International Journal of Cardiology 294 (2019) 1–5

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Climate changes and ST-elevation myocardial infarction treated with primary percutaneous coronary angioplasty

Francesco Versaci [a,1], Giuseppe Biondi-Zoccai [b,c,*,1], Angela Dei Giudici [a], Enrica Mariano [d], Antonio Trivisonno [e], Sebastiano Sciarretta [b,f], Valentina Valenti [a], Mariangela Peruzzi [b,c], Elena Cavarretta [b,c], Giacomo Frati [b,f], Massimiliano Scappaticci [a], Massimo Federici [g], Francesco Romeo [d]

[a] *Unità Operativa Complessa di Cardiologia, Ospedale Santa Maria Goretti, Latina, Italy*
[b] *Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy*
[c] *Mediterranea Cardiocentro, Napoli, Italy*
[d] *Cattedra di Cardiologia, Tor Vergata University, Rome, Italy*
[e] *Unità Operativa Complessa di Cardiologia, Ospedale Antonio Cardarelli, Campobasso, Italy*
[f] *IRCCS NEUROMED, Pozzilli, Italy*
[g] *Department of Systems Medicine, Tor Vergata University, Rome, Italy*

A R T I C L E I N F O

Article history:
Received 10 March 2019
Received in revised form 20 June 2019
Accepted 2 July 2019
Available online 3 July 2019

Keywords:
Acute myocardial infarction
Atherothrombosis
Climate
Coronary artery disease
Primary percutaneous coronary intervention

A B S T R A C T

Background: The impact of seasonal changes on the incidence of acute myocardial infarction has been incompletely appraised, especially in the modern era of primary percutaneous coronary intervention (PPCI). We aimed to appraise the overall and season-specific impact of climate changes on the daily rate of PCCI.
Methods: Details on PPCI and climate changes were retrospectively collected in three high-volume Italian institutions with different geographical features. The association between rate of PPCI and temperature, atmospheric pressure (ATM), humidity and rainfall was appraised with Poisson models, with overall analyses and according to season of the year.
Results: Details on 6880 days with a total of 4132 PPCI were collected. Overall adjusted analysis showed that higher minimum atmospheric pressure 3 days before PPCI were associated with lower risk (regression coefficient = 0.999 [95% confidence interval 0.998–1.000], $p = 0.030$). Focusing on season, in Winter PPCI rates were increased by lower same day mean temperature (0.973 [0.956–0.990], $p = 0.002$) and lower rainfall (0.980 [0.960–1.000], $p = 0.049$). Conversely, in Spring greater changes in atmospheric pressure 3 days before PPCI were associated with increased risk (1.023 [1.002–1.045], $p = 0.032$), with similar effects in Summer for minimum temperature on the same day (1.022 [1.001–1.044], $p = 0.040$).
Conclusions: Climate has a significant impact on the risk of PPCI in the current era, with a complex interplay according to season. Higher risk risk is expected with lower minimum atmospheric pressure in the preceding days, lower rainfall in Winter, greater changes in atmospheric pressure in Spring, and higher temperatures in Summer. These findings have important implications for prevention strategies.

1. Introduction

Atherothrombosis remains a major cause of morbidity and mortality worldwide [1]. Despite many discoveries in underlying pathophysiology and improvements in prediction, diagnosis, risk-stratification and management, several unresolved issues persist [2]. Indeed, there are many atherothrombotic triggers which have been the focus of intense research [3], but limited evidence has been accrued on the impact of climate on the chronopathophysiology of atherothrombosis [4,5]. Light, temperature, humidity, and atmospheric pressure may all impact significantly on neurobiology, hormone physiology and cardiovascular functions [6]. Accordingly, seasonal and circadian changes in the incidence and severity of cardiovascular disease have been reported for several conditions such as angina, pulmonary thromboembolism, aneurysmal rupture, and sudden cardiac death [4,7–9].

Most studies reported so far on the association between coronary atherothrombosis and climate have highlighted a J- or U-shaped association, with increased risk for temperatures which are too high or too low, whereas limited and conflicting data are available for humidity, pressure and rainfall [4,7,10–14]. In addition, the vast majority of the

* Corresponding author at: Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Corso della Repubblica 79, 04100 Latina, Italy.
E-mail address: giuseppe.biondizoccai@uniroma1.it (G. Biondi-Zoccai).
[1] Equal contribution.

https://doi.org/10.1016/j.ijcard.2019.07.006
0167-5273/

Table 1
Descriptive analysis.

