Influence of Meteorological Temperature and Pressure on the Severity of Heart Failure Decompensations

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OBJECTIVE: To investigate the relationship between ambient temperature and atmospheric pressure (AP) and the severity of heart failure (HF) decompensations.

METHODS: We analysed patients coming from the Epidemioloy Acute Heart Failure Emergency (EAHFE) Registry, a multicentre prospective cohort study enrolling patients diagnosed with decompensated HF in 26 emergency departments (EDs) of 16 Spanish cities. We recorded patient and demographic data and maximum temperature (T_{max}) and AP (AP_{max}) the day before ED consultation. Associations between temperature and AP and severity endpoints were explored by logistic regression. We used restricted cubic splines to model continuous non-linear associations of temperature and AP with each endpoint.

RESULTS: We analysed 16,545 patients. Daily T_{max} and AP_{max} (anomaly) of the day before patient ED arrival ranged from 0.8 to 41.6° and from − 61.7 to 69.9 hPa, respectively. A total of 12,352 patients (75.2%) were hospitalised, with in-hospital mortality in 1171 (7.1%). The probability of hospitalisation by HF decompensation showed a U-shaped curve versus T_{max} and an increasing trend versus AP_{max}. Regarding temperature, hospitalisation significantly increased from 20 °C (reference) upwards (25 °C: OR = 1.12, 95% CI = 1.04–1.21; 40 °C: 1.65, 1.13–2.40) and below 5.4 °C (5 °C: 1.21, 1.01–1.46). Concerning the mean AP of the city (anomaly = 0 hPa), hospitalisation increased when AP_{max} (anomaly) was above + 7.0 hPa (atmospheric anticyclone; + 10 hPa: 1.14, 1.05–1.24; + 30 hPa: 2.02. 1.35–3.03). The lowest probability of mortality also corresponded to cold-mild temperatures and low AP, with a significant increased risk only found for T_{max} above 24.3 °C (25 °C: 1.13, 1.01–1.27; 40 °C: 2.05, 1.15–3.64) and AP_{max} (anomaly) above + 3.4 hPa (+ 10 hPa: 1.21, 1.07–1.36; + 30 hPa: 1.73, 1.06–2.81). Sensitivity analysis confirmed the main analysis results.

CONCLUSION: Temperature and AP are independently associated with the severity of HF decompensations, with possible different effects on the need for hospitalisation and in-hospital mortality.

KEY WORDS: climate; temperature; atmospheric pressure; acute heart failure; mortality; emergency departments.

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INTRODUCTION

Climate change is expected to increase the frequency and intensity of extreme meteorological conditions, in a scenario in which severe cold weather may anomalously alter warm temperatures in winter, whereas heat waves may become more intense from spring to autumn.[1] This scenario represents a threat to public health, since increases in mortality by cardiovascular and respiratory diseases are typically observed during both hot and cold weather conditions.[2,3] Among cardiovascular diseases, extreme temperatures have been associated with increased risk of myocardial infarction as well as larger infarct size.[4–6] On the other hand, a failing heart is one of the leading cardiovascular causes of death associated with extreme ambient conditions, and in this context, individuals with heart failure (HF) are likely to be unable to

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compensate for the increased circulatory demand induced by heat exposure.[7]

Heart failure (HF) is a highly prevalent cardiovascular condition in people over 65 years old.[4,5] Mortality associated with HF decompensations (acute HF, AHF) is high, with in-hospital all-cause mortality ranging from 5 to 10%.[6,7] Many variables related to patient baseline characteristics and to the acute episode of decompensation with potential to predict such adverse outcomes have been unequivocally defined.[6–10] Conversely, the importance of meteorological conditions on the immediate prognosis of patients with AHF has been poorly investigated. Many previous reports are epidemiological studies based on time-series analysis in general populations investigating the incidence of certain cardiovascular diseases, such as acute coronary syndrome,[11] or the overall or cardiovascular patterns of mortality related to meteorological conditions. However, these studies mainly focus on the effect of high temperatures in hot regions of the world, or analyse the impact on mortality during heatwave episodes. Alahmad et al. recently reported a threefold increased risk of cardiovascular mortality during periods of maximum risk temperature (42.7 °C) with respect to those of minimum risk temperature (34.7 °C) in Kuwait.[12] Remarkably, no previous study has analysed the severity of decompensations and the risk of adverse events for AHF, and neither has the effect of atmospheric pressure (AP) on top of the effect of temperature been investigated. Therefore, we aimed to investigate the relationship between ambient air temperature and AP and the severity of HF decompensations.[2,3]

METHODS

Setting, Study Design and Patient Inclusion

This study is a subanalysis of the Epidemioloy Acute Heart Failure Emergency (EAHFE) Registry,[13] a prospective, multicentre, cohort study initiated in 2007 (see supplementary material). The authors designed the study and gathered and analysed the data according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary Table 1).

