The Impact of Environmental Factors on the Mortality of Patients With Chronic Heart Failure

Persio D. Lopez, MD[a,b], Eder H. Cativo-Calderon, MD[a,c], Diana Otero, MD[a,b], Mahjabeen Rashid, MD[a,b], Steven Atlas, MD[c,d], and Clive Rosendorff, MD, PhD[a,c,d,*]

Outcomes of acute heart failure hospitalizations are worse during the winter than the rest of the year. Seasonality data are more limited for outcomes in chronic heart failure and the effect of environmental variables is unknown. In this population-level study, we merged 20-year data for 555,324 patients with heart failure from the national Veterans Administration database with data on climate from the National Oceanic and Atmospheric Administration and air pollutants by the Environmental Protection Agency. The outcome was the all-cause mortality rate, stratified by geographical location and each month. The impact of environmental factors was assessed through Pearson's correlation and multiple regression with a family-wise $\alpha = 0.05$. The monthly all-cause mortality was 13.9% higher in the winter than the summer, regardless of gender, age group, and heart failure etiology. Winter season, lower temperatures, and higher concentrations of nitrogen dioxide were associated with a higher mortality rate in multivariate analysis of the overall population. Different environmental factors were associated in regions with similar patterns of temperature and precipitation. The only environmental factor associated with the mortality rate of patients dwelling in large urban centers was the air quality index. In conclusion, the mortality in chronic heart failure exhibits a seasonal pattern, regardless of latitude or climate. In this group of patients, particularly those of male gender, a higher mortality was associated with environmental factors and incorporating these factors in treatment plans and recommendations could have a favorable cost-benefit ratio. **(Am J Cardiol 2021;146:48−55)**

Heart failure (HF) affects an estimated 6.2 million patients in the United States (US).[1] Acute HF requiring hospitalization is more common during the winter in the US[2,3] and the prognosis of a HF-related hospitalization is worse during this season compared with the rest of the year.[2,4] Several large studies have confirmed this pattern in various countries throughout the world, including Japan,[5,6] Nigeria,[7] Italy,[8] and Brazil.[9] A similar pattern has been described in patients with chronic HF,[10,11] however, the data are more limited. Further, there is ongoing debate regarding the factors underlying the seasonal changes in HF mortality. Some have suggested that the answer lies in seasonal variations in the prevalence of respiratory[12,13] and acute cardiovascular diseases,[14,15] and in the levels of circulating catecholamines and systemic inflammation.[14,16] However, climate variables and air pollutants have also been associated with an increase in the rate of hospitalizations due to acute HF[17,18] and with a higher mortality rate (MR) in chronic HF.[19] We hypothesized that climate and pollution variables (collectively referred to as environmental variables hereon) contribute to the seasonal changes observed in HF mortality. We present the findings of a nation-wide study spanning nearly 20 years across a variety of climate regions.

Methods

The national Veterans Administration (VA) patient database contains records of approximately 23 million patients followed in 1,600 sites across the US and it can be accessed through the VA Informatics and Computing Infrastructure (VINCI). We performed a cross-sectional analysis of VINCI starting one month after database inception (November 1, 1999) and ending on September 30, 2019. The first and the last month were excluded from the analysis to ensure data accuracy. The protocol was approved by the Bronx Veterans' Affairs Institutional Review Board #1 and the study was performed in accordance with the 2013 Declaration of Helsinki. A full waiver of informed consent was obtained from the institutional review board to complete this study. All authors had access to the data.

We surveyed VINCI and included patients residing in the continental US if they had 1 admission with a primary diagnosis related to HF at discharge (ICD-9 code 428 and its derivations or ICD-10 code I50 and its derivations) or if they had 2 outpatient encounters with a HF code.[20] Data regarding demographics, co-morbidities, vital status, and geographical location were obtained. In the VA system, the vital status is determined from 4 sources to ensure accuracy: the Beneficiary Identification Records Locator Subsystem, the inpatient datasets, the Death Index from the Social Security Administration, and the Medicare Vital Status File.

