ARTICLE IN PRESS
IJCA-24358; No of Pages 5
International Journal of Cardiology xxx (2016) xxx–xxx
Contents lists available at ScienceDirect
International Journal of Cardiology
journal homepage: www.elsevier.com/locate/ijcard

Within-summer variation in out-of-hospital cardiac arrest due to extremely long sunshine duration

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ARTICLE INFO

Article history:
Received 11 October 2016
Received in revised form 18 December 2016
Accepted 21 December 2016
Available online xxxx

Keywords:
Epidemiology
Cardiac arrest
Environmental medicine
Statistical analysis
Sudden death
Sunshine

ABSTRACT

Background: Although several studies have reported the impacts of extremely high temperatures on cardiovascular diseases, no studies have examined whether variation in out-of-hospital cardiac arrest (OHCA) due to extremely long sunshine duration changes during the summer.

Methods: We obtained daily data on all cases of OHCA and weather variations for all 47 prefectures of Japan during the summer (June to September) between 2005 and 2014. A distributed lag non-linear model combined with a quasi-Poisson regression model was used to estimate within-summer variation in OHCA due to extremely long sunshine duration for each prefecture. Then, multivariate random-effects meta-analysis was performed to derive overall effect estimates of sunshine duration at the national level.

Results: A total of 166,496 OHCAs of presumed cardiac origin met the inclusion criteria. The minimum morbidity percentile (MMP) was the 0th percentile of sunshine duration at the national level. The overall cumulative relative risk (RR) at the 99th percentile vs. the MMP was 1.15 (95% CI: 1.05–1.27) during the summer. The effect of extremely long sunshine duration on OHCA in early summer was acute and did not persist, whereas an identical effect was observed in late summer, but it was delayed and lasted for several days.

Conclusions: During summer periods, excessive sunshine duration could increase the risk of OHCA. Timely preventive measures to reduce the OHCA risk due to extremely long sunshine duration are important in early summer, whereas these measures could include a wider time window of several days to reduce the risk in late summer.

1. Introduction

An association has been established between seasonal and weather variations and sudden cardiac arrest. Sudden cardiac death and coronary heart disease events demonstrate highly significant seasonal variations, with maximum incidence during the winter [1], and sudden cardiac mortality is strongly associated with cold temperatures [2]. A multi-city study has also found that both extreme heat and cold are associated with an increase in the risk of out-of-hospital coronary death [3]. Regarding the population attributable risk, cold temperature is responsible for the highest proportions of temperature-related cardiovascular disease mortality and emergency cardiovascular hospitalization [4,5]. However, no studies have investigated the impact of sunshine duration on the incidence of out-of-hospital cardiac arrest (OHCA), with adjustments for mutual confounding among sunshine durations and potential confounding by seasonally varying factors.

Specifically, in recent years, many studies have noted that the impact of extreme weather conditions on cardiovascular disease mortality and morbidity may change over time. With respect to long-term variations, the incidence of heat–related cardiovascular deaths has decreased over time, whereas an increasing trend in the effect of heat on cardiovascular disease mortality has also been reported [6,7]. However, changes in the susceptibility of a population may also occur within shorter periods of time, such as within seasons, and this susceptibility could be affected by factors causing of cardiovascular diseases. Additionally, with growing concerns about climate change and global warming in recent years, many studies have provided evidence that heat events during summer months cause serious public health problems [8]. Thus, obtaining a better understanding of temporal variations in the relationship between extreme weather events and cardiovascular diseases during summer season is essential to elucidate how changes in the level of exposure and public health strategies modify exposure-response association. Although several studies have evaluated variations in mortality risk during the summer [9,10], no studies have investigated within-summer variations in the effects of extremely long sunshine duration on OHCA.

In the present study, we obtained Japanese national registry data for all OHCA cases occurring between 2005 and 2014 in the 47 prefectures of Japan to investigate within-summer variations in the association

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http://dx.doi.org/10.1016/j.ijcard.2016.12.179
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between extremely long sunshine duration and OHCA. To accomplish this, we used flexible statistical models based on distributed lag non-linear models and multivariate random-effects meta-regression models.

2. Methods

2.1. Data collection

In Japan, emergency medical service (EMS) is provided by municipal governments at ~800 fire stations with dispatch centers under Japan's Fire Service Act. As EMS providers are not allowed to terminate resuscitation in the field, all patients with OHCA who are treated by EMS personnel are then transported to a hospital [11]. Following the standardized Utstein-style reporting guidelines for cardiac arