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ORIGINAL PAPER

Mean air temperature as a risk factor for stroke mortality in São Paulo, Brazil

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Abstract

In Brazil, chronic diseases account for the largest percentage of all deaths among men and women. Among the cardiovascular diseases, stroke is the leading cause of death, accounting for 10% of all deaths. We evaluated associations between stroke and mean air temperature using recorded mortality data and meteorological station data from 2002 to 2011. A time series analysis was applied to 55,633 mortality cases. Ischemic and hemorrhagic strokes (IS and HS, respectively) were divided to test different impact on which subgroup. Poisson regression with distributed lag non-linear model was used and adjusted for seasonality, pollutants, humidity, and days of the week. HS mortality was associated with low mean temperatures for men relative risk (RR) = 2.43 (95% CI, 1.12–5.28) and women RR = 1.39 (95% CI, 1.03–1.86). RR of IS mortality was not significant using a 21-day lag window. Analyzing the lag response separately, we observed that the effect of temperature is acute in stroke mortality (higher risk among lags 0–5). However, for IS, higher mean temperatures were significant for this subtype with more than 15-day lag. Our findings showed that mean air temperature is associated with stroke mortality in the city of São Paulo for men and women and IS and HS may have different triggers. Further studies are needed to evaluate physiologic differences between these two subtypes of stroke.

Keywords Stroke · Mean temperature · Time series · DLNM · São Paulo

Introduction

In 2015, more than 56 million people died worldwide; the most fatal diseases were myocardial infarction and stroke, which together totaled more than 15 million deaths, the largest number occurred in peripheral countries ("{WHO} {\textbar} {The} top 10 causes of death," 2015). The main characteristic of CVDs is the presence of atherosclerosis, which is plaque buildup of fat in the arteries over the years that prevents the passage of blood (Mendis et al. 2011).

Stroke is a type of CVD and can be defined as sudden focal neurological deficit resulting from vascular injury (restriction of blood supply to the brain), causing cell injury and damage in neurological functions (Hu et al. 2008). Stroke has two distinct subtypes with different mortality rates, risk factors, and outcomes. Ischemic stroke (IS) is the most common subtype, accounting for 80% of cases of stroke, caused by a vascular occlusion (Schellinger et al. 2003). Ischemic stroke occurs more frequently in the elderly. Its main risk factors are thrombosis, embolism, and lacunar stroke (Lim et al. 2013).

Hemorrhagic stroke (HS) occurs when a vessel in the brain ruptures and spills blood into it. Cases of hemorrhagic stroke are more common in young people and are associated with a high mortality rate compared to those of ischemic stroke (Schellinger et al. 2003). The most

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common cause present in cases of hemorrhagic stroke is hypertension (Galimanis et al. 2009).

A component of the physical environment that potentially influences circulatory system diseases is the local meteorological variables. This influence is direct and indirect and may act in a positive or negative way. High temperatures cause excessive sweating leading to reduced plasma volume and blood pressure drop. The sudden rise in temperature also causes an increase in viscosity of the blood concentration of cholesterol and the number of erythrocytes and platelets (Keatinge et al. 1984).

The effect of meteorological variables on CVDs has been observed in temperate climate localities (Ebi et al. 2004; Turin et al. 2008; Abe et al. 2008; Zhang et al. 2014). Because annual air temperature variation in tropical context is much lower than that in high-latitude environments, few studies have addressed this issue in the tropics (Wang et al. 2009; Coelho et al. 2010). Nevertheless, high daily air temperature variation may have an impact on the physiology mainly in the most vulnerable group of elderly people. Thus, the aim of this study was to verify possible associations between each stroke subtype (HS and IS) and mean air temperature using recorded mortality data and meteorological station data from 2002 to 2011 in the city of São Paulo, which has the subtropical climate and is the largest city of Brazil.

Material and methods

Study area

The city of São Paulo was chosen because is a megacity, with almost 12 million inhabitants, and located in the Tropic of Capricorn (Fig. 1). Its average annual temperature varies between 19 and 27 °C. The hottest period is between the months of December and March, which are also when the highest rainfall volumes of the year are recorded.

Mortality data

Daily records of deaths are due to the following: total stroke (International Codes of Disease 10th Revision—ICD 10th:

Fig. 1 Location of the city of São Paulo

I60–I69), to hemorrhagic (International Codes of Disease 10th Revision—ICD 10th: I60–I62) and ischemic (ICD 10th: I63, I65, and I66) strokes which were obtained from the Death Records Improvement Program (PROAIM), the official health statistics source for the municipality.