Feature		Count (%) or mean ± standard deviation
Days		6088
Daily number of primary PCI	0	3241 (53.2%)
	1	1838 (30.2%)
	2	783 (12.9%)
	3	182 (3.0%)
	4	40 (0.7%)
	5	2 (0.03%)
	6	2 (0.03%)
Center	Latina	2008 (35.8%)
	Campobasso	2024 (28.9%)
	Rome	2467 (35.3%)
Gender	Male	2804 (76.3%)
	Female	869 (23.7%)
Age (year)		64.5 ± 13.2
Temperature (°C)	Minimum	11.9 ± 6.9
	Maximum	20.3 ± 7.9
	Mean	14.0 ± 7.1
	Delta	8.4 ± 3.4
Atmospheric pressure (bar)	Minimum	1013.2 ± 7.7
	Maximum	1017.3 ± 6.8
	Mean	1015.3 ± 9.0
	Delta	4.1 ± 4.3
Humidity (%)	Minimum	51.0 ± 17.8
	Maximum	90.5 ± 9.5
	Mean	71.5 ± 13.8
	Delta	39.5 ± 15.9
Rainfall (mm)	AM	1.09 ± 4.32
	PM	1.27 ± 4.47
	Total daily	2.33 ± 6.84

evidence on this topic risks being outdated, not valid given changes in primary prevention approaches and reperfusion strategies, or limited to specific geographic areas characterized by peculiar meteorologic features [15–17].

We thus aimed to appraise in detail the association between several climate features on a daily and seasonal basis, with the ultimate goal of providing practical guidance to identify which variables and their corresponding changes may predict peaks in coronary atherothrombotic events.

2. Methods

This study is a retrospective analysis of anonymized data on primary percutaneous coronary intervention (PPCI) collected for administrative purposes in three high-volume Italian institutions with large catchment areas: Latina province, Rome province, and Molise region. Detailed data were obtained on occurring between June 2012 and June 2017. Cases in which the procedure was limited to emergency coronary angiography or percutaneous coronary intervention for non-ST-elevation acute coronary syndrome were excluded from data collection. No ethical approval was sought given the use of anonymized data only.

Climate features were provided by the Meteorologic Center of Italian Military Aviation, Pratica di Mare, Italy. In particular, the following variables were collected: atmospheric temperature (expressed in °C; mean, minimum, maximum), relative humidity (representing the ratio the partial pressure of water vapor to the equilibrium vapor pressure of water at a given temperature; expressed as %; mean, minimum, maximum), rainfall (expressed in mm; mean, minimum, maximum), atmospheric pressure (ATM; expressed in bar; mean, minimum, maximum). They were recorded as values for the same day of PPCI, the day preceding the PPCI, 3 days before the PPCI, or the mean of the 3 days preceding the PPCI. Specifically, PPCI was defined as emergent coronary angiography followed by percutaneous revascularization for ST-elevation myocardial infarction or non-ST-elevation myocardial infarction complicated by clinical instability.

Variables were described as count (%) or mean ± standard deviation. The association between meteorologic features and number of daily PPCI was inferentially appraised with a mixed-effect generalized linear model with Poisson likelihood and logit link, forcing center as random effect, in order to appraise clusters of multiple PPCI occurring in the same day while adjusting for within-center correlation. Accordingly, an overall analysis was conducted, and then subgroup analyses according to season, to explore the potential mediating effects of this feature. In addition, the impact of gender on the association between meteorologic variables and risk of PPCI was appraised with generalized estimating equations with a logit link, using date as clustering feature, thus exploring in detail the impact of center-wise features. Statistical significance was set at the 2-tailed 0.05 level, without multiplicity adjustment. Computations were performed with Stata 13 (StataCorp, College Station, TX, USA).

Table 2
Poisson analysis for the association between same day meteorologic variables and daily number of primary percutaneous coronary interventions.*