Exposure Variables

The primary exposure variables of interest were the daily values of maximum temperature ($T_{\max}$) and maximum AP ($AP_{\max}$) for the day before patient consultation to the ED. Maximum temperature and pressure were chosen the day before ED consultation in order to ensure they had an effect on the severity of decompensation (as those registered on the day of ED consultation could not affect patients arriving to the ED early in the morning). These meteorological variables were recorded by the Meteorological State Agency at stations near the hospital. We compiled $T_{\max}$ in degrees Celsius (°C) and $AP_{\max}$ in hectopascals (hPa). The AP is a meteorological variable which decreases with altitude, and therefore, cities located at sea level have a higher mean AP than those located at a higher altitude (i.e., the mean AP is 1018 hPa in Barcelona, located at 13 m above sea level, and 917 hPa in Burgos, placed at 859 m above sea level; see Fig. 1), The statistical analysis was performed using the anomaly of the $AP_{\max}$ [$AP_{\max}$ (anomaly)] for each day. The concept of $AP_{\max}$ anomaly was used and calculated in a similar way as that used in many climate studies: $AP_{\max}$ anomaly (for day d) was obtained as the result of the average value of $AP_{\max}$ during a certain period (in the current study, the $AP_{\max}$ of all days included in the study) minus the value of $AP_{\max}$ of day d. Accordingly, a day with an $AP_{\max}$ (anomaly) equal to zero means that the $AP_{\max}$ was equal to the mean $AP_{\max}$ in that city; similarly, a negative value means a day with a low $AP_{\max}$ and a positive value represents a day with a high $AP_{\max}$ for every particular city. These negative and positive $AP_{\max}$ values are generally associated with changes in weather, i.e. the passage of a cyclone (or depression or heat low) for negative $AP_{\max}$ or an anticyclonic weather situation for positive $AP_{\max}$ values. In Spain, the day-to-day variability in temperature and AP is regularly associated with the shifting of the Azores anticyclone and mid-latitude depressions/cyclones.

Covariates

We considered demographic factors including age, sex, and 6 clinical risk factors: diabetes mellitus, hypertension, coronary artery disease, chronic renal disease, cerebrovascular disease, and chronic obstructive pulmonary disease. These comorbidities have been considered to impact prognosis in general as well as in previous studies analysing the effects of temperature on mortality. We also considered three demographic data consisting in day of the week and season of the year of patient arrival to the ED (there were no inclusions in the summer due to logistic issues—vacation time of most of ED staff; the EAHFE Registry never includes summer periods for patient recruitment) and the climate type of the city where the ED is located according to official Spanish climate data.[14]

Outcomes

We considered two different outcomes to assess the severity of the AHF episode: (1) need for hospitalisation (accounting for every patient who, after ED evaluation and treatment, required hospitalisation, irrespective of the department in charge of the admission) and (2) in-hospital all-cause mortality.

Statistical Analysis

Continuous variables are expressed as mean and standard deviation (SD) or median and interquartile range (IQR), and categorical variables as absolute values and percentages. Confidence intervals of proportions were computed using the Wilson method.[15] Binary logistic regression analysis was used to investigate the potential association of $T_{\max}$ and $AP_{\max}$ (anomaly) with each outcome. To avoid dichotomizing $T_{\max}$ and $AP_{\max}$ (anomaly) into a few discrete, ordered levels and to