[a]Mount Sinai Heart, Icahn School of Medicine at Mount Sinai, New York, New York; [b]Cardiology Department, James J. Peters V. A. Medical Center, Bronx, New York; [c]Cardiology/Hypertension Research Program, James J. Peters V. A. Medical Center, Bronx, New York; and [d]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York. Manuscript received October 21, 2020; revised manuscript received and accepted January 5, 2021.

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*Corresponding author: Tel: 212-865-3674.

E-mail address: clive@rosendorff.com (C. Rosendorff).

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To assess the impact of meteorological variables on patients with HF, we retrieved weather data for the study period from the Global Historical Climatology Network (Daily) dataset,[21] which is maintained by the National Oceanic and Atmospheric Administration. A description of the database and its methods has been published elsewhere.[22] The continental US weather information is obtained from over 49,000 climate monitoring stations and is the most comprehensive collection of US daily weather data available. Climatological information is updated in real-time and undergoes daily automated quality checks with semiautomated and manual confirmations when significant outliers are detected. We retrieved hourly and daily nation-wide values for the temperature, snowfall, snow depth, amount of precipitation (which includes all forms of rain, snow, and hail), weather conditions, and wind speed.

In addition, air quality data was obtained from the Air Quality System database, which is maintained by the US Environmental Protection Agency,[23] the federal agency responsible for monitoring and regulating the use of chemicals and pollutants. This database gathers hourly and daily concentrations for criteria pollutants from over 4,000 stations nationwide. The overall air pollution is also expressed through the air quality index, a pollutant-specific standardized scale that directly relates the contaminant concentration with its healthy impact in the community; lower is better. The pollutant with the highest air quality index is used to define the overall index for a specific location. We retrieved hourly values for the air quality index, the mass of suspended particulate matter, and the air concentrations of ozone, sulfur dioxide, carbon monoxide, and nitrogen dioxide. These pollutants were chosen based on literature review[17] and data availability.

Continuous variables were expressed as mean ± standard deviation or median and interquartile ranges, depending on their distribution, while categorical variables were expressed as counts and percentages. All analyses were run with SAS v.7.15 (SAS Institute Inc, Cary, North Carolina) with 95% confidence intervals. Given the large number of environmental factors and geographical locations, we used Bonferroni's correction for a family-wise $\alpha = 0.05$, resulting in $\alpha = 4.63\text{E-}5$ per comparison.

For each month of the study period, we calculated the following parameters: the MR; the number of incident cases of acute coronary syndromes, hypertensive crises, and pneumonia and/or influenza; the mean age of the cohort; and mean values for environmental variables. The MR, expressed per 1,000 patients with HF, was calculated as the ratio between the number of deaths and the number of patients in the cohort in a given month. To account for the variability caused by unusual weather events, the longitudinal data were used to calculate representative values for each of the 12 calendar months for every geographic stratum. We also used them to calculate representative seasonal values; the 4 seasons were defined using the meteorological classification for the Northern Hemisphere.

We stratified the data by county, state, and climatically-consistent regions. Climate regions are geographic areas in the continental US within which environmental variables exhibit a common pattern. They were defined through temporal and spatial analysis of temperature and precipitation data collected over the course of 86 years.[24,25] In addition to Alaska, the continental US has 9 climatically consistent regions; a map is available at the National Oceanic and Atmospheric Administration website.[26] These regions were used to assess the impact of environmental factors on the MR in a geographical area sharing a common climatological pattern, thus controlling for weather events that might not impact other areas in the US. In addition, they allowed us to compare the effect of environmental factors across different climatological patterns.

The primary outcome for this study was the monthly all-cause MR in patients with HF. Because the number of patients with HF in some counties was known to be insufficient to calculate an accurate MR, pre-specified analyses were performed using state-level data. We used Pearson's correlation and scatter plots to assess the relationship between the MR and the environmental variables, the mean age of the cohort, and the mean number of incident cases of acute coronary syndromes, hypertensive crises, and pneumonia/influenza. We ordered the seasons of the year by their average temperature and used Spearman's correlation to assess the relationship between them and the MR. Multiple regression was used to assess the effect of variables that were significant on univariate analyses while controlling for other factors. The seasons were included in the regression equation using dummy variables with summer as the reference season. A pre-specified geographical analysis was performed comparing the effect of environmental variables on the MR across the 10 climatically-consistent regions and within each of them.

