analysis incorporating age, sex, race, primary payer status, socio-economic stratum, hospital characteristics, comorbidities, organ failure, AMI-type, cardiac rhythm (shockable vs. non-shockable), cardiac procedures and non-cardiac procedures was performed for assessing association of seasons with in-hospital mortality and temporal trends

of in-hospital mortality. For the multivariable modeling, regression analysis with purposeful selection of statistically (liberal threshold of $P < 0.20$ in univariate analysis) and clinically relevant variables was conducted. Two-tailed $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS v25.0 (IBM Corp., Armonk, NY).

Best practices relating to the use of the HCUP-NIS database, such as not assessing individual hospital-level volumes (due to changes to sampling design detailed above), treating each entry as an 'admission' as opposed to individual patients, restricting the study details to inpatient factors since the HCUP-NIS does not include outpatient data and limiting administrative codes to those previously validated and used for similar studies, were adhered to during data analysis.²⁰

Results

There were a total of 10 880 856 AMI admissions with information on admission month available between 1 January 2000 and 31 December 2017 in the HCUP-NIS database. Among these, 546 334 (5.0%) were complicated by CA overall, and incidence of CA was 4.9% in spring, 5.0% in summer, 5.1% in fall and 5.1% in winter

AMI admissions. Among those complicated with CA ($n = 546\,334$), incidence of IHCA was 30.2% in spring, 29.6% in summer, 30.3% in fall and 31.5% during winter. Unadjusted temporal trends over 18-years of the study period demonstrated a significant increase in STEMI-CA admissions and a slight increase in NSTEMI-CA admissions across all seasons (Figure 1A). Adjusted trends, however, identified a steady increase in STEMI-CA admissions with a relatively stable or declining trend for NSTEMI-CA admissions across all seasons (Figure 1B). Baseline characteristics of AMI-CA admissions admitted in various seasons were largely similar, but those admitted in summer were less often female, had lower comorbidity, more often presented with STEMI and had higher rates of shockable rhythms compared to AMI-CA admissions in spring, fall and winter (Table 1). Similar findings of lower comorbidity and higher rates of STEMI were seen in subgroups of IHCA and non-IHCA (Supplementary Tables S2 and S3).

Compared to AMI-CA admissions in other seasons, those admitted in winter had slightly lower rates of coronary angiography (61.4% vs. 63.3–64.3%) and PCI (45.6% vs. 47.2–48.4%) ($P < 0.001$). Temporal trends revealed an increase in use of early coronary angiography, coronary angiography, PCI and mechanical circulatory support across all seasons over the study period