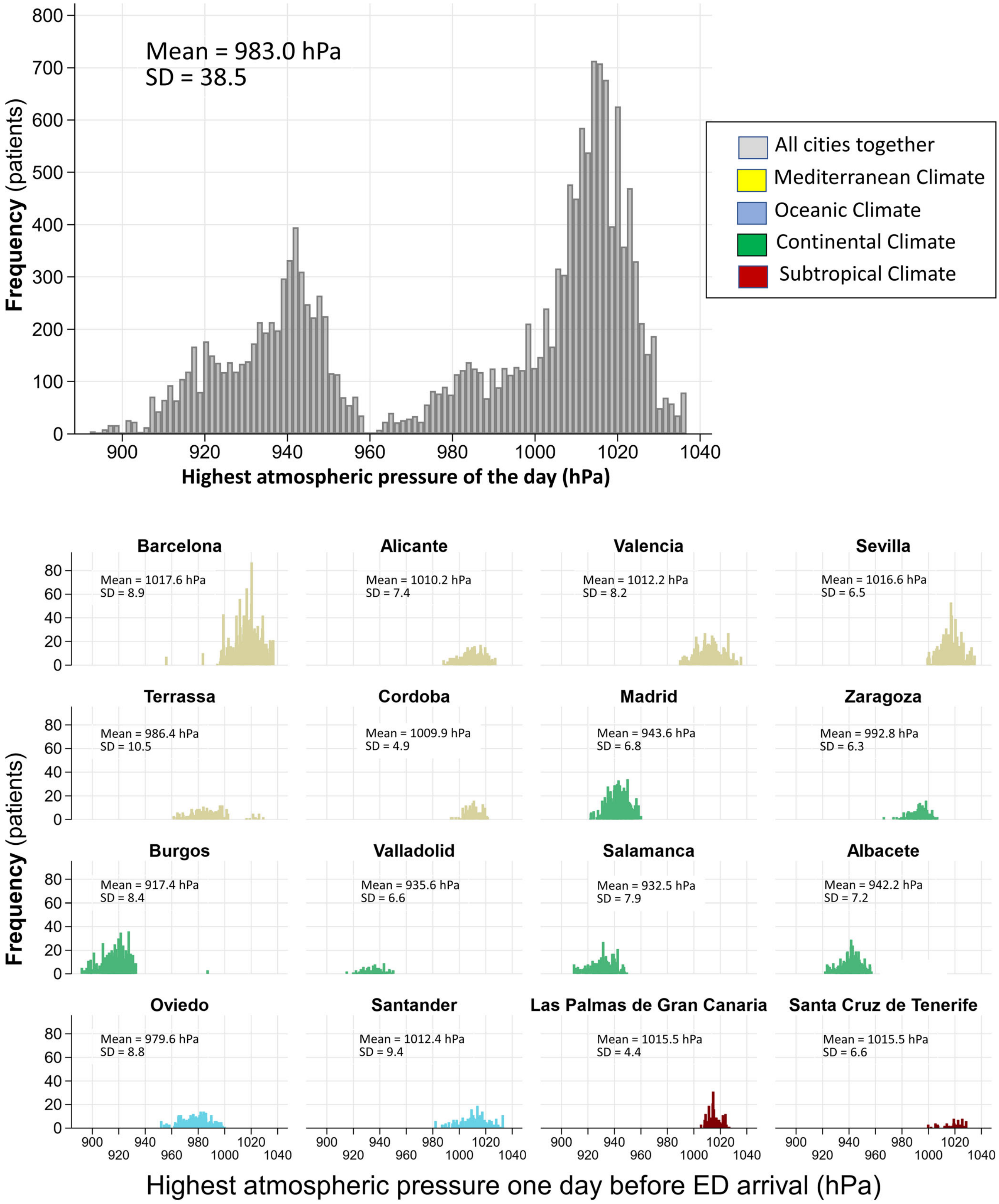

Fig. 1 Distribution of patients, according to the maximum atmospheric pressure of the day before arrival to the emergency department, considering all cities together (upper image) and individually (lower image).

avoid imposing linearity, we used a restricted cubic spline function to model the continuous association of $T_{\max}$ and $AP_{\max}$ (anomaly) with each outcome. Four spline knots were placed at the 0.05, 0.35, 0.65 and 0.95 percentiles of each continuous variable marginal distribution, following the recommendations of Harrel.[16] Adjustment was performed for age, sex, patient comorbidities, demographic data (day of the week, season of the year and city climate) and daily $T_{\max}$ and $\mathrm{AP}_{\max}$ (anomaly). The magnitude of the effect of each $T_{\max}$ and $\mathrm{AP}_{\max}$ (anomaly) unit change was graphically assessed. Because both continuous variables were modelled with restricted cubic splines, their adjusted associations were expressed in a dose-response manner for probability or odds ratio (OR) with 95% confidence intervals (CI) for each outcome of interest. In order to compute an OR for the dose-response plots, we chose a priori a $T_{\max}$ of 20.0 °C and an $\mathrm{AP}_{\max}$ (anomaly) of 0 hPa as the reference values. These reference values were chosen arbitrarily, as there are no previous studies suggesting any theory-based reference value for temperature and atmospheric pressure in patients with AHF. Two-dimension plots (heat maps) were constructed to assess the relationship between $T_{\max}$ and $\mathrm{AP}_{\max}$ (anomaly) for each endpoint.

Two sensitivity analyses were performed to assess the robustness of the main analysis: first, we included an interaction between temperature and AP in the multivariable model used for the main analysis (sensitivity analysis A), and second, we adjusted for chronic HF as an additional covariate in the main multivariable model (sensitivity analysis B). In addition, we performed a subgroup analysis based on the four climates (Mediterranean, continental, oceanic or subtropical) in the cities studied.

All hypothesis testing was two-tailed, and p values < 0.05 or ORs 95% CI excluding 1 were considered statistically significant. All analyses were performed using observed cases without imputation of missing data due to the extremely low missing rate (0.25%). Data analysis was performed using Stata version 16.1 (Stata Corp, College Station, TX, USA) and R version 3.6.3 (R foundation for Statistical Computing, Vienna, Austria).

RESULTS

Characteristics of Patients, Temperature and Pressure

A total of 16,447 patients with AHF were available for this analysis (Supplementary Figure 1). The median age was 83 years, 56% were women, and the most frequent comorbidities were hypertension and diabetes mellitus (Table 1). ED consultation was more frequent during weekdays than during weekends, and a higher proportion of patients (68%) were included in winter. Most patients were attended at the EDs of Mediterranean and continental cities, whilst less than 15% corresponded to EDs of cities with an oceanic or subtropical climate (Table 1).

The mean $T_{\max}$ and $\mathrm{AP}_{\max}$ the day before patient arrival to the ED were 16.4 °C (range: 0.8 to 41.6) and 983.0 hPa (range: 892.1 to 1036.7), respectively. After $\mathrm{AP}_{\max}$ transformation, the mean $\mathrm{AP}_{\max}$ (anomaly) was − 0.2 hPa (range: − 61.7 to 69.9) (Fig. 2).

Table 1 Patient and Demographic Data

	Total ***N* = 16,447** ***n* (%)**	**Missing data** ***n* (%)**
Patient data		
Age (years) [median (IQR)]	83 (77–88)	22 (0.1)
Female sex	9147 (55.8)	43 (0.3)
Arterial hypertension	13,676 (83.5)	63 (0.4)
Diabetes mellitus	6769 (41.3)	64 (0.4)
Coronary artery disease	4532 (27.7)	65 (0.4)
Chronic renal disease	4356 (26.6)	62 (0.4)
Chronic obstructive pulmonary disease	3882 (23.7)	73 (0.4)
Cerebrovascular disease	2047 (12.5)	64 (0.4)
Demographic data		
Day of the week		3 (0.0)
Monday	2922 (17.8)	
Tuesday	2702 (16.4)	
Wednesday	2580 (15.6)	
Thursday	2557 (15.5)	
Friday	2499 (14.9)	
Saturday	1638 (10.0)	
Sunday	1616 (9.8)	
Season of the year		34 (0.2)
Autumn	2283 (13.9)	
Winter	11,226 (68.4)	
Spring	2904 (17.7)	
Climate type		0 (0)
Mediterranean	8273 (50.3)	
Barcelona	*3207 (19.5)*	
Sevilla	*1637 (10.0)*	
Valencia	*1341 (8.2)*	
Alicante	*966 (5.9)*	
Terrassa	*724 (4.4)*	
Córdoba	*398 (2.4)*	
Continental	6217 (37.8)	
Madrid	*2059 (12.5)*	
Burgos	*1509 (9.2)*	
Albacete	*1019 (6.2)*	
Salamanca	*979 (6.0)*	
Zaragoza	*449 (2.7)*	
Valladolid	*202 (1.2)*	
Oceanic	1387 (8.4)	
Oviedo	*832 (5.1)*	
Santander	*555 (3.4)*	
Subtropical	570 (3.5)	
Las Palmas de Gran Canaria	*454 (2.8)*	
Santa Cruz de Tenerife	*116 (0.7)*	