We performed the following post-hoc sensitivity analyses. We selected counties with ≥100 patients with HF to reassess the relationship between environmental variables and the MR at a county level controlling for their Köppen climate type. The Köppen climate classification is commonly used to classify the world into 5 major climate groups −tropical, dry, temperate, continental, and polar. We also selected urban counties with ≥1 million habitants and reanalyzed the data to assess the impact of air pollutants in metropoles with a high population density. We analyzed the subset of patients followed since 2009 to see if our findings remained valid in a more contemporary group. Lastly, we performed a sensitivity analysis assessing the relationship between environmental variables and the MR using the longitudinal values instead of the summarized ones.

Results

After duplicates and records with missing information were removed, we identified 555,324 patients with HF across 130 centers over the course of 19 years and 9 months. The median length of follow-up was 45.2 months and there were 447,391 deaths. The baseline characteristics of this cohort and its geographical distribution are presented in Table 1. The mean yearly values of both overall precipitation and snowfall trended up during the study period; temperatures and wind speed trends remained unchanged. The air quality index and air pollutants exhibited an improvement during the study period; the exception was ozone, which remained essentially unchanged.

Every year of the study, the MR peaked during winter months and was at its lowest in the summer (see Figure 1A).

Table 1
Baseline characteristics and geographic distribution of the study cohort (n = 556,550)

Male	542,542 (97.70%)	Hypertension	480,564 (86.54%)
Female	12,782 (2.30%)	Hyperlipidemia	384,696 (69.27%)
Age (years)	74.90 ± 10.71	Diabetes mellitus	297,541 (53.58%)
<65	94,829 (17.04%)	CAD	398,206 (71.71%)
65-79	257,437 (46.26%)	PAD	135,449 (24.39%)
≥80	203,058 (36.49%)	CVA	103,175 (18.58%)
Asian	1,596 (0.29%)	AF/AFlut	246,695 (44.42%)
Black	86,217 (15.53%)	COPD	269,754 (48.58%)
Native American	2,996 (0.54%)	Climate Region	
Pacific Islander	3,416 (0.62%)	Alaska	779 (0.14%)
White	354,571 (63.85%)	Central	93,124 (16.77%)
Unknown	106,528 (19.18%)	East North Central	42,774 (7.70%)
Hispanic	14,871 (3.11%)	Northeast	83,620 (15.06%)
Single	48,702 (8.77%)	Northwest	37,123 (6.68%)
Married	257,199 (46.32%)	South	90,550 (16.31%)
Separated/Divorced	159,130 (28.66%)	Southeast	109,103 (19.65%)
Widowed	89,306 (16.08%)	Southwest	32,574 (5.87%)
Unknown	987 (0.17%)	West	51,802 (9.33%)
Urban-Rural Classification		West North Central	13,875 (2.50%)
Urban large city	153,792 (27.69%)		
Suburban large city	104,504 (18.82%)		
Medium-small city	176,003 (31.69%)		
Micropolitan & rural	120,300 (21.66%)		
Unknown	811 (0.15%)		

All statistics are expressed as n (%) or mean ± standard deviation. AF/AFlut = atrial fibrillation/atrial flutter; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; PAD = peripheral artery disease.

On average, the MR in winter months was 13.9% higher than in the preceding summer months. The smallest difference was between winter 2009 and the preceding summer (8.9%), while the greatest increase was seen in winter 2000 (18.9%). This seasonality was observed regardless of gender, age group, and HF etiology (Figure 1B-D), but it was not present in regions that spent most of the winter in below-freezing point temperatures −Alaska and the West North Central region (see online supplement). There was no association between the MR and the number of cases of acute coronary syndromes (r = 0.02; p = 0.6003), hypertensive crises (r = 0.00; p = 0.9626), or pneumonia/influenza (r = 0.09; p = 0.0331) in our sample.

Several environmental variables were significantly correlated with the MR on univariate analysis and we present them in Table 2. We used multiple regression to assess the impact of each environmental variable while controlling for other relevant variables (Table 2); only factors significant on univariate and scatter plot analyses were included. Since the different temperature variables (i.e., maximum, average, and minimum), the amount of snowfall, and the season of the year had a strong correlation between each other, we ran separate models substituting these variables to avoid collinearity. Winter season, lower maximum monthly temperatures, higher air concentrations of nitrogen dioxide, and higher age were independently associated with higher MR.