Feature		Overall	Winter-only	Spring-only	Summer-only	Fall-only
Temperature (° C)	Minimum	1.002 (0.994–1.009), $p = 0.674$	0.991 (0.974–1.008), $p = 0.274$	1.000 (0.987–1.014), $p = 0.955$	**1.022 (1.001–1.044), p = 0.040**	1.002 (0.989–1.016), $p = 0.756$
	Maximum	0.998 (0.990–1.005), $p = 0.575$	0.984 (0.966–1.002), $p = 0.083$	0.995 (0.982–1.008), $p = 0.426$	1.019 (0.999–1.040), $p = 0.065$	1.000 (0.986–1.013), $p = 0.971$
	Mean	**0.992 (0.985–1.000), p = 0.043**	**0.972 (0.955–0.988), p = 0.001**	0.991 (0.978–1.005), $p = 0.189$	1.007 (0.986–1.028), $p = 0.521$	1.000 (0.987–1.012), $p = 0.950$
	Delta	0.993 (0.982–1.003), $p = 0.175$	0.995 (0.975–1.014), $p = 0.581$	0.988 (0.969–1.007), $p = 0.206$	0.998 (0.975–1.021), $p = 0.881$	0.993 (0.969–1.017), $p = 0.548$
Atmospheric pressure (bar)	Minimum	0.998 (0.994–1.003), $p = 0.443$	0.999 (0.993–1.005), $p = 0.801$	0.996 (0.986–1.006), $p = 0.400$	0.989 (0.975–1.002), $p = 0.108$	1.001 (0.993–1.008), $p = 0.815$
	Maximum	0.999 (0.994–1.004), $p = 0.686$	0.999 (0.992–1.006), $p = 0.719$	1.001 (0.990–1.013), $p = 0.835$	0.994 (0.977–1.012), $p = 0.524$	0.999 (0.991–1.008), $p = 0.897$
	Mean	1.000 (0.996–1.004), $p = 0.968$	1.001 (0.994–1.007), $p = 0.838$	0.997 (0.988–1.006), $p = 0.485$	1.004 (0.985–1.023), $p = 0.700$	1.001 (0.993–1.009), $p = 0.775$
	Delta	1.003 (0.995–1.012), $p = 0.450$	0.998 (0.982–1.014), $p = 0.789$	**1.024 (1.002–1.045), p = 0.031**	1.006 (0.993–1.019), $p = 0.397$	0.993 (0.976–1.011), $p = 0.434$
Humidity (%)	Minimum	0.999 (0.997–1.001), $p = 0.183$	**0.994 (0.991–0.998), p = 0.001**	0.999 (0.995–1.002), $p = 0.460$	1.002 (0.997–1.007), $p = 0.492$	1.003 (0.999–1.007), $p = 0.194$
	Maximum	1.000 (0.996–1.004), $p = 0.911$	**0.993 (0.987–0.999), p = 0.030**	1.004 (0.997–1.011), $p = 0.326$	0.999 (0.992–1.006), $p = 0.771$	1.009 (0.999–1.020), $p = 0.091$
	Mean	0.999 (0.997–1.002), $p = 0.621$	**0.993 (0.988–0.998), p = 0.002**	1.001 (0.996–1.006), $p = 0.666$	1.002 (0.997–1.008), $p = 0.423$	1.004 (0.998–1.011), $p = 0.207$
	Delta	1.002 (0.999–1.004), $p = 0.166$	**1.005 (1.001–1.009), p = 0.016**	1.003 (0.999–1.007), $p = 0.162$	0.997 (0.992–1.003), $p = 0.350$	0.999 (0.994–1.003), $p = 0.536$
Rainfall (mm)	AM	0.993 (0.985–1.002), $p = 0.112$	**0.979 (0.959–0.999), p = 0.041**	0.994 (0.977–1.012), $p = 0.530$	1.006 (0.989–1.024), $p = 0.506$	0.993 (0.980–1.007), $p = 0.312$
	PM	1.003 (0.996–1.010), $p = 0.375$	1.004 (0.988–1.019), $p = 0.658$	1.010 (0.999–1.021), $p = 0.066$	0.993 (0.973–1.014), $p = 0.506$	1.000 (0.987–1.012), $p = 0.941$
	Total daily	0.999 (0.994–1.004), $p = 0.671$	0.995 (0.984–1.006), $p = 0.345$	1.004 (0.996–1.012), $p = 0.335$	1.000 (0.987–1.012), $p = 0.968$	0.997 (0.988–1.005), $p = 0.449$

* A regression coefficient <1 indicates lower risk, and >1 indicates higher risk; bold type indicates significant associations (i.e. $p < 0.05$).

Table 3
Poisson analysis for the association between prior day meteorologic variables and daily number of primary percutaneous coronary interventions.*