Association of Temperature and Atmospheric Pressure with Hospitalisation

Hospitalisation was necessary in 12,352 HF patients with decompensation (75.2%; this data was unknown in 12 cases). The expected probability of hospitalisation due to HF versus $T_{\max}$ exhibited a U-shaped curve, with lower probabilities with a $T_{\max}$ between 10 and 20 °C (minimum probability at $T_{\max}$ at ~ 16 °C, Fig. 3), and cold and warm temperatures significantly increasing the need for hospitalisation. Specifically, with respect to a temperature of 20 °C (reference), hospitalisation significantly increased above this point (for 25 °C: OR = 1.12, 95% CI = 1.04–1.21; 30 °C: 1.27, 1.07–1.52; 35 °C: 1.45, 1.10–1.91; 40 °C: 1.65, 1.13–2.40) as well as below 5.4 °C (5 °C: 1.41, 1.17–1.71) (Fig. 3 and Table 2).

The probability of hospitalisation rose with increasing $\mathrm{AP}_{\max}$ (anomaly). In this sense, with respect to the mean $\mathrm{AP}_{\max}$ of the

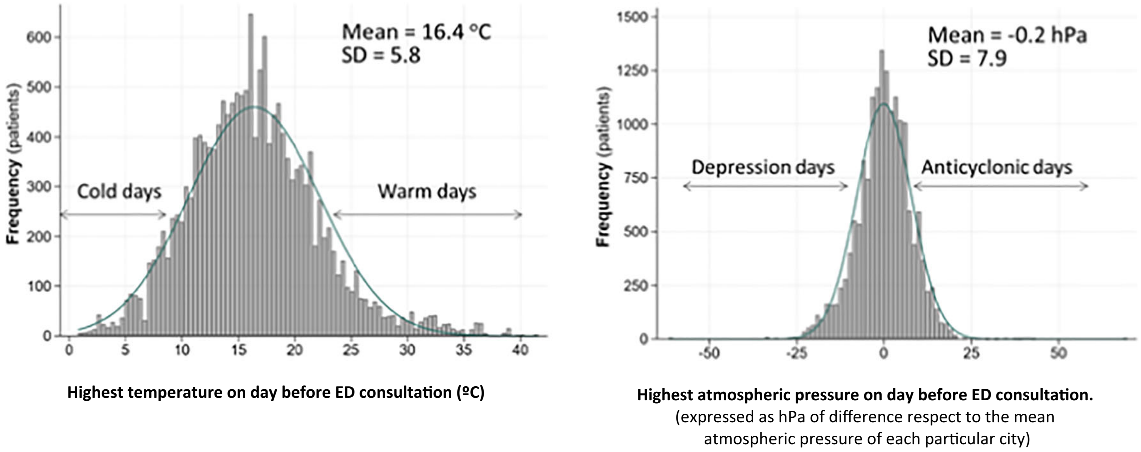

Fig. 2 Distribution of patients, according to daily maximum temperature values (left) and maximum atmospheric pressure anomaly (right) of the day before patient arrival to the ED.

corresponding city [0 hPa of AP_{max} (anomaly)], hospitalisation significantly increased when the AP_{max} (anomaly) was above + 7.0 hPa (anticyclonic condition; + 10 hPa: 1.14, 1.05–1.24; + 20 hPa: 1.52, 1.20–1.91; + 30 hPa: 2.02, 1.35–3.03) (Fig. 3 and Table 2). Sensitivity and subgroup analyses showed very similar results compared to the main analysis (Table 2 and Supplemental Figures 2, 3 and 4).

The contour plot (Fig. 3) shows that the probability of hospitalisation due to HF decompensation was (1) minimum (< 68%) when the T_{max} was mild (12–19 °C) and the AP_{max} (anomaly) was negative (~ − 20 hPa), a scenario frequently associated with southern warm winds in autumn and spring linked to an approaching cyclone from the Atlantic, and (2) high (~ 75–80%) when the T_{max} was low (< 5 °C) and the AP_{max} (anomaly) was positive (> 7 hPa), a typical scenario of cold weather linked to anticyclonic conditions in winter, often associated with inversions near ground level and fog, and (3) is maximum (80%) when the T_{max} is high (> 30 °C), irrespective of the AP_{max} (anomaly), a typical scenario of hot weather in early autumn and the end of spring.