When we compared the impact of environmental variables across the 10 regions climatically-consistent regions, univariate analysis revealed that the season of the year (Spearman r = 0.65; p = 1.78E-15), the maximum temperature (r = -0.51; p = 3.41E-09), the amount of snowfall (r = 0.48; p = 2.52E-08), the number of days with heavy fog (r = 0.38; p = 1.71E-05), and the amount of particulate matter ≤10 μm in diameter (r = -0.38; p = 1.93E-05) were correlated with the MR in all regions. On multivariate analysis, only the winter remained significantly associated with the MR throughout the different regions: compared with the summer, the winter resulted in an increase in the MR of 1.82 deaths per thousand patients (CI 1.19 to 2.46; p = 1.12E-07). We then analyzed the effect of environmental factors (other than seasons) within each climate region. Since the climate regions are defined by common patterns in temperature and precipitation, these variables were not included in this analysis. As expected from the results from the across-region analysis, the factors associated with the MR differed from one region to the other (Figure 2).

We performed 4 post-hoc sensitivity analyses. We identified 387 counties with ≥100 patients with HF, most of which had a temperate climate (68.3%). We used dummy variables to include the Köppen climate types on a linear regression model with other significant environmental factors. After controlling for other environmental variables, none of the Köppen climate types was significantly associated to the MR. We also assessed the role of environmental variables within each climate type. In counties with a continental climate type, sulfur dioxide was the only environmental factor associated with the MR (b = 41.9; CI 28.9 to 55.0; p = 6.30E-10). In counties with a dry climate type, only the amount of precipitation had an effect on the MR (b = 0.31; CI 0.24 to 0.38; p = 7.52E-16). In temperate climates, wintertime was the predominant factor associated with a higher MR (b = 146.6; CI 78.1 to 215.1; p = 2.85E-05), followed by the air quality index (b = 6.68; CI 4.44 to

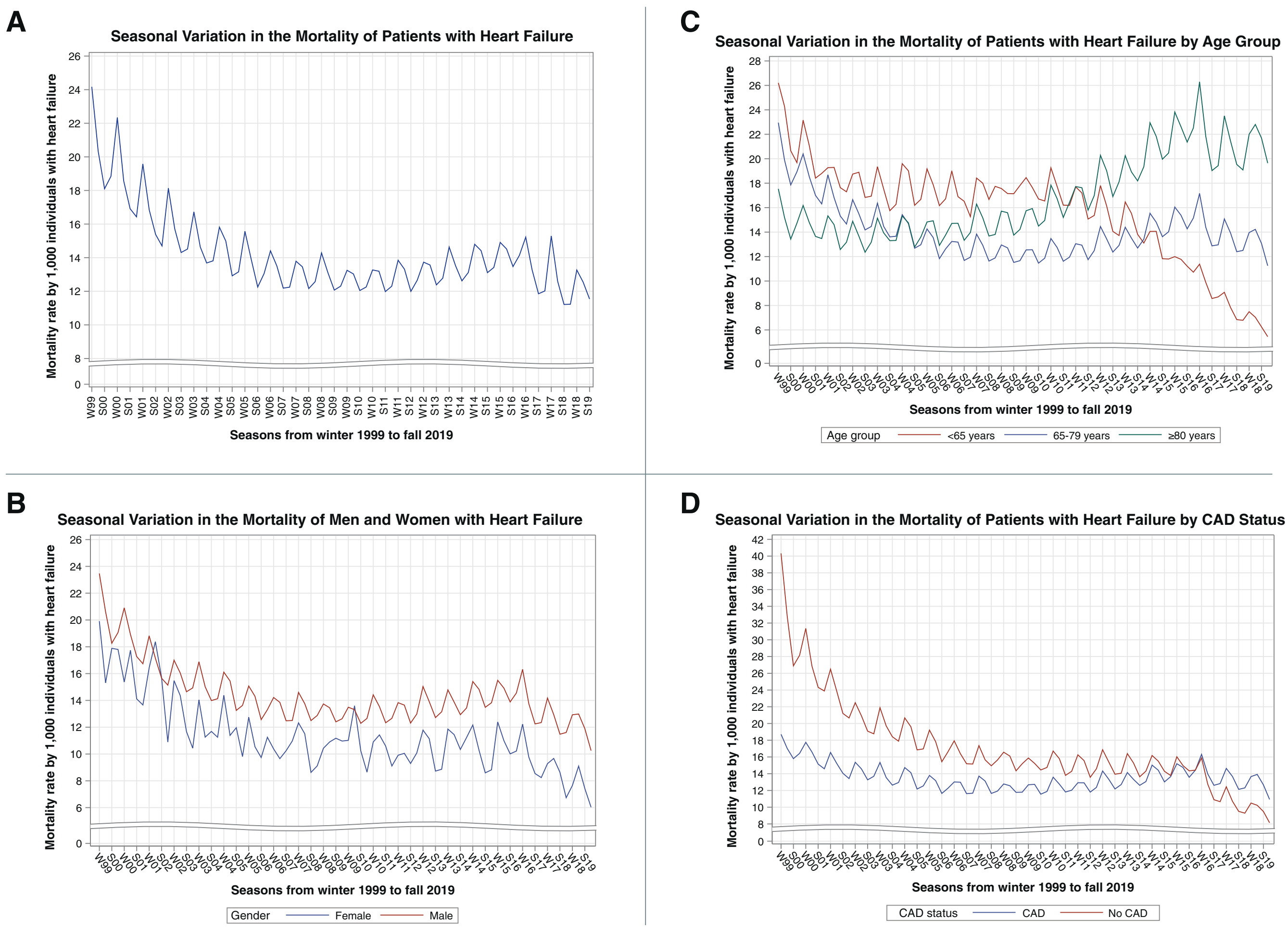

Figure 1. **Twenty-year trend of the mortality rate in chronic HF.** All seasons are represented, though only winter and summer are labeled. **(A)** The overall MR has improved in patients with chronic HF. However, every winter, the MR is higher than the preceding summer by approximately 14% on average. **(B)** This pattern is less consistent in women than in men, possibly due to gender-related variations in the exposure to climate conditions, but also possibly due to the low prevalence of female gender in our cohort. **(C)** This seasonal pattern is also well preserved throughout age groups, though patients <65 years-old are less affected. The elderly are likely to be more susceptible to changes in their environment. **(D)** Patients with HF with CAD and without CAD alike are more susceptible to die during the winter than in the summer. CAD, coronary artery disease; HF, heart failure; MR, mortality rate.

8.91; p = 5.82E-09) and the amount of precipitation (b = 0.05; CI 0.03 to 0.07; p = 3.48E-06). None of the environmental factors was associated with the MR in counties with a tropical climate type.

There were 445 counties with ≥1 million inhabitants and 175 of them had ≥100 patients in our cohort. On univariate analyses, the MR in these counties was affected by different environmental factors than in the general cohort and their impact was more subdued. Unlike in the general cohort, the temperature or the amount of snowfall was not associated with the MR in these counties; instead, the MR was correlated with the amount of available sunlight (r = -0.34; p = 2.56E-05) and the total precipitation (r = 0.15; p = 9.62E-10). Similarly, in these counties, nitrogen dioxide did not affect the MR; rather, the MR was correlated with the overall air quality index (r = 0.19; p = 1.86E-14), the amount of particulate matter ≤10 μm (r = 0.19; p = 2.04E-11, and the amount of particulate matter ≤2.5 μm (r = 0.19; p = 3.15E-07). The season of the year remained correlated with the MR (Spearman's r = 0.24; p = 9.83E-23). On multivariate analysis, only the air quality index remained significantly associated with the MR (b = 13.8; CI 8.05 to 19.55; p = 5.64E-06).

In the subset of patients followed since 2009, the weather variables associated with the MR were the same ones as in the general cohort. However, the air quality index (r = -0.18; p = 2.34E-05) and the amount of particulate matter ≤10 μm (r = -0.36; p = 6.41E-18) were the only air pollutant indicators correlated with the MR in this subset. The results of multivariate analysis in this data subset revealed that winter season, the temperature (maximum, average, and minimum), and the amount of snowfall were all independently associated with the MR.