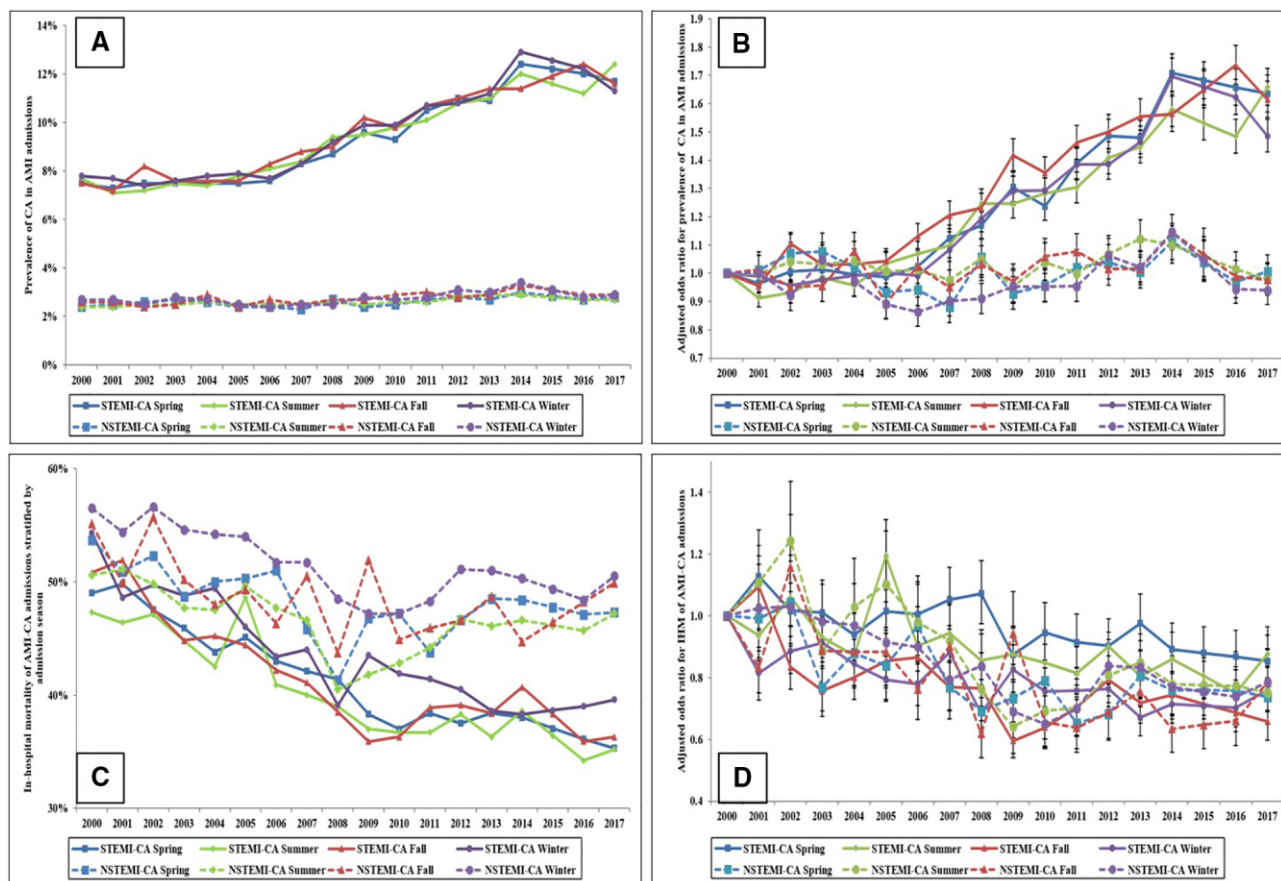


Figure 1. Trends in the prevalence and in-hospital mortality in AMI-CA admissions stratified by the type of AMI. (A) Unadjusted temporal trends of the proportion of AMI admissions with CA stratified by the type of AMI during spring, summer, fall and winter ($P < 0.001$ for trend over time); (B) adjusted odds ratio for STEMI and NSTEMI admissions with CA by year (with 2000 as the referent); adjusted for age, sex, race, comorbidity, primary payer, socio-economic status, hospital region, hospital location and teaching status and hospital bed-size ($P < 0.001$ for trend over time); (C) unadjusted in-hospital mortality in AMI-CA admissions stratified by the type of AMI during spring, summer, fall and winter ($P < 0.001$ for trend over time); and (D) adjusted odds ratio for in-hospital mortality by year (with 2000 as the referent) in AMI-CA admissions stratified by type of AMI; adjusted for age, sex, race, comorbidity, primary payer, socio-economic status, hospital region, hospital location and teaching status, hospital bed-size, multiorgan failure, cardiogenic shock, influenza and pneumonia infections, coronary angiography, PCI, pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation and acute hemodialysis ($P < 0.001$ for trend over time). AMI, acute myocardial infarction; CA, cardiac arrest; NSTEMI, non-ST-segment-elevation myocardial infarction; STEMI, ST-segment-elevation myocardial infarction.

Table 1. Baseline and in-hospital characteristics of AMI-CA admissions stratified by admission season