Association of Temperature and Atmospheric Pressure with In-Hospital Mortality

In-hospital mortality was observed in 1241 patients (7.5%). The probability of mortality is quite low on days when the T_{max} is within the range of 2 to 25 °C and with a negative AP_{max} (anomaly). For this particular outcome, only high (but not low) temperatures were associated with increased in-hospital mortality (Fig. 4), with a significantly high risk when the T_{max} was above 24.3 °C (25 °C: 1.13, 1.01–1.27; 30 °C: 1.38, 1.05–1.79; 35 °C: 1.68, 1.10–2.57; 40 °C: 2.05, 1.15–3.64). Mortality also increased when the AP_{max} (anomaly) was higher than + 3.4 hPa (+ 10 hPa: 1.21, 1.07–1.36; + 20 hPa: 1.44, 1.09–1.91; + 30 hPa: 1.73, 1.06–2.81) (Fig. 4 and Table 2). Sensitivity and subgroup analyses showed very similar results compared to the main analysis (Table 2 and Supplemental Figures 2, 4 and 5).

The contour plot (Fig. 4) shows that the probability of in-hospital mortality by HF was (1) high (10%) when the T_{max} was ~ 12 °C and the AP_{max}(anomaly) was high (~ + 20 hPa), a typical meteorological scenario of "good weather", from the end of autumn to early spring, due to an anticyclonic situation, and (2) maximum (~ 12%) when the T_{max} was higher than 35 °C and the AP_{max} (anomaly) was slightly negative (~ − 5 hPa).

DISCUSSION

The relationship between the variability of meteorological ambient air, temperature and mortality is a topic of worldwide interest in a changing climate with a warming trend.[17] A recent global study found that the minimum mortality temperature tends to be close to the most frequent local temperature, data demonstrating human adaptability to the local climate.[17,18] A recent study in Spain showed that the minimum mortality temperature has progressively increased during the last four decades (at the rate of 0.64 °C/decade), suggesting biological adaptation to climate change and/or the adoption of mitigation measures (i.e., the use of air conditioning).[18] Our study specifically focused on a particular cardiovascular syndrome, HF, and investigated the potential connection between weather conditions and the severity of decompensations presented by a cohort of patients with HF. We found that the T_{max} and AP_{max} (anomaly) the day before patient ED consultation for decompensated HF were independently associated with the severity of the decompensation. Moreover, even adjusting for the two values, they could exert a different influence on disease severity, with possible different effects on the need for hospitalisation and mortality, the two outcomes investigated in the present study to assess the severity of HF decompensation.

The need for hospitalisation and mortality progressively and significantly increased from a not very high maximal temperature (around 25 °C) upwards. This means that an increase in temperatures above a certain threshold (and not