When we assessed the longitudinal data instead of the summarized values, several variables (i.e., elevation, average wind speed, air quality index, carbon monoxide, particulate matter ≤2.5 μm, and number of cases of hypertensive crises) were correlated with the MR on univariate analyses in addition to the ones identified in the summarized analysis. The results of the multivariate analysis are presented in Table 3.

Table 2
Factors correlated with the mortality rate in univariate analyses and included in multivariate analyses

	Univariate Analyses		Multivariate Analyses		
	R	p Value	B	CI	p Value
TAvg	-0.44	1.75E-27	-0.02	-0.04 to -0.01	4.31E-03
TMin	-0.36	2.09E-18	-0.01	-0.02 to 0.00	1.22E-01
TMax	-0.55	5.00E-44	-0.08	-0.10 to -0.05	3.27E-10*
Snowfall	0.42	1.26E-25	0.05	0.02 to 0.09	1.07E-03
TPrecip	-0.28	1.92E-11	3.49E-07	-6.41E-06 to 7.11E-06	9.19E-01
MDHF	0.25	1.90E-09	0.08	-0.02 to 0.19	1.14E-01
NO_2	0.39	2.12E-21	0.12	0.09 to 0.15	7.53E-12*
SO_2	0.29	5.82E-12	0.02	-0.08 to 0.13	6.59E-01
Ozone	-0.18	1.24E-05	29.94	8.62 to 51.26	6.00E-03
PM10[†]	-0.33	1.38E-15	-0.05	-0.07 to -0.02	1.37E-03
Age	0.38	8.69E-21	0.32	0.24 to 0.41	1.75E-12*
Season[‡]	0.50	8.97E-38	1.23	0.80 to 1.66	3.68E-08*
Intercept	−	−	-7.77	-14.09 to -1.45	1.61E-02

† Statistically significant at the pre-specified α in all other models.

‡ Spearman's R. The seasons were ranked from warmest to coldest based on their average temperature (summer=1, fall=2, spring=3, winter=4). For multivariate analysis, we used dummy variables with summer as the reference; the values for winter are reported.

Asterisk indicates statistical significance in multivariate analysis at the pre-specified significance level of family-wise α=0.05, equivalent to 4.63E-5 per comparison. Pearson's R is provided unless otherwise specified. Separate models were run for variables with strong correlation to avoid collinearity. The results of the regression model that used TMax are presented (AIC 373.10; R^2 0.44). The values for TAvg, TMin, snowfall, and season are provided from the models that included them.

B = parameter; CI = 95% confidence interval; MDHF = median days with heavy fog; NO_2 = nitrogen dioxide; PM10 = particulate matter ≤10 μm in diameter; TAvg = average temperature; TMax = maximum temperature; TMin = minimum temperature; TPrecip = total precipitation; SO_2 = sulfur dioxide.

We also used the longitudinal data to assess the impact of Köppen climate types on the MR. A one-way analysis of variance with Tukey's correction for multiple comparisons suggested a significant difference between the MR of counties with continental climate and those with dry or tropical climate. However, this association did not reach statistical significance on multivariate analysis. Finally, we used the longitudinal data to reexamine the effect of environmental factors in major urban centers. In counties with ≥1 million inhabitants, carbon monoxide, and sulfur dioxide concentrations were significantly associated with a higher MR in multivariate analysis (p = 2.06E-12 and 1.93E-42, respectively). For every increase in 1 ppm of carbon monoxide, the MR increased by 2.75 deaths per 1,000 patients (CI 1.99 to 3.52); every increase in 1 ppb of sulfur dioxide lead to 0.59 more deaths per 1,000 patients (CI 0.50 to 0.67).