Meteorological data

Daily mean air temperatures and relative air humidity were obtained from the Meteorological Observatory of the Institute of Astronomy, Geophysics and Atmospheric Sciences of the University of São Paulo, which is considered representative of all city. As we used relative humidity, cloudy days are likely to have lower diurnal temperature ranges that can result in a higher average relative humidity due to lower temperatures throughout the day.

In order to adjust the effects of air pollution on mortality, daily 24-h averages of particulate matter with an aerodynamic diameter of less than 10 μm (PM_{10}), ozone (O_3), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2) were collected from the environmental agency in São Paulo (Environmental Company Of The State Of São Paulo) from 14 stations spread over the city, although not all of them being fit to measure all types of pollutants. We thus adopted the average of all stations that measured each pollutant as a citywide exposure level.

Statistical analysis

Descriptive analysis was performed to observe the behavior of the time series and the distribution and autocorrelation of the dependent variables. Correlation was tested between independent variables. Quasi-Poisson regression models with generalized linear model (GLM) were built to estimate the effects of mean temperature on mortality for stroke and its subtypes in the total population and for people above 65 years old. Distributed lag non-linear model (DLNM) was also used. DLNM methodology was originally developed for linear models with pollutant effects and has recently been expanded to the non-linear context (Armstrong 2006; Gasparrini 2011).

This type of modeling uses a crossbasis, which is defined with a two-dimensional space describing the association over the predictor space and lag. The crossbasis is specified by two bases, among a set of possible options such as splines, polynomials, and step functions (Gasparrini and Armstrong 2013).

The final model was controlled for relative humidity, pollution variables, and day of the week. Cubic B-splines were built to control for seasonality and trend, with 10 degrees of freedom (df) per year; a time window of 21 days was tested. The software R (R Development Core Team 2014) was used for all statistical analyses and the following packages were used: stats, splines, dlnm, Epi, foreign, and tsModel.

Results

Monthly mean air temperature in the city of São Paulo, for the 10 years of study, was 21 °C, ranging from 15 to 25 °C depending on the season. Concentration of PM_{10} pollutant ranged from 8.30 to 140.3 μg/m^3 (Table 1), with an inverse association with air temperature (highest concentrations with low temperatures). Annual variation of relative humidity ranged from minimum of 34% to maximum of 97.3%.

In the period from 2002 to 2011, 55,663 people died from stroke in São Paulo. IS accounted for 12,183 deaths and HS, 17,250; the difference between the total value of stroke cases with the sum of the hemorrhagic and the ischemic stroke was the cases classified as those not specified as hemorrhagic or ischemic or other cerebrovascular diseases. The daily average was 15.24 cases (Table 2) in total age group for all types of stroke, being slightly higher in women (7.99). For the entire period of study, this slight difference becomes expressive, about 2000 deaths more than in men. For HS subtype, the daily mortality average was 4.72 cases and for IS, 3.34, for all ages, both also higher in women. Cases in elderly were also analyzed with a daily mean of 5.81 cases for women and 4.6 for men.

Figure 2 contains the mean of relative risks for the 21 analyzed lags separated by percentiles of temperature calculated for seven mean temperature percentile ranges: 2.5, 5, 10, 25, 50, 75, 97.5 RR varied according to the type of stroke and sex.

In general, for all stroke types, RR was higher when mean temperature was low, (first percentiles). When the mean temperature recorded is in the range of 17 to 24 °C, the RR was not significant. However, when the mean temperature is above 26 °C, the RR is significant as a risk factor for male over 65 years (RR = 2.12; 95% CI 1.21–3.71), being the highest risk for total stroke.

RR results for HS show that lower temperatures seem to be a risk factor for this subtype, especially below 10 °C both in men (RR = 2.43; 95% CI, 1.12–5.28) and in women (RR = 1.39; 95% CI, 1.03–1.86). Over 65 years, low

Table 1 Variability of the environmental variables for the period of 2002 to 2011

Variable	Mean	Min	SD	Max
Mean daily temperature (°C)	19.45	8.4	3.31	27.6
Max daily temperature (°C)	25.45	11.4	4.54	35.2
Minimum daily temperature (°C)	15.22	2.4	3.38	21.8
Mean daily air pressure	925.99	914.9	3.49	937.9
Mean daily humidity	80.17	34.3	8.51	97.3
PM_{10}	40.74	8.3	19.52	140.3