Feature		Overall	Winter-only	Spring-only	Summer-only	Fall-only
Temperature (°C)	Minimum	1.004 (0.996–1.011), $p = 0.326$	0.994 (0.977–1.010), $p = 0.454$	1.003 (0.990–1.017), $p = 0.628$	1.011 (0.993–1.030), $p = 0.225$	1.008 (0.994–1.022), $p = 0.277$
	Maximum	0.996 (0.989–1.003), $p = 0.237$	**0.980 (0.963–0.997), $p = 0.023$**	0.995 (0.984–1.007), $p = 0.436$	1.007 (0.992–1.023), $p = 0.375$	0.998 (0.985–1.011), $p = 0.719$
	Mean	0.994 (0.987–1.001), $p = 0.093$	**0.978 (0.961–0.994), $p = 0.009$**	0.993 (0.980–1.006), $p = 0.295$	0.997 (0.981–1.014), $p = 0.729$	1.003 (0.990–1.015), $p = 0.743$
	Delta	**0.984 (0.974–0.994), $p = 0.002$**	0.984 (0.965–1.003), $p = 0.107$	0.982 (0.964–1.001), $p = 0.060$	0.998 (0.976–1.020), $p = 0.847$	**0.970 (0.947–0.993), $p = 0.012$**
Atmospheric pressure (bar)	Minimum	0.997 (0.992–1.001), p = 0.107	0.995 (0.989–1.002), $p = 0.146$	**0.989 (0.979–0.998), 0.022**	0.999 (0.982–1.017), $p = 0.947$	1.002 (0.995–1.010), $p = 0.539$
	Maximum	0.998 (0.993–1.003), $p = 0.355$	0.997 (0.990–1.004), $p = 0.353$	0.990 (0.979–1.001), $p = 0.086$	1.003 (0.989–1.018), $p = 0.649$	1.002 (0.993–1.011), $p = 0.623$
	Mean	0.997 (0.993–1.002), $p = 0.205$	0.995 (0.989–1.002), $p = 0.154$	0.991 (0.981–1.001), $p = 0.063$	1.005 (0.986–1.025), $p = 0.589$	1.004 (0.996–1.012), $p = 0.345$
	Delta	1.007 (0.999–1.015), p = 0.096	1.013 (0.998–1.029), $p = 0.085$	1.018 (0.997–1.040), p = 0.096	1.004 (0.990–1.018), $p = 0.591$	0.996 (0.980–1.013), $p = 0.669$
Humidity (%)	Minimum	0.99 (0.997–1.001), $p = 0.320$	**0.995 (0.991–0.998), $p = 0.002$**	0.998 (0.994–1.002), $p = 0.233$	1.003 (0.998–1.008), $p = 0.240$	**1.004 (1.000–1.009), $p = 0.045$**
	Maximum	0.998 (0.995–1.002), $p = 0.348$	0.994 (0.988–1.001), $p = 0.090$	0.999 (0.992–1.006), p = 0.743	1.003 (0.995–1.010), $p = 0.462$	0.997 (0.987–1.006), $p = 0.500$
	Mean	0.999 (0.997–1.002), 0.626	**0.994 (0.989–0.998), p = 0.007**	1.000 (0.995–1.005), $p = 0.965$	1.003 (0.997–1.009), $p = 0.293$	1.004 (0.998–1.011), $p = 0.211$
	Delta	1.001 (0.998–1.003), 0.598	**1.005 (1.001–1.009), p = 0.011**	1.002 (0.998–1.006), $p = 0.276$	0.998 (0.993–1.004), 0.503	0.994 (0.990–0.999), $p = 0.014$
Rainfall (mm)	Total	1.002 (0.997–1.006), $p = 0.471$	1.003 (0.993–1.013), $p = 0.550$	1.002 (0.993–1.011), p = 0.743	1.005 (0.994–1.016), $p = 0.388$	1.000 (0.992–1.008), $p = 0.920$

* A regression coefficient <1 indicates lower risk, and >1 indicates higher risk; bold type indicates significant associations (i.e. $p < 0.05$).

3. Results

A total of 4132 PPCI occurred during a total of 6880 days (Table 1). Patient age was 64.5 ± 13.2 years, and 25.7% were women. Whereas most days (53%) were uneventful, 1, 2 or ≥3 PPCI occurred in 30%, 13%, and 4% of days. Daily temperature ranged between 11.9° and 20.3°, ATM between 1013.2 and 1017.3 bar, and humidity between 51.0% and 90.5%, whereas mean daily rainfall was 2.33 ± 6.84 mm. Overall analysis for the impact of climate on PPCI rates showed that lower mean temperature on the same day was associated with a significant increase in risk ($p = 0.043$), whereas greater changes in temperature occurring on the prior day appeared associated with lower risk ($p = 0.002$) (Table 2; Table 3; Figs. 1S–4S). Minimum ATM 3 days before PPCI was inversely associated with PPCI rates ($p = 0.049$), suggesting that ATM may be the proxy by which temperature changes in the day before the event may impact on incidence (Table 4).

Season-specific analysis showed further significant associations between climate changes and PPCI rates. Specifically, in Winter PPCI rates were higher in days with lower same day mean temperature ($p = 0.001$) and in days with same day lower humidity (p = 0.001 for

Table 4
Poisson analysis for the association between meteorologic variables three days before and daily number of primary percutaneous coronary interventions.*