Characteristics		Spring (N = 139 363)	Summer (N = 132 050)	Fall (N = 131 251)	Winter (N = 143 669)	P
Age (years)		66.7 ± 13.6	66.3 ± 13.5	66.8 ± 13.5	67.2 ± 13.4	<0.001
Female		35.6	34.2	35.0	35.3	<0.001
Race	White	63.6	62.8	63.0	63.8	<0.001
	Black	7.8	8.2	8.0	8.0	
	Others ^a	28.6	29.0	29.0	28.3	
Primary payer	Medicare	55.3	54.2	55.6	57.2	<0.001
	Medicaid	7.0	7.2	6.8	6.7	
	Private	29.0	29.2	28.5	27.4	
	Others ^b	8.7	9.4	9.2	8.7	
Quartile of median household income for zip code	0–25th	24.0	23.9	23.3	24.1	<0.001
	26th–50th	26.1	26.4	26.5	26.4	
	51st–75th	24.9	24.9	24.9	24.4	
	75th–100th	24.9	24.8	25.3	25.1	
Charlson comorbidity index	0–3	38.1	39.6	35.6	35.9	<0.001
	4–6	46.7	46.1	48.1	48.0	
	≥7	15.2	14.4	16.3	16.0	
Hospital teaching status and location	Rural	9.2	9.0	8.8	8.8	<0.001
	Urban non-teaching	38.6	37.8	38.8	39.1	
	Urban teaching	52.2	53.2	52.4	52.1	
Hospital bed-size	Small	9.8	9.8	9.7	9.9	0.21
	Medium	25.7	25.7	25.4	25.5	
	Large	64.5	64.4	64.9	64.6	
Hospital region	Northeast	18.4	18.1	18.5	18.4	<0.001
	Midwest	24.5	25.0	23.8	23.7	
	South	35.6	36.2	36.4	35.9	
	West	21.5	20.8	21.3	22.0	
AMI-type	STEMI	66.8	67.2	65.9	65.9	<0.001
	NSTEMI	33.2	32.8	34.1	34.1	
Atrial fibrillation or flutter		22.4	22.3	22.6	23.2	<0.001
Cardiogenic shock		27.7	28.0	27.3	27.8	0.001
Cardiac rhythm	Shockable	52.6	53.8	53.4	51.4	<0.001
	Non-shockable	47.4	46.2	46.6	48.6	
Respiratory infections	Influenza	0.1	0.0	0.1	0.3	<0.001
	Pneumonia	11.1	10.0	10.8	12.1	<0.001
Multorgan failure		43.1	43.6	42.6	44.1	<0.001
Mechanical circulatory support		21.0	20.5	20.6	20.5	0.003
Pulmonary artery catheterization		3.3	3.3	3.4	3.4	0.17
Invasive mechanical ventilation		46.9	47.2	46.4	48.0	<0.001
Acute hemodialysis		1.7	1.5	1.9	1.7	<0.001

Represented as percentage or mean ± standard deviation.

AMI, acute myocardial infarction; CA, cardiac arrest; NSTEMI, non-ST-segment-elevation myocardial infarction; STEMI, ST-segment-elevation myocardial infarction.

^aHispanic, Asian or Pacific Islander, Native American and others.

^bSelf-pay, no charge and others.

(Figure 2A–D). The lower use of coronary angiography and PCI among winter admissions was consistent in subgroups of IHCA and non-IHCA (Supplementary Tables S4 and S5). Unadjusted in-hospital mortality was higher among winter AMI-CA admissions (46.8%) compared to spring (44.2%), summer (43.0%) and fall (44.4%) AMI-CA admissions ($P < 0.001$) (Table 2). Compared to those admitted in the spring, adjusted in-hospital mortality was higher for winter [OR 1.08 (95% CI 1.06–1.10); $P < 0.001$], lower for summer [OR 0.97 (95% CI 0.95–0.98); $P < 0.001$] and comparable for fall [OR 1.01 (95% CI 0.99–1.02); $P = 0.31$] AMI-CA admissions (Supplementary Table S6). These results were consistent when the admissions were further sub-divided into monthly data (Supplementary Table S7). In subgroup analyses stratified by type of AMI and type of CA, the winter season was associated with higher in-hospital mortality for AMI-CA admissions in NSTEMI-IHCA, STEMI-non-IHCA and NSTEMI-non-IHCA subgroups

(Supplementary Figure S1A–D). Similarly, the winter season was associated with higher in-hospital mortality for AMI-CA admissions compared to spring across all four geographic regions of the USA, with a relatively greater effect size in the Northeast and South regions (Supplementary Figure S2A–D). A decline in in-hospital mortality was seen in both STEMI-CA and NSTEMI-CA categories across all seasons in unadjusted and adjusted temporal trends (Figure 1C and D). Length of hospital stay, total hospitalization charges and discharge dispositions for AMI-CA admissions were comparable across the seasons (Table 2).

Discussion

In this study evaluating outcomes and management of AMI-CA admissions across seasons, we identified that winter admissions