Table 2 Descriptive statistics of the studied outcomes: daily deaths from stroke, hemorrhagic stroke, and ischemic stroke (mean, minimum value, standard deviation, maximum value, and sum of total deaths for 2002 to 2011)

	Mean	Min	SD	Max	Sum
Stroke	15.24	2	4.16	32	55,663
Stroke female	7.99	0	2.90	19	29,197
Stroke male	7.25	0	2.79	19	26,465
Stroke > 65	10.41	1	3.41	23	38,017
Stroke > 65 female	5.81	0	2.46	16	21,219
Stroke > 65 male	4.60	0	2.22	13	16,798
HS	4.72	0	2.24	15	17,250
HS female	2.49	0	1.58	12	9085
HS male	2.24	0	1.52	10	8165
HS > 65	1.99	0	1.43	10	7275
HS > 65 female	1.13	0	1.06	6	4137
HS > 65 male	0.86	0	0.94	6	3138
IS	3.34	0	1.93	12	12,183
IS female	1.75	0	1.37	8	6379
IS male	1.59	0	1.30	8	5804
IS > 65	2.55	0	1.69	11	9307
IS > 65 female	1.43	0	1.23	7	5236
IS > 65 male	1.11	0	1.08	8	4071

mean temperatures presented a higher risk for women (RR = 1.94; 95% CI, 1.25–2.99).

Evaluating the graphs of lag response curves calculated for different temperatures (Fig. 3), we can see a significant distribution between the 21-day window lag exposures to mean temperatures, but generally, higher values of RR are within 5-day lag display, showing the quick influence of mean temperature on mortality from chronic diseases.

For all types of stroke, temperatures of 10, 15, and 25 °C demonstrated a higher RR in the first 5 days after temperature exposure. The second lag was the one that presented the highest RR value for temperature of 10 °C. After 5 days of exposure, the temperature is no longer a risk factor, except for low temperatures (10 °C). For men and women, the first 5 days of exposure was also the ones that registered higher RR values; however, with highest lags (more than 15 days), the cold affects women more. For men, the opposite occurred; the heat had increased the risk with increased lags.

For IS, cold (10 °C) appears to be a risk factor not only for the first 5 days but also after 10 to 15 days of lag. Heat has acute effect for women and men and a delayed effect for men for whom risk increases with more than 15 days of lag.

HS showed a higher risk with the cold. Exposure to 10 °C of mean temperature showed high RR for overall population and for females in all 21 lags analyzed and for men up to 12 days. For high mean temperatures, only men were affected for up to 3-day lags.

Fig. 2 Relative risks by temperature percentile for the studied outcomes: stroke, hemorrhagic stroke, and ischemic stroke, for female and male, for overall population and the elderly ▶