Feature		Overall	Winter-only	Spring-only	Summer-only	Fall-only
Temperature (°C)	Minimum	1.000 (0.997–1.008), $p = 0.322$	1.002 (0.986–1.019), $p = 0.781$	1.005 (0.994–1.017), $p = 0.366$	1.005 (0.996–1.015), $p = 0.277$	0.999 (0.999–1.008), $p = 0.796$
	Maximum	1.001 (0.997–1.005), $p = 0.601$	1.002 (0.990–1.013), $p = 0.786$	1.003 (0.995–1.012), $p = 0.401$	1.003 (0.996–1.009), $p = 0.402$	0.997 (0.990–1.004), $p = 0.410$
	Mean	0.990 (0.995–1.004), $p = 0.770$	0.993 (0.979–1.007), $p = 0.323$	1.002 (0.993–1.012), $p = 0.646$	1.001 (0.994–1.009), $p = 0.729$	0.997 (0.989–1.006), $p = 0.525$
	Delta	0.999 (0.992–1.006), $p = 0.769$	1.001 (0.987–1.015), $p = 0.919$	1.003 (0.989–1.017), $p = 0.717$	1.002 (0.988–1.016), $p = 0.798$	0.990 (0.976–1.005), $p = 0.182$
Atmospheric pressure (bar)	Minimum	**1.000 (1.000–1.000), $p = 0.049$**	0.999 (0.999–1.000), $p = 0.472$	0.999 (0.999–1.000), $p = 0.225$	0.999 (0.999–1.000), $p = 0.487$	0.999 (0.999–1.000), $p = 0.163$
	Maximum	1.000 (1.000–1.000), $p = 0.102$	0.999 (0.999–1.000), $p = 0.683$	0.999 (0.999–1.000), $p = 0.429$	0.999 (0.999–1.001), $p = 0.431$	0.999 (0.999–1.000), $p = 0.156$
	Mean	1.000 (1.000–1.000), $p = 0.086$	0.999 (0.999–1.000), $p = 0.631$	0.999 (0.999–1.000), $p = 0.374$	0.999 (0.999–1.001), $p = 0.440$	1.000 (0.999–1.001), $p = 0.157$
	Delta	1.003 (0.994–1.011), p = 0.460	1.003 (0.988–1.019), $p = 0.676$	**1.021 (1.000–1.043), p = 0.041**	1.005 (0.991–1.019), $p = 0.474$	0.989 (0.972–1.006), $p = 0.203$
Humidity (%)	Minimum	0.999 (0.997–1.000), $p = 0.173$	0.997 (0.994–1.001), $p = 0.131$	0.999 (0.995–1.003), $p = 0.624$	0.998 (0.993–1.003), $p = 0.409$	1.000 (0.996–1.005), $p = 0.885$
	Maximum	0.998 (0.994–1.002), $p = 0.243$	0.998 (0.991–1.004), $p = 0.489$	0.997 (0.990–1.004), $p = 0.432$	0.997 (0.990–1.004), $p = 0.470$	1.000 (0.989–1.010), $p = 0.986$
	Mean	0.999 (0.996–1.001), p = 0.345	0.997 (0.992–1.002), $p = 0.192$	1.000 (0.995–1.004), $p = 0.972$	0.999 (0.993–1.005), $p = 0.714$	0.999 (0.993–1.006), $p = 0.866$
	Delta	1.000 (0.999–1.003), p = 0.426	1.003 (0.999–1.007), $p = 0.187$	1.000 (0.996–1.004), $p = 0.954$	1.001 (0.995–1.006), $p = 0.758$	0.999 (0.995–1.004), $p = 0.871$
Rainfall (mm)	Total	0.998 (0.993–1.003), p = 0.443	1.008 (0.999–1.018), p = 0.086	0.995 (0.985–1.006), $p = 0.352$	0.995 (0.981–1.008), p = 0.440	0.994 (0.986–1.003), $p = 0.202$

* A regression coefficient <1 indicates lower risk, and >1 indicates higher risk; bold type indicates significant associations (i.e. $p < 0.05$).

minimum values, $p = 0.030$ for maximum values, and $p = 0.002$ for mean values, and $p = 0.016$ for same day change), whereas same day AM rainfall appeared associated with lower risk ($p = 0.041$) (Table 1S; Figs. 5S–8S). Lower temperatures on the prior day also significantly increased risk ($p = 0.023$ for maximum temperature and $p = 0.009$ for mean temperature). Lower humidity had similar effects (p $= 0.002$ for minimum values, $p = 0.007$ for mean values, and $p = 0.011$ for change). Focusing on the 3 days prior to PPCI, lower temperature was still associated with adverse effects ($p = 0.017$) (Table 2S ex 5). In Spring, daily PPCI rates were associated with greater changes in ATM on the same day ($p = 0.031$), lower ATM on the prior day ($p = 0.022$), and greater changes in ATM ($p = 0.041$). In Summer, greater risk was conferred by higher minimum temperature on the same day ($p = 0.040$). Finally, in Fall, smaller changes in prior day temperature were associated with increased risk ($p = 0.012$).