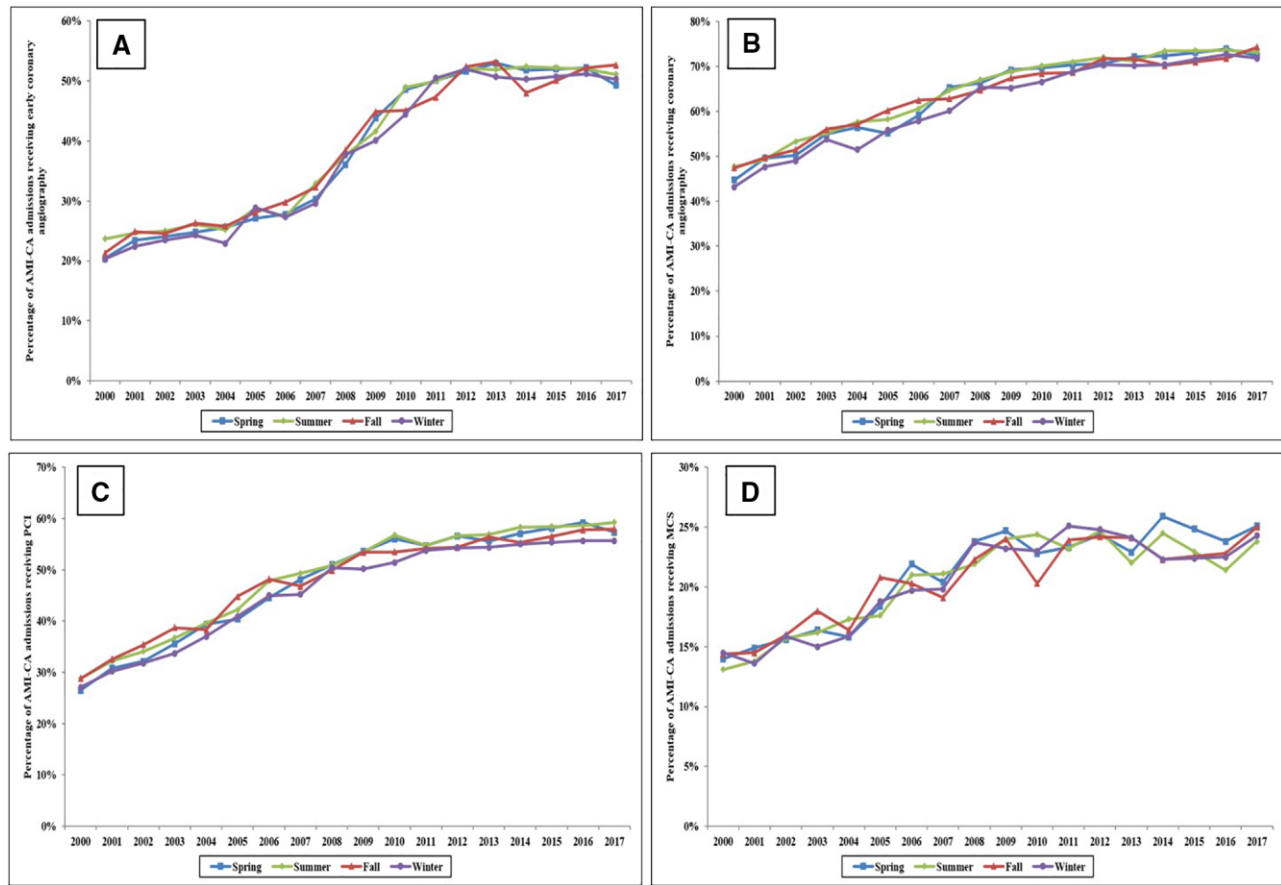


Figure 2. Temporal trends in the use of coronary angiography and PCI stratified by admission season. The 18-year temporal trends in the use of early coronary angiography (A); coronary angiography (B); PCI (C); and MCS (D); all $P < 0.001$ for trend over time. AMI, acute myocardial infarction; CA, cardiac arrest; MCS, mechanical circulatory support; NSTEMI, non-ST-segment-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation myocardial infarction.

Table 2. Clinical outcomes of AMI-CA admissions stratified by admission season

Characteristics	Spring (N = 139 363)	Summer (N = 132 050)	Fall (N = 131 251)	Winter (N = 143 669)	P
Coronary angiography	63.3	64.3	63.3	61.4	<0.001
Percutaneous coronary intervention	47.2	48.4	47.4	45.6	<0.001
Coronary artery bypass grafting	10.2	9.7	9.6	10.0	<0.001
In-hospital mortality	44.2	43.0	44.4	46.8	<0.001
Length of stay (days)	7.7 ± 10.3	7.6 ± 9.8	7.6 ± 10.1	7.8 ± 10.3	<0.001
Palliative care consultations	4.7	4.9	4.7	4.9	0.02
Do-not-resuscitate status	6.0	6.0	6.0	6.2	0.10
Hospitalization costs ($\times 1000$ USD)	106.5 ± 146.1	107.2 ± 145.9	105.0 ± 144.7	106.9 ± 156.9	0.001
Discharge disposition					<0.001
Home	54.9	55.8	56.5	54.6	
Transfer	12.3	11.9	11.8	11.7	
Skilled nursing facility	20.6	20.9	20.4	21.7	
Home with HHC	11.7	10.9	10.7	11.4	
Against medical advice	0.5	0.6	0.7	0.6	

Represented as percentage or median (interquartile range).