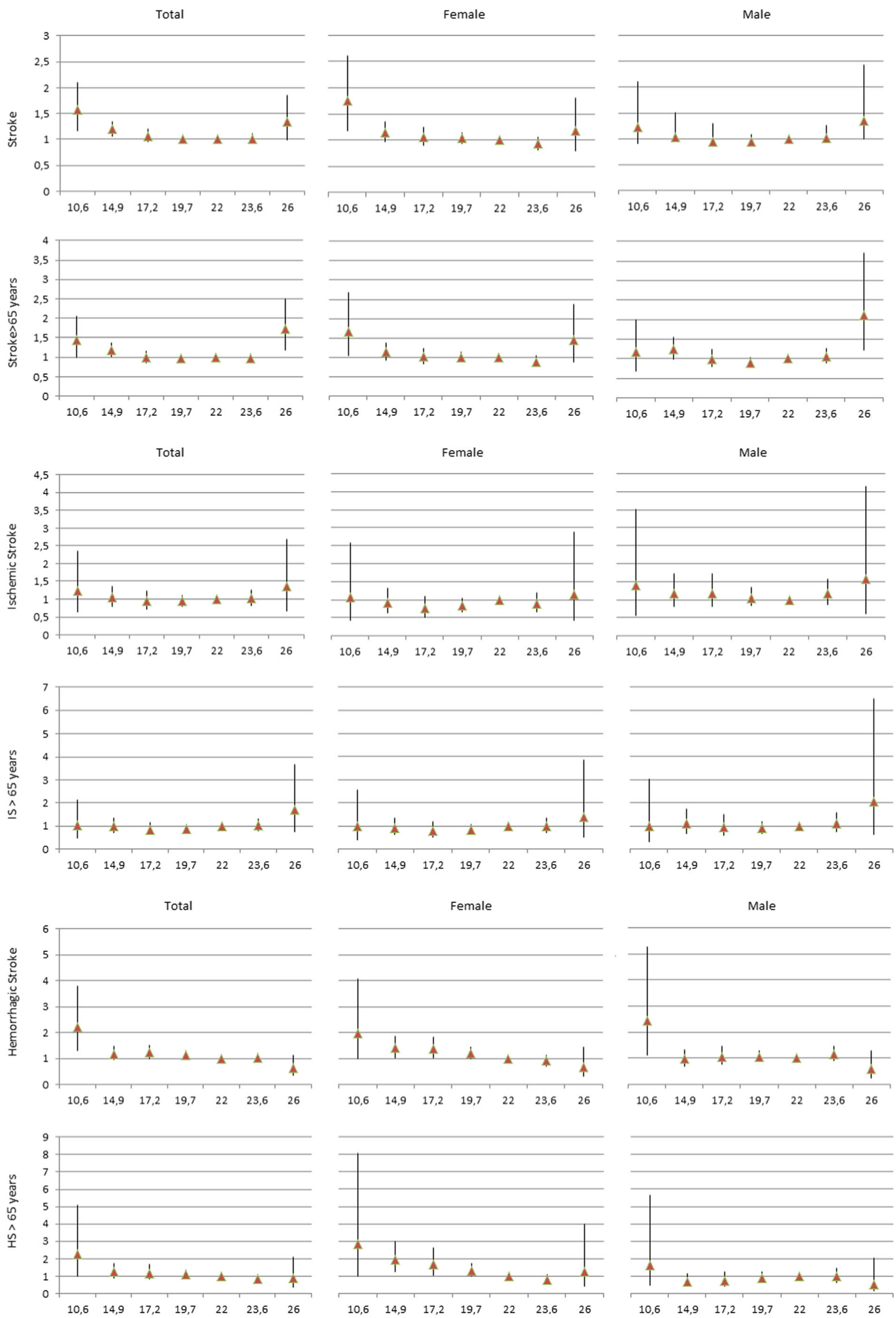
Discussion

This study showed that daily mean temperature is associated with stroke mortality in the city of São Paulo and that relative risk varied by age and sex. As results, we found that lower temperatures (below 15 °C) were statistically more significant with stroke mortality than higher temperatures (above 22 °C). Also, the lagged effect of temperature on relative risk of stroke was higher with up to 5-day exposure for both low and high temperatures.

The effect of temperature has long been analyzed on human health. Potential risks for respiratory (Braga et al. 2002) and cardiovascular diseases are already well explored (Rothwell et al. 1996; Hu and Rao 2009; Wang et al. 2009; Gasparrini 2011; Zanobetti et al. 2012; Lim et al. 2013). Several studies have shown the influence of meteorological variables on hospital admissions and deaths from strokes (Goggins et al. 2012; Morabito et al. 2011; Khan et al. 2005; Berginer et al. 1989; Inagawa et al. 2000). In temperate locations in the USA, relationships were found between hospital admissions and deaths from stroke and atmospheric variables (minimum or maximum temperature, atmospheric pressure, relative humidity) (Ebi et al. 2004). However, other studies conducted in temperate regions, Brussels, the UK, and Canada, found no association between atmospheric variables in the incidence of stroke (Capon et al. 1992; Rothwell et al. 1996; Field et al. 2004; Cowperthwaite and Burnett 2011).

In subtropical and tropical climates where people are acclimated to the hot weather and low thermal amplitude, few studies are available concerning the relationship between temperature and stroke. In Brisbane, a subtropical city in Australia, it was found that the temperature variation was significantly associated with emergency admissions for stroke, with variable impact according to the type, whether ischemic or hemorrhagic (Wang et al. 2009). In Hong Kong, Goggins et al. (2012) found that a variation of 1 °C lower in mean daily temperature over the same day and until lag 4 was associated with an increase (2.7%) in stroke admission.