Further exploratory analysis appraising the impact of gender did not identify any significant role of this variable on the association between meteorologic variables and risk of PPCI (all $p > 0.05$). Conversely, multivariable analysis including data from all seasons showed that higher minimum ATM 3 days before PPCI was associated with lower risk ($p = 0.030$) (Table 3S ex 6). Limiting the analysis to Winter showed that PPCI rates were increased by lower same day mean temperature ($p = 0.002$) and lower AM rainfall ($p = 0.049$). In Spring greater changes in ATM 3 days before PPCI were associated with increased risk ($p = 0.032$), whereas in Summer higher minimum temperature on the same day was associated with increased risk ($p = 0.040$). Additional sensitivity analyses according to gender are provided in Table 4S.

4. Discussion

This observational study, appraising in detail the association between daily PPCI rates in three high-volume tertiary care centers with different catchment areas in terms of geography and environment, and focusing on several important climate features, has the following main findings. First, analysis of the impact of climate changes on coronary atherothrombotic events cannot disregard season-specific patterns and the trends in climate features in the days preceding the acute event. Second, when appraisal takes into account season, higher risk is of acute myocardial infarction is expected with lower temperatures, lower minimum ATM and lower rainfall in Winter, greater changes in ATM and greater humidity in Spring, and higher temperatures in Summer. Accordingly, preventive strategies should aim at minimizing exposure in cold and dry days in Winter, days with extreme ATM and humidity changes in Spring, and hot days in Summer.

The pathophysiology of atherothrombosis remains a complex conundrum, and complexity increases when focusing on the potential impact of climate on acute myocardial infarction [1–3]. Indeed, climate may be indirectly associated with several untoward events, ranging from subclinical infections with proinflammatory effects to cold-mediated vasoconstriction, or increased cardiac output requirements due to sweating in hot Summer days, with even worse effects in fragile subjects [18]. In addition, climate changes may impact on risk factor control as, for instance, cold Winter days may limit daily activity and promote excessive or high calorie food intake, alcohol consumption, weight gain, or indoor smoking with subsequent secondhand smoke, whose detrimental effects on blood pressure, heart rate, endothelial function and platelet activation are well established [14,19,20]. Yet, the analysis of the interplay between climate and atherothrombotic risk has provided to date conflicting results.

Several previous reports have indeed suggested that higher temperature is associated with increased risk. For instance, the MINAP study has reported on the increased risk in acute coronary events associated with higher tempera1ure [21]. Conversely, the MONICA and the SWEDEHEART studies, among many others, have suggested that lower temperatures may lead to increased risk of acute myocardial infarction [15,16,22]. This controversy has been partly solved by assuming non-linear associations between climate and events [17]. Our study indeed provides a coherent and season-specific framework showing that lower Winter temperatures and higher Summer temperatures may be similarly detrimental.

A number of studies have already been focused on the interplay between ATM and atherothrombosis. Specifically, Danet et al. and the SWEDEHEART study have reported on the J-shaped association between ATM and acute myocardial infarction, while others have not found significant independent effects of this climate feature on outcomes [16,22]. Yet, it is conceivable that, despite the risk of confounding due to concomitant changes with temperature and humidity, increased ATM may lead to increases in blood pressure, especially among hypertensive and prehypertensive patients.

The clinically relevant impact of humidity and rainfall on acute coronary events has been debated extensively. Recent findings from other studies, such as SWEDEHEART, are indeed in agreement with our owns in highlighting the potential detrimental impact of extremes of humidity or low rainfall [22]. Still, the risk of confounding, interaction and/or interplay between these environmental variables is difficult to disentangle with simple unidimensional appraisals.

In light of our findings and others reported in the scholarly literature, several preventive strategies can be envisioned to minimize the detrimental impact of climate on the risk of coronary events. First, exposure to cold dry air should be limited in Winter, using clothing and ambient heating as appropriate. In addition, frail subjects could consider avoiding outdoor activities during very cold and dry days, or altogether consider moving (temporarily or permanently) in warmer locations. Spring days with extreme atmospheric ATM changes should be considered a harbinger of increased risk. Accordingly, hot days in Summer should be viewed with caution, leading to limited outdoor activities, liberal use of air conditioning, and extensive water intake to counterbalance excessive sweating. The detrimental impact of excessive changes in humidity is less immediately actionable, but limiting outdoor activities and liberal use of air conditioning.