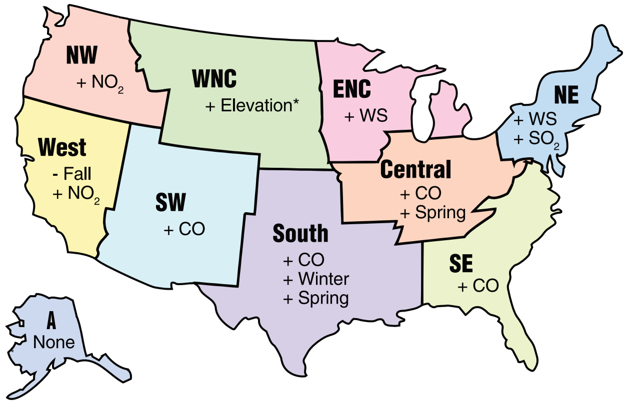

Figure 2. **Region-stratified analysis of environmental factors associated with the mortality rate in patients chronic heart failure.** The factors associated with the MR varied among regions, although nitrogen dioxide was more predominant in the western US and carbon monoxide in the southern regions. The factors are ordered in decreasing size of effect. Crosses indicate a direct relationship with the MR while hyphens indicate an inverse relationship. The asterisk indicates a minimal effect (<0.01 deaths per thousand patients). The seasons were assessed using summer as the reference season. A, Alaska; CO, carbon monoxide; ENC, East North Central; NO_2, nitrogen dioxide; NE, Northeast; NW, Northwest; SW, Southwest; SE, Southeast; SO_2, sulfur dioxide; WNC, West North Central; WS, wind speed.

Table 3
Factors associated with the mortality rate in multivariate analyses using longitudinal data

	B	CI	p Value
Elevation	-7.52E-04	1.01E-03 to -4.98E-04	6.99E-09
TMax	-0.05	-0.07 to -0.04	9.52E-09
TAvg	-0.05	-0.07 to -0.04	1.28E-10
TMin	-0.04	-0.05 to -0.03	7.26E-13
Total Precipitation	-6.97E-06	1.01E-05 to -3.88E-06	1.04E-05
CO	4.46	3.80 to 5.13	1.20E-38
SO_2	0.47	0.39 to 0.54	1.39E-33
Spring	1.16	0.85 to 1.47	2.27E-13
Winter	0.79	0.43 to 1.15	2.06E-05
Age	0.35	0.28 to 0.42	3.02E-22
Intercept	-14.22	-19.33 to -9.10	5.24E-08

Family-wise significance level of α=0.05, equivalent to 4.63E-5 per comparison. The seasons were included as dummy variables with summer as the reference. Separate models were run for variables with strong correlation to avoid collinearity. The results of the regression model that used seasons are presented (AIC 10,979; R^2 0.27). The values for TMax, TAvg, and TMin are provided from the models that included them.

B = parameter; CI = 95% confidence interval; CO = carbon monoxide; TAvg = average temperature; TMax = maximum temperature; TMin = minimum temperature; SO_2 = sulfur dioxide.

Discussion

Using US nation-wide data spanning nearly 20 years, we found that the risk of death of patients with chronic HF is higher during winter months than during any other season of the year. Although there is significant variability in the size of the effect, these results fall in line with the pattern observed in Australia,[10] France,[11] and the province of Quebec, Canada.[27] The 13.8% seasonal increase in all-cause mortality that we observed in our study is the smallest reported so far and it contrasts with the 35% wintertime increase documented in France. Nonetheless, wintertime resulted in an increase of 1.23 deaths per month per thousand patients with chronic HF after controlling for environmental factors and climate types. The seasonality of the MR in our cohort was present throughout all subgroups of age, gender, and etiology of HF.

Acute respiratory diseases,[12,13] myocardial infarctions, and hypertensive crises[14,15,28] have been associated with greater morbidity and mortality during an acute HF hospitalization. In our cohort of patients with chronic HF, these factors were not correlated with the MR, suggesting that these factors are not the primary drivers for the seasonal variation on all-cause MR in this population. Influenza is noteworthy in that its incidence has evident seasonality, but we did not find it to be associated with the MR in our cohort. Since the effectiveness of influenza vaccination in reducing overall mortality in the elderly has recently been questioned,[29] our results highlight the need for further assessment of the impact of influenza in chronic HF.