AMI, acute myocardial infarction; CA, cardiac arrest; HHC, home health care; USD, United States Dollars.

with AMI-CA had higher in-hospital mortality in comparison to those admitted during the summer months. We also identified lower rates of guideline-directed therapies (coronary angiography and PCI) among winter AMI-CA admissions while highest

rates were seen among summer AMI-CA admissions. Overall, an increase in the use of these cardiac procedures and a decline in the in-hospital mortality of AMI-CA admissions were noted in both STEMI and NSTEMI admissions across all seasons.

The observations from this largest study exploring the seasonal patterns in AMI-CA are consistent with that reported in the literature for other presentations of AMI.^{5–8} In our study, not only the prevalence of AMI-CA is increased but the outcomes are also worse during the winter months.^{8,21–25} From this database, causation cannot be determined; however, we can theorize the role of cold climate on hemodynamics, blood coagulation parameters, increased systemic vascular resistance and myocardial oxygen consumption, as possible explanations for the increased prevalence of AMI during winter months.^{6,26,27} Concurrent respiratory infections during the winter months and even air pollution have also been postulated as triggers for acute cardiovascular events leading to AMI and subsequent CA. In addition, worse transportation and road conditions, social isolation, and emotional and social influences on mental and physical health during the colder months may also have influenced the observed outcomes.^{4,5} We are, however, not able to rule out the possibility of reduction of AMI-CA during the summer months relative to winter and other seasons, which may provide alternate explanations to the noted higher rates of winter CA admissions.

These data are consistent with higher rates of CA from diverse settings, such as Europe, Asia and various parts of the USA.^{5–8} In epidemiological data from the Olmsted County Minnesota, Gerber et al.⁵ demonstrated higher rates of sudden cardiac death in the winters between 1979 and 2002. They report a stepwise increase in the incidence of CA with amount of snowfall, suggestive of the impact of temperature. Furthermore, infarct sizes from AMI are largest in the winter and smallest in the summer, which may additionally contribute to the higher rates of CA and worse outcomes in this population.²⁸ In a recent study from the HCUP-National Emergency Department Sample, El Sibai et al.²⁹ noted highest rates of out-of-hospital CA during the December and January months, which is also associated with higher in-hospital mortality. These patients were all comers with out-of-hospital CA, as compared to our study, which is specific to admissions with AMI. In addition, the results of our study were consistent across the subgroups stratified by location of arrest (IHCA vs. non-IHCA) and type of AMI (STEMI and NSTEMI). Despite the differences in winter temperatures across the continental United States, the mortality in the winter season was consistently high across all geographic regions, suggestive of chronobiological influences independent of the temperature.^{2,3} The in-hospital outcomes are worse in AMI-CA admissions during winter months even as the temporal trends show improvement over time. Lower rates of guideline-directed therapies such as coronary angiography and percutaneous or surgical revascularization along with higher comorbidity burden in patients presenting during winter months likely contribute to the worse outcomes. The cardiogenic shock rates were similar across all the seasons and interestingly, infections including influenza or higher presentation with NSTEMI during winter months were not associated with adverse outcomes. Importantly, this study shows that winter admissions were older and had higher rates of comorbidities, higher rates of NSTEMI and more frequent non-shockable rhythms, alluding to the role of seasons as precipitants for CA in AMI independent of cardiac disease.

Limitations

This study has several limitations, despite the HCUP-NIS database's attempts to mitigate potential errors by using internal and external quality control measures. Echocardiographic data,

angiographic variables and hemodynamic parameters were unavailable in this database, which limits physiological assessments of disease severity. We are unable to assess further detailed metrics, such as receipt of bystander CPR, witnessed nature of CA, total ischemic time and door-to-balloon time. Important factors such as the delay in presentation from time of onset of AMI symptoms, timing of cardiogenic shock, CA and acute organ failure, reasons for not receiving aggressive medical care and treatment-limiting decisions of organ support could not be reliably identified in this database. It is possible that despite best attempts at controlling for confounders by a multivariate analysis, winter admission was a marker of greater illness severity due to residual confounding. Despite these limitations, this study addresses an important knowledge gap highlighting the national temporal evolution of the seasonal effect and the impact of concomitant influenza infection on AMI.

Conclusions

AMI-CA hospitalizations during winter had lower use of guideline-directed therapies and higher in-hospital mortality whereas summer admissions had lower in-hospital mortality. The influence of season on the pathobiology of acute cardiac processes and the logistical delays to travel and care in the winter season are worthy of further study using granular data.

Supplementary material

[Supplementary material](#) is available at *QJMED* online.

Conflict of interest. None declared.

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