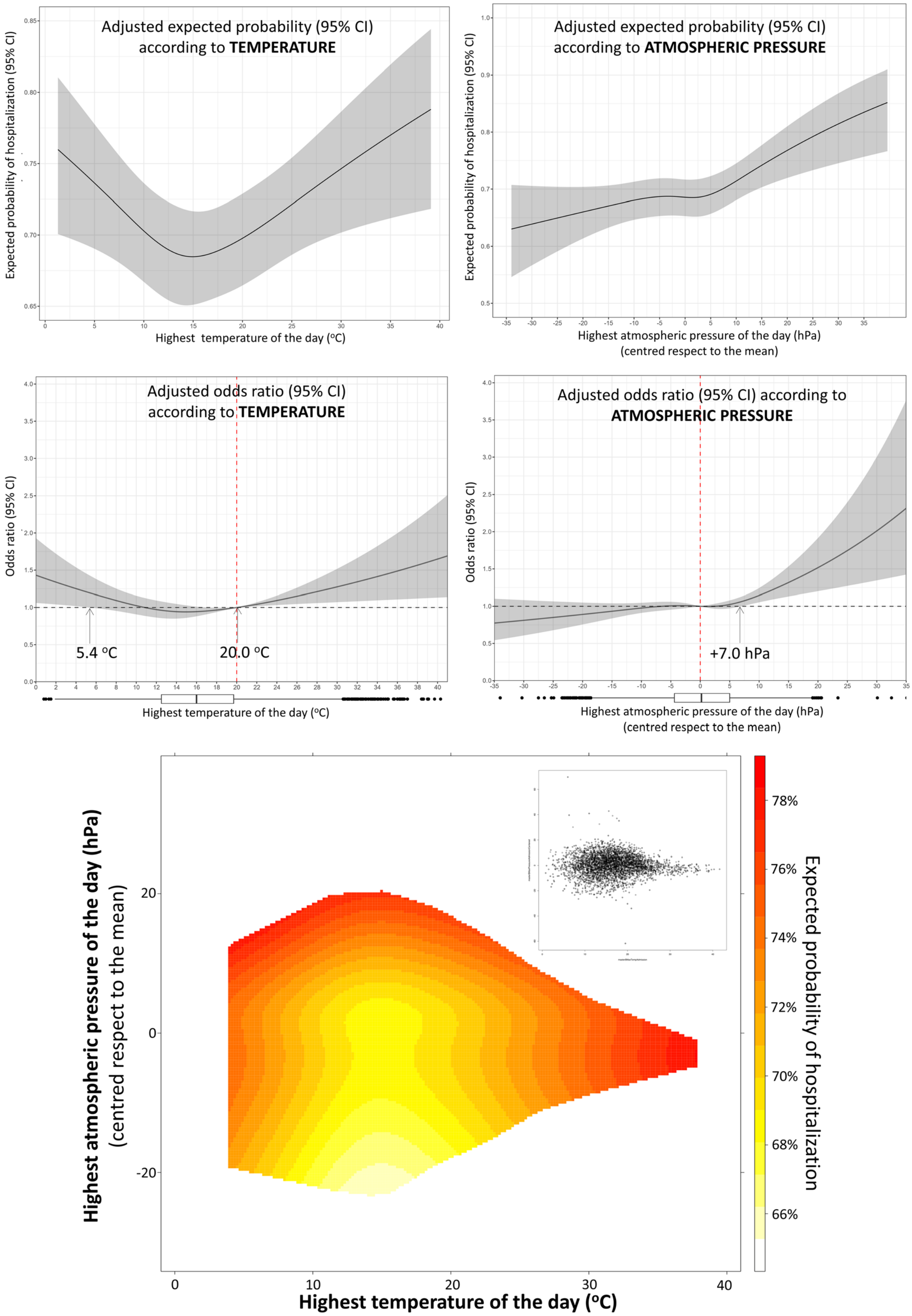

Fig. 3 Adjusted effects of temperature and atmospheric pressure on the need for hospitalisation of patients with AHF. Upper panels correspond to restricted cubic spline curves for predicted probabilities, and middle panels correspond to the odds ratio of hospitalisation for every temperature and atmospheric pressure value, choosing as reference a temperature value of 20 °C and an atmospheric pressure value of 0 HPa. The bottom panel corresponds to the heat map for probability of hospitalisation according to temperature and atmospheric pressure [inside, dot plot including the whole range of temperatures (from 0.8 to 41.6 °C) and atmospheric pressure anomalies (from − 61.7 to 69.9 hPa)]. The multivariable regression model was adjusted for median age (82 years), gender (reference Female), weekday (reference Monday), season (reference Winter), climate (reference Mediterranean), hypertension, diabetes mellitus, chronic kidney disease, coronary heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease (for all risk factors, the reference was *No*).

only during heatwave periods) is associated with a clear increase of risk, and this should be put into the perspective of the global warming linked to climate change. Remarkably, we found a minimum probability of hospitalisation and mortality at a $T_{\max}$ of ~ 20 °C, a temperature slightly lower than the minimum mortality temperature (for all natural causes) typically found in Spain, which ranges between 25 and 30 °C.[18] This suggests a higher susceptibility (or less adaptive capacity) of HF patients to high temperatures than the general population or those with other diseases.

We found that, whilst a significant increase in hospitalisation was seen in patients who presented to the ED when temperatures were low, there was no increase in mortality in these patients. The apparent inconsistence between these two markers of severity was not observed for high temperatures, for which the effects on hospitalisation and mortality mirrored each other. We have no solid explanation for this. We can hypothesise that this incongruence observed for low temperatures could be because part of the decompensations during cold spells are facilitated by infections for which (bacterial) there are effective treatments. Alternatively, a lower threshold for hospitalisation during cold spells could also have accounted for the difference.

In contrast with the large number of reports analysing the impact of ambient temperature on health, the number of studies on AP are very scarce. Anticyclones (associated with high AP) typically result in stable, fine weather, with clear skies, whilst depressions (associated with low AP) are associated with cloudier, wetter, and windier conditions. Additionally, there are some relationships between AP and temperature, as high temperature is generally associated with low AP. In Spain, high temperatures are associated with meteorological scenarios characterised by a weak pressure gradient and the formation of a thermal low (i.e. relatively low pressure due to the strong heating of terrain and the consequent formation of a thermal low—meteorological terminology). This is a well-known feature on the Spanish mainland.[19] However, although it is intuitive to consider anticyclonic conditions more favourable for health, we found that anticyclones were, in fact, associated, with a significant excess of hospitalisations and in-hospital deaths in patients with AHF. Our results partially disagree with those of Plavcová and Kyselý,[20] who reported that sudden AP drops in winter were associated with a significant rise in hospital admissions and also with a significant excess of cardiovascular mortality in Prague (Czech Republic). It is remarkable that whilst patients can manage extreme external temperatures using air conditioning or heating devices to adjust ambient

Table 2 Adjusted Odds Ratio for Different Temperatures and Atmospheric Pressures with Respect to Their Reference Value in the Main Analysis and in the Two Sensitivity Analyses (A and B)