This work has several important limitations, which should be borne in mind when applying its findings. First, this is an observational study relying on angiographically appraised events, and thus can only appraise association without stringently implying causation. Second, convenience sampling at the level of PPCI hubs may lead to a distorted sample due to selection bias, with catchment population varying according to various factors (e.g. vacation time). Indeed, it is evident that patients with paucisymptomatic syndromes, those dying before admission or those admitted too late to be eligible for PPCI were not included in the study. Yet, this focus on PPCI also represents a unique strength of our work, given the ensuing emphasis on clinically sanctionable events. Third, only aggregate climate data were measured, thus limiting the appraisal of the association between individual risk and local climate features. Moreover, no data were collected on patient features (e.g. cardiovascular risk factors or medical therapy), nor post-PPCI events, nor additional environment details (e.g. sunlight or pollution). Indeed, air pollution is an important environmental risk factor for cardiovascular disease, and recently Luo et colleagues [23] demonstrated that the association between temperature variability and cardiovascular admissions for cardiovascular disease was attenuated but remained significant after adjustment of air pollutants, suggesting that air pollution is a confounder of the association. Furthermore, and despite our study being preceded by several other analyses, our work has many unique and original strengths. First, focusing on PPCI, it uses clinically valid and poignant event directly related with acute coronary atherothrombosis, at odds with prior works focusing simply on fatal events (typically lacking adjudication details) or clinically (but not angiographically) defined acute myocardial infarction, which is at risk of adjudication bias. In addition, we focused on the same-day comparison of three different Italian areas with similarities (as they are <250 km apart) but differences, as they have different climate and urbanization patterns (with different particulate matter exposures). Finally, the statistical methods capable of recognizing temporal differences as well as regional differences adjusting for potential confounders further strengthen our work impact. Indeed, our goal was to seek climatic features that could predict an increase in clinically relevant acute coronary events, in order to inform healthcare organizations and patients alike.

In conclusion, despite the existence of a notable number of previous publications regarding relationship between meteorological conditions and coronary artery disease yielding similar. I reduce the clinical relevance of our work, we originally report data on a selected group of patients with ST-elevation myocardial infarction treated with PPCI in three tertiary care hospitals.

Indeed, we found that climate has a significant impact on the risk of PPCI in the current era, with a complex interplay according to season. Higher risk risk is expected with lower minimum ATM in the preceding days, lower rainfall in Winter, greater changes in ATM in Spring, and higher temperatures in Summer. These findings have thus important implications for prevention strategies and also for public health organization.

Funding

None.

Conflicts of interest

Prof. Biondi-Zoccai has consulted for Abbott Vascular and Bayer. All other authors have nothing to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.07.006.