In Brazil, there are few studies of this nature; the theme has been explored by some national authors but using a data series of very limited time. Rumel et al. (1993) found that 2.8% of the annual hospitalizations for stroke in the emergency department of clinics hospital in São Paulo were due to high air temperatures. In more recent studies, Rufca et al. (2009) evaluated the influence of circadian variations and temperature on 100 patients with ischemic stroke in São José do Rio Preto, state of São Paulo. As a result, the authors found a strong relationship between the prevalence of ischemic stroke and the negative change of temperature. In São Paulo, a study


Total
Female
Male
Stroke
Stroke>65 years
Ischemic Stroke
IS > 65 years
Hemorrhagic Stroke
HS > 65 years
10,6
14,9
17,2
19,7
22
23,6
26

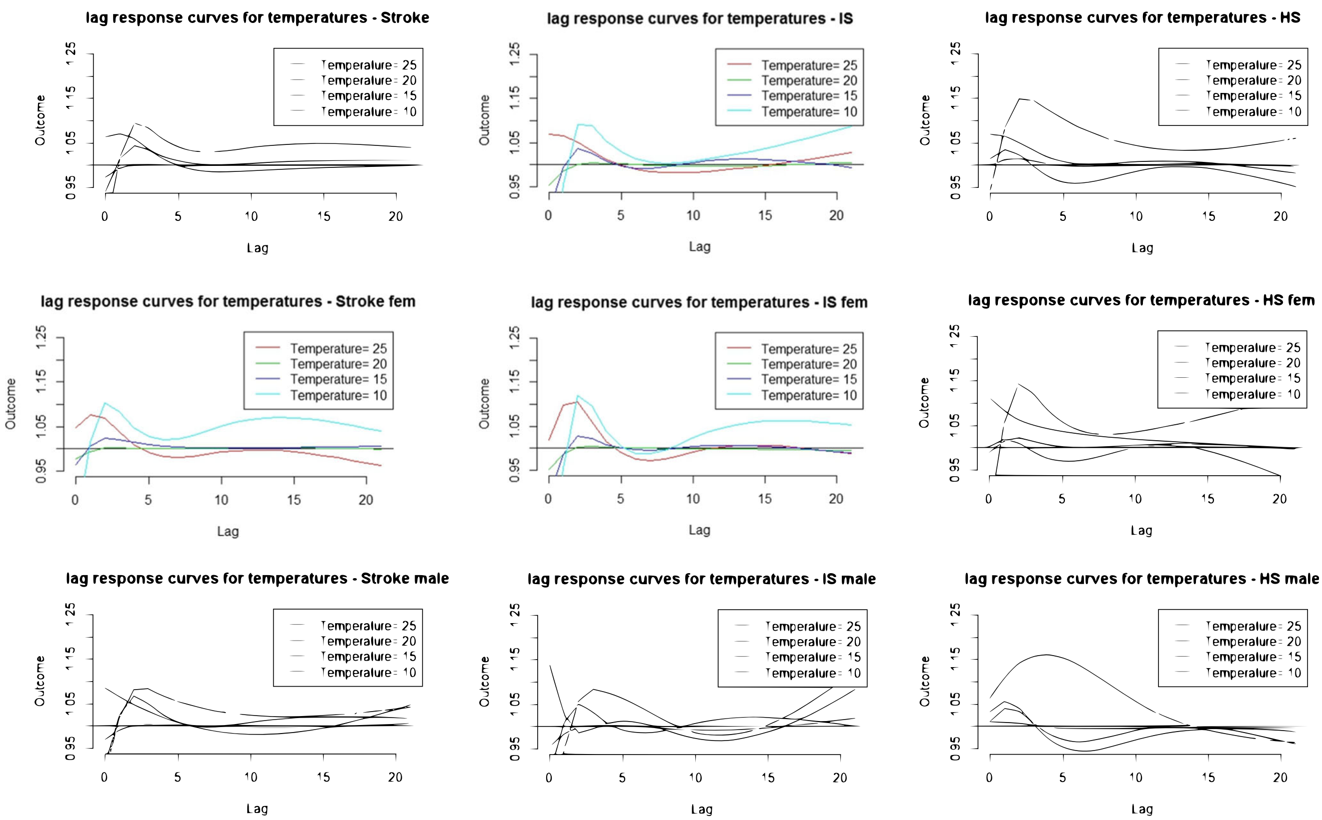


Fig. 3 Lag response curves for air temperatures and stroke mortality in all strokes, subtype groups, and sex (95%CI)

showed that 3 °C variation of the air temperature in the 24 h preceding the onset of symptoms may have been an important factor in stroke occurrence for the case studies (Coelho et al. 2010). Recently, Bando et al. (2012) analyzed the seasonality of mortality from coronary heart disease, heart failure, stroke, suicide, and homicide in São Paulo and found that the stroke does not have a set pattern.