Endpoint	Exposure	Value	Main analysis	Sensitivity analyses	
			OR (95% CI)	Analysis A* OR (95% CI)	Analysis B† OR (95% CI)
Hospitalisation	Temperature (°C)	5	**1.21 (1.01–1.46)**	**1.28 (1.03–1.58)**	**1.24 (1.02–1.50)**
		10	1.02 (0.91–1.16)	1.05 (0.91–1.20)	1.04 (0.92–1.18)
		15	0.94 (0.86–1.03)	0.94 (0.86–1.03)	0.95 (0.87–1.04)
		20	1.00 (reference)	1.00 (reference)	1.00 (reference)
		25	**1.12 (1.04–1.21)**	**1.13 (1.03–1.23)**	**1.13 (1.05–1.22)**
		30	**1.27 (1.07–1.52)**	**1.28 (1.05–1.57)**	**1.30 (1.09–1.55)**
		35	**1.45 (1.10–1.91)**	**1.46 (1.06–2.01)**	**1.49 (1.13–1.97)**
		40	**1.65 (1.13–2.40)**	**1.67 (1.08–2.58)**	**1.71 (1.17–2.52)**
	Pressure (hPa of anomaly) (difference with respect to the mean pressure of the city)	− 30	0.81 (0.61–1.08)	0.87 (0.64–1.19)	0.84 (0.62–1.13)
		− 20	0.89 (0.75–1.05)	0.94 (0.78–1.13)	0.90 (0.76–1.07)
		− 10	0.98 (0.91–1.05)	1.01 (0.93–1.10)	0.97 (0.90–1.04)
		0	1.00 (reference)	1.00 (reference)	1.00 (reference)
		10	**1.14 (1.05–1.24)**	**1.13 (1.04–1.24)**	**1.16 (1.06–1.26)**
		20	**1.52 (1.20–1.91)**	**1.53 (1.20–1.96)**	**1.52 (1.20–1.93)**
		30	**2.02 (1.35–3.03)**	**2.06 (1.35–3.14)**	**2.02 (1.34–3.04)**
In-hospital death	Temperature (°C)	5	0.92 (0.69–1.24)	0.90 (0.65–1.26)	0.93 (0.69–1.27)
		10	1.10 (0.90–1.33)	1.09 (0.87–1.35)	1.10 (0.90–1.35)
		15	1.12 (0.97–1.29)	1.12 (0.96–1.30)	1.12 (0.96–1.30)
		20	1.00 (reference)	1.00 (reference)	1.00 (reference)
		25	**1.13 (1.01–1.27)**	1.08 (0.95–1.24)	**1.15 (1.02–1.30)**
		30	**1.38 (1.05–1.79)**	1.25 (0.91–1.71)	**1.43 (1.09–1.87)**
		35	**1.68 (1.10–2.57)**	1.44 (0.88–2.36)	**1.77 (1.16–2.73)**
		40	**2.05 (1.15–3.64)**	1.65 (0.84–3.26)	**2.20 (1.23–3.93)**
	Pressure (hPa of anomaly) (difference with respect to the mean pressure of the city)	− 30	0.82 (0.48–1.38)	0.75 (0.43–1.29)	0.78 (0.45–1.34)
		− 20	0.85 (0.63–1.16)	0.79 (0.57–1.09)	0.83 (0.61–1.14)
		− 10	**0.89 (0.80–1.00)**	**0.83 (0.72–0.96)**	**0.89 (0.79–1.00)**
		0	1.00 (reference)	1.00 (reference)	1.00 (reference)
		10	**1.21 (1.07–1.36)**	**1.22 (1.07–1.40)**	**1.21 (1.07–1.36)**
		20	**1.44 (1.09–1.91)**	1.36 (0.96–1.92)	**1.45 (1.09–1.93)**
		30	**1.73 (1.06–2.81)**	1.50 (0.83–2.70)	**1.74 (1.07–2.85)**

Bold numbers denote statistical significance ($p < 0.05$)

**Sensitivity analysis A consisted of including the interaction between temperature and atmospheric pressure as covariate into the adjusted model of the main analysis*

†Sensitivity analysis B consisted of including chronic heart failure as covariate into the adjusted model of the main analysis