The effect of environmental factors on outcomes of patients with chronic HF is an area of research with paucity of data. A single-center study found that air temperature, nitrogen oxides, and sulfur dioxide contributed to worse outcomes in patients with chronic HF.[17] Our findings from a larger, more diverse sample corroborate that lower monthly temperatures and higher concentrations of nitrogen dioxide result in a higher MR in patients with chronic HF after adjusting for potential confounders. In the sensitivity analysis using longitudinal data, we also found that higher concentrations of carbon monoxide and sulfur dioxide could result in a higher all-cause MR, particularly in densely populated cities. These findings are consistent with those from other large cities where exposure to nitrogen oxide increased the risk of non-accidental death by 2.3% to 3% in patients with chronic HF[19] and exposure to carbon monoxide resulted in a higher rate of acute HF hospitalizations.[30] The effect of environmental temperature on the MR in chronic HF is likely due to its inverse correlation with adrenergic activity and systemic inflammation.[14,16] The impact of exposure to air pollutants could be explained by their myocardial toxicity,[31] the resulting increase in systemic inflammation,[32] and pollutant-specific effects on the hemoglobin dissociation curve and the immune system.[17] The amount of particulate material <10 μm in diameter is noteworthy because it appeared to be non-significantly associated with a reduction in the MR in our study. Its effect on cardiovascular outcomes is not clear, as contradictory results have been observed in different countries[33] or even cities within the same country.[34] These differing findings likely reflect the heterogeneity in the components of local particulate matter, as well as the effect of other local factors, as discussed below.

The large geographical distribution of this study allowed us to compare regions with homogeneous patterns of temperature and precipitation, areas with similar climate types, and areas with different population density. While these analyses are post-hoc and predisposed to selection bias, they suggest that the effect of a given environmental variable is modified by local factors, as reported elsewhere.[34] The analysis by Köppen climate type indicates that the underlying climate and ecology of the region is one of the relevant local factors. As an example, climate differences between Bilbao and the cities of the US and Canada could underlie the differences in the impact of air pollutants on HF hospitalizations among these locations.[17,30] It follows that as climate change alters regional ecologies, we should expect that the relative impact of patient environmental factors on HF mortality will also change. Alternatively, it is possible that the impact of environmental variables is affected by the patient and local communal responses to cold temperatures. Chronic exposure to cold induces physiological adaptations[16] and results in behavioral changes[27] that may ameliorate the impact of the environment. Our data appear to support this idea and fall in line with observations from other populations.[10,27] Our subgroup analysis of large urban centers is consistent with the idea that local lifestyles and behaviors modify the impact of environmental factors. While maximum temperature and air concentrations of nitrogen dioxide had a significant impact on all-cause mortality in the general cohort, they did not have a perceptible effect on the MR when dense urban centers were considered in isolation. In these locations, only the overall air quality index was associated with the MR, suggesting that improving air quality could have a positive effect on the MR in urban-dwelling patients with chronic HF. Taking environmental factors into account when designing treatment plans for these patients can result in solutions that are easily implementable in the digital age. Some wearable devices, like the Apple Watch, already provide automated notifications about local air quality, which can be harnessed alongside clinical and pharmacological data through apps in healthcare systems to provide more comprehensive management and guidance to patients.

In summary, the MR of US patients with chronic HF is approximately 14% higher in the winter than in the summer, regardless of their gender, age group, and HF etiology. After controlling for potential environmental confounders, winter season, the maximum monthly temperature, and air concentrations of nitrogen dioxide are associated with the MR. While the seasonal effect persists even after adjusting for regions with a similar climate pattern, the impact of other environmental factors differs between regions. Finally, post-hoc analyses suggest that the underlying climate type and the degree of urbanization modify the effect of environmental factors on the MR.

Our findings should be interpreted within the limitations of this study. Because of the retrospective design of this study and its reliance on administrative data, we cannot draw definitive conclusions or rule out residual confounders. Many patients in the US travel every year to avoid the winter temperatures in the north and the seasonality of their migrations could result in bias. Finally, women and some racial groups had a low prevalence in our sample, which limits the generalization of our results. Despite its limitations, this study emphasizes the importance of a comprehensive approach in the management of chronic HF and suggests that these patients may benefit from increased surveillance (by themselves, their families, and their healthcare providers) in the winter months. Our findings also highlight that policies addressing this topic should be considered throughout geographical locations, as the impact of the seasons on mortality is not limited to areas with harsh winters. The possibility of significantly reducing morbidity, as well as therapy costs by identifying and facilitating effective winter habits cannot be overlooked.

Disclosures

The authors have no conflicts of interest to disclose.

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.01.019.

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