In this study, the mean temperature was used, instead of minimum and maximum because it is an average of several observations on the same day, and it can be a good estimate of exposure and can be less affected by measurement errors, compared to other temperature data. Some studies that used mean temperature have shown that this variable was associated with hospitalization and mortality (Braga et al. 2007; Keatinge et al. 2000).

For the city of São Paulo, mean temperature was associated with total stroke and stroke subtype mortality. The hemorrhagic subtype presented higher risk toward the cold in men and women for all ages and over 65 years in women. According to Goggins et al. (2012), as a result of decreased metabolism, the elderly are poorly able to maintain homeostasis in response to changes in usual temperatures. This result is consistent with that found in tropical localities such as Australia (Wang et al. 2009) and subtropical climate areas in China (Pan et al. 1995a), Korea (Lim et al. 2013), and Italy (Morabito et al. 2011). These studies found a negative association between hospitalization or mortality due to hemorrhagic stroke and the temperature. This subtype of stroke seems not to be very susceptible to high temperatures even with lag; a similar result was found by Lim et al. (2013) in Korea for hemorrhagic stroke.

IS at the 21 lag window did not show significant risk for total IS and for women. On the contrary, for men, the heat seems to be a risk factor for ischemic stroke (Fig. 3). These results reinforce the concept that the subgroups of stroke, ischemic and hemorrhagic, may present different pathophysiologic mechanisms and, hence, different risk factors (Pan et al. 1995b; Lim et al. 2013).

When evaluating lag response for mean temperature, we notice that relative risk was more significant with up to 5-day lags in all types of stroke showing an acute effect of temperature on stroke mortality. This result can be sustained by Goggins et al. (2012) whose study showed that association between stroke subtypes and mean temperature in Hong Kong was stronger and significant with lags (0–4).

For the ischemic subtype, higher mean temperatures presented a significant risk value for men with a delay of more than 15 days. In a recent study, Vodonos et al. (2017) analyzed the effect of the maximum hourly temperature in cases of ischemic stroke in Israel and found that temperature was associated with IS in men and not in women.

Overall, at the sex analysis, we found that for total stroke and HS, the most vulnerable sex was women. The data of the descriptive statistics show that women have the highest mean of mortality, even if slightly. The relative risk of stroke calculated for mean temperature variations was also higher (1.75, CI 1.17–2.61) in women than in men (1.04, CI 1.02–1.51). The lowest mean temperatures caused more impact on women from both subtypes, and for low and high lags. The stress for cold, according to Keatinge et al. (1984), results in increased blood pressure, as well as increased blood viscosity and platelet counts, thus increasing blood pressure that may cause HS. Recent studies have explained main factors why women are more susceptible than men in cases of stroke. Cordonnier et al. (2017) have shown that the influence of some risk factors are stronger in women, such as diabetes mellitus and high blood pressure, because "women differ from men in a multitude of ways, including anatomy, vascular biology, immunity, neuroprotective factors, coagulation, hormonal profiles, vascular risk factors, lifestyle factors and societal roles." Still according to the authors, WHO reported an excess of stroke in women compared to men in the period of 1996–2006.

These results focus on an ecological study design, and part of this design has some limitations like lack of information on individual medical history or personal alimentation and exercise habits, and others contributors to health effects. The data used in this research are from mortality and not from hospital admissions, which can impair the analysis even using time lag, since a patient may have a stroke and not come immediately to death, and may be hospitalized for months. Another limitation is the use of air temperature and humidity data measured in outdoor environments which may not correctly express the temperature and humidity in addition to the concentration of pollutants that individuals are subjected when indoors, such as office and home.

We consider the results found in this research, to be important. Firstly, it is because this study contributes to understanding the impact of temperature on stroke mortality in a tropical setting, where temperature is not supposed to be a concern. Secondly, it is because the amount of deaths in the city gives power to the statistical analysis. Additionally, for the health managers of the city of São Paulo, this knowledge may be useful to alert people about risks, mainly the elderly at home or in asylums where efforts could be made to improve thermal comfort, reducing hospitalizations and avoidable deaths. Social inequality in low- and middle-income countries is an important issue that needs to be addressed and affects mainly a population that is aging.

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Compliance with ethical standards

Competing interests The authors declare they have no competing interests.

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