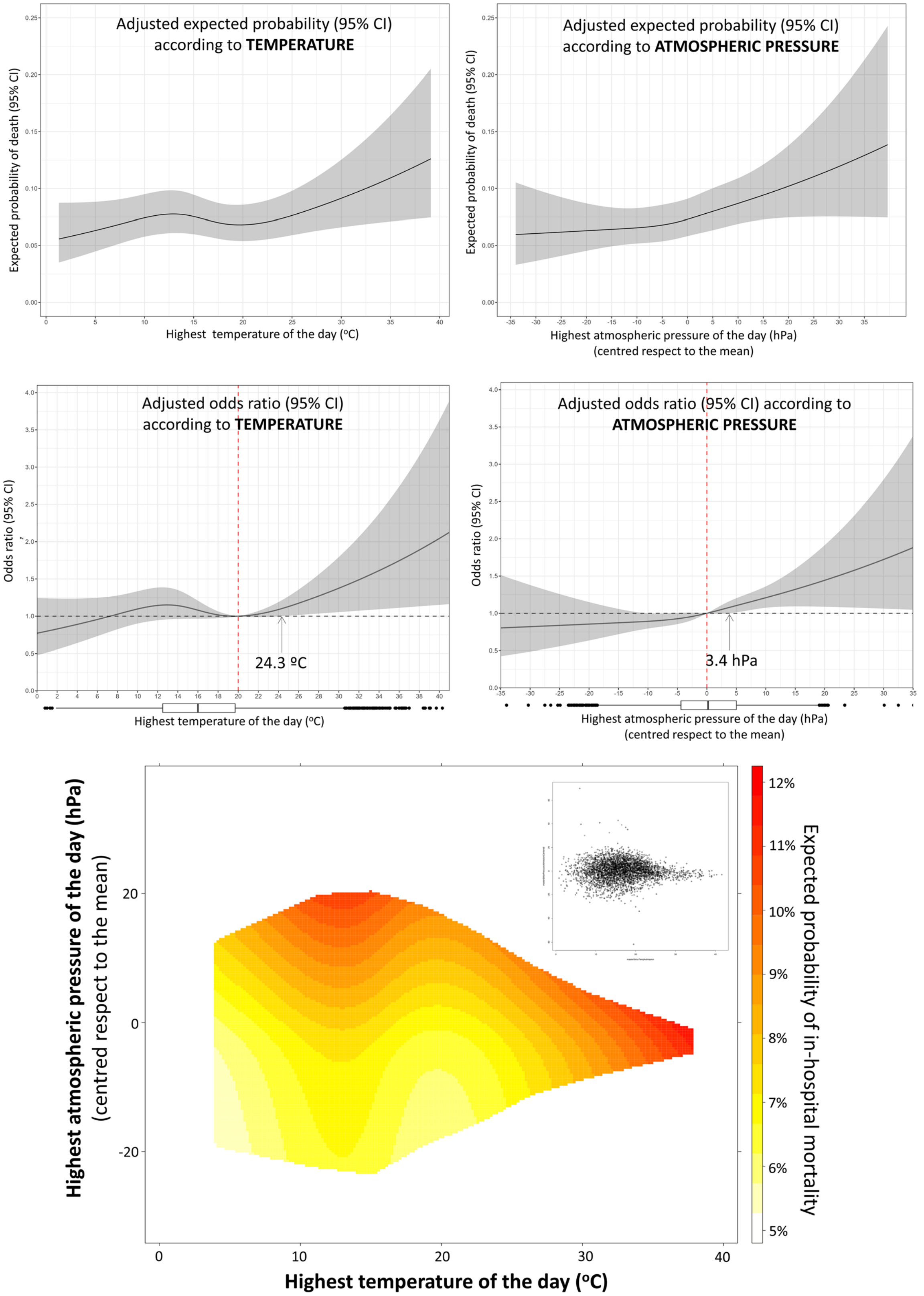

Fig. 4 Adjusted effects of temperature and atmospheric pressure on in-hospital all-cause mortality of patients with AHF. Upper panels correspond to restricted cubic spline curves for predicted probabilities, and middle panels correspond to the odds ratio of mortality for every temperature and atmospheric pressure value, choosing as reference a temperature value of 20 °C and an atmospheric pressure value of 0 HPa. The bottom panel corresponds to the heat map for probability of mortality according to temperature and atmospheric pressure [inside, dots plot including the whole range of temperatures (from 0.8 to 41.6 °C) and atmospheric pressures (from − 61.7 to 69.9 hPa)]. The multivariable regression model was adjusted for median age (82 years), gender (reference Female), weekday (reference Monday), season (reference Winter), climate (reference Mediterranean), hypertension, diabetes mellitus, chronic kidney disease, coronary heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease (for all risk factors, the reference was *No*).

temperature to one that is more comfortable according to their own preferences/necessities, extreme AP conditions cannot be modulated. Accordingly, the impact of AP on health could be greater and more difficult to palliate than the effect of temperature. Indeed, when the AP was higher than + 30 hPa over the mean AP of the city, excesses of hospitalisation and mortality were similar to those observed with very high temperatures (40 °C). Therefore, the effects of AP on health merit thorough study in the next years.

The pathophysiology of adverse effects of extreme temperatures and AP on health is complex. For temperature, several biological mechanisms have been postulated for populations (particularly the elderly) susceptible to heat-related mortality, a condition highly present in HF patients.[21] Increased blood viscosity, elevated cholesterol levels associated with higher temperatures, and a higher sweating threshold may also trigger heat-related mortality. For the particular case of HF patients, certain chronic medications such as diuretics or beta-blockers could exacerbate this disruption in homeostatic mechanisms. Furthermore, thermoregulation can also be influenced by acclimatisation: heat waves earlier in the year or affecting areas where high temperatures are unusual are more likely to impact the health of the population. Similarly, people living next to the sea are used to a very high AP, whilst people leaving at high altitudes are used to a very low AP. In this sense, it has been reported that residing at higher altitudes is associated with a lower mortality from cardiovascular diseases, and moderate altitudes would be even more protective.[22]

Limitations

First, as in every observational study, causal relationships cannot be inferred. Therefore, the results of the current analysis are limited by the retrospective design and should be considered as hypothesis generating. Second, several confounding factors make it difficult to study weather-related morbidity and mortality. In this sense, daily changes in temperature and AP, and other meteorological conditions such as wind, humidity or trends in changes along the immediate previous or posterior days, were not included in our models. Air pollutants were not considered in our study either. Nevertheless, an extensive review analysing the relationship between elevated temperature and mortality concluded that although some contaminants such as PM_{10} and $PM_{2.5}$ particles and ozone can act as confounders and/or modifiers of the temperature effect, the independent negative effect of high temperatures and mortality is retained.[12] Additionally, ozone is an air pollutant with a strong seasonal cycle, with high levels in summer and low levels in the other seasons, especially in the winter, and our study did not include summertime. Moreover, this study focuses on populations of urban areas, whereas ozone typically shows high levels in rural areas on a regional scale, due to the reaction of fresh nitric oxide (linked to vehicle exhaust emissions) with ozone which results in ozone titration. Therefore, we do not believe that our findings were influenced by changes in ozone levels not measured in the present study. Third, we only recorded all-cause mortality, without distinguishing between cardiovascular and non-cardiovascular causes of death. A more detailed analysis of cause of death could have contributed to better delimiting the “harvesting” effect from the inherent effect of extreme meteorological conditions in patients with AHF. Fourth, patient socioeconomic status is not included in the EAHFE Registry, and therefore, the potential effect of these socioeconomic factors is not accounted for in the present study. However, although this could be relevant, air conditioning and heat devices are present in the majority of Spanish homes, and we believe that differences in the impact of extreme external temperatures due to socioeconomic factors were minimal. Fifth, the prevalence of certain diseases, primarily outbreaks of respiratory infection, is increased during winter season and could potentially impact mortality. However, a previous study has demonstrated that HF patients decompensated by infection actually have a better prognosis than the remaining HF patients.[23] Sixth, although cases with AHF related to acute coronary syndrome other than STEMI were included (non-STEMI, angina), exclusion of STEMI could partly mask the impact meteorological conditions have on outcomes, as myocardial infarction is a cardiovascular condition that is negatively impacted by extreme meteorological conditions. Finally, we did not explore the effect of very hot temperatures, as HF patients consulting the ED in the summer were not included.

Conclusions

Maximal temperatures and AP are independently associated with the severity of HF decompensations, with possible different effects on the need for hospitalisation and in-hospital mortality.

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Declarations:

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