References

[1] G.G. Biondi-Zoccai, A. Abbate, G. Liuzzo, L.M. Biasucci, Atherothrombosis, inflammation, and diabetes, J. Am. Coll. Cardiol. 41 (2003) 1071–1077.
[2] Y.C. Chen, A.L. Huang, T.S. Kyaw, A. Bobik, K. Peter, Atherosclerotic plaque rupture: identifying the straw that breaks the camel's back, Arterioscler. Thromb. Vasc. Biol. 36 (2016) e63–e72.
[3] M.A. Munger, D.W. Hawkins, Atherothrombosis: epidemiology, pathophysiology, and prevention, J. Am. Pharm. Assoc. 44 (2004) S5–12 (2003).
[4] B. Marchant, K. Ranjadayalan, R. Stevenson, P. Wilkinson, A.D. Timmis, Circadian and seasonal factors in the pathogenesis of acute myocardial infarction: the influence of environmental temperature, Br. Heart J. 69 (1993) 385–387.
[5] N. Rumana, Y. Kita, T.C. Turin, Y. Murakami, H. Sugihara, Y. Morita, N. Tomioka, A. Okayama, Y. Nakamura, H. Ueshima, Seasonal pattern of incidence and case fatality of acute myocardial infarction in a Japanese population (from the Takashima AMI Registry, 1988 to 2003), Am. J. Cardiol. 102 (2008) 1307–1311.
[6] J.D. Li, W.P. Hu, Q.Y. Zhou, The circadian output signals from the suprachiasmatic nuclei, Prog. Brain Res. 199 (2012) 119–127.
[7] F.A. Spencer, R.J. Goldberg, R.C. Becker, J.M. Gore, Seasonal distribution of acute myocardial infarction in the second National Registry of Myocardial Infarction, J. Am. Coll. Cardiol. 31 (1998) 1226–1233.
[8] C. Spielberg, D. Falkenhahn, S.N. Willich, K. Wegscheider, H. Völler, Circadian, day-of-week, and seasonal variability in myocardial infarction: comparison between working and retired patients, Am. Heart J. 132 (1996) 579–585.
[9] V. Nagarajan, G.C. Fonarow, C. Ju, M. Pencina, W.K. Laskey, T.M. Maddox, A. Hernandez, D.L. Bhatt, Seasonal and circadian variations of acute myocardial infarction: findings from the Get With The Guidelines-Coronary Artery Disease (GWTG-CAD) program, Am. Heart J. 189 (2017) 85–93.
[10] P. Dilaveris, A. Synetos, G. Giannopoulos, E. Gialafos, A. Pantazis, C. Stefanadis, CLimate impacts on myocardial infarction deaths in the Athens TErritory: the CLIMATE study, Heart 92 (2006) 1747–1751.
[11] V.L.S. Crawford, M. McCann, R.W. Stout, Changes in seasonal deaths from myocardial infarction, Q. J. Med. 96 (2003) 45–52.
[12] T. Honda, K. Fujimoto, Y. Miyao, Influence of weather conditions on the frequent onset of acute myocardial infarction, J. Cardiol. 67 (2016) 42–50.
[13] D.B. Panagiotakos, C. Chrysohoou, C. Pitsavos, P. Nastos, A. Anadiotis, C. Tentolouris, C. Stefanadis, P. Toutouzas, A. Paliatsos, Climatological variations in daily hospital admissions for acute coronary syndromes, Int. J. Cardiol. 94 (2004) 229–233.
[14] H. Marti-Soler, C. Gubelmann, S. Aeschbacher, L. Alves, M. Bobak, V. Bongard, E. Clays, G. de Gaetano, A. Di Castelnuovo, R. Elosua, J. Ferrieres, I. Guessous, J. Igland, T. Jørgensen, Y. Nikitin, M.G. O'Doherty, L. Palmieri, R. Ramos, J. Simons, G. Sulo, D. Vanuzzo, J. Vila, H. Barros, A. Borglykke, D. Conen, D. De Bacquer, C. Donfrancesco, J.M. Gaspoz, S. Giampaoli, G.G. Giles, L. Iacoviello, F. Kee, R. Kubinova, S. Malyutina, J. Marrugat, E. Prescott, J.B. Ruidavets, R. Scragg, L.A. Simons, A. Tamosiunas, G.S. Tell, P. Vollenweider, P. Marques-Vidal, Seasonality of cardiovascular risk factors: an analysis including over 230 000 participants in 15 countries, Heart 100 (2014) 1517–1523.
[15] The Eurowinter Group, Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe, Lancet 349 (1997) 1341–1346.
[16] S. Danet, F. Richard, M. Montaye, S. Beauchant, B. Lemaire, C. Graux, D. Cottel, N. Marécaux, P. Amouyel, Unhealthy effects of atmospheric temperature and pressure on the occurrence of myocardial infarction and coronary deaths. A 10-year survey: the Lille-World Health Organization MONICA project (monitoring trends and determinants in cardiovascular disease), Circulation 100 (1999) E1–E7.
[17] R. Chen, P. Yin, L. Wang, C. Liu, Y. Niu, W. Wang, Y. Jiang, Y. Liu, J. Liu, J. Qi, J. You, H. Kan, M. Zhou, Association between ambient temperature and mortality risk and burden: time series study in 272 main Chinese cities, BMJ 363 (2018) k4306.
[18] G. Biondi Zoccai, A. Abbate, F. D'Ascenzo, D. Presutti, M. Peruzzi, E. Cavarretta, A.G. Marullo, M. Lotrionte, G. Frati, Percutaneous coronary intervention in nonagenarians: pros and cons, J. Geriatr. Cardiol. 10 (2013) 82–90.
[19] L. Loffredo, R. Carnevale, L. Perri, E. Catasca, T. Augelletti, R. Cangemi, F. Albanese, C. Piccheri, C. Nocella, P. Pignatelli, F. Violi, NOX2-mediated arterial dysfunction in smokers: acute effect of dark chocolate, Heart 97 (2011) 1776–1781.
[20] C. Nocella, G. Biondi-Zoccai, S. Sciarretta, M. Peruzzi, F. Pagano, L. Loffredo, P. Pignatelli, C. Bullen, G. Frati, R. Carnevale, Impact of tobacco versus electronic cigarette smoking on platelet function, Am. J. Cardiol. 122 (2018) 1477–1481.
[21] K. Bhaskaran, B. Armstrong, S. Hajat, A. Haines, P. Wilkinson, L. Smeeth, Heat and risk of myocardial infarction: hourly level case-crossover analysis of MINAP database, BMJ 345 (2012), e8050.
[22] M.A. Mohammad, S. Koul, R. Rylance, O. Fröbert, J. Alfredsson, A. Sahlén, N. Witt, T. Jernberg, J. Muller, D. Erlinge, Association of weather with day-to-day incidence of myocardial infarction: a SWEDEHEART nationwide observational study, JAMA Cardiol. 3 (2018) 1081–1089.
[23] K. Luo, R. Li, Z. Wang, R. Zhang, Q. Xu, Effect modification of the association between temperature variability and daily cardiovascular mortality by air pollutants in three Chinese cities, Environ. Pollut. 230 (2017) 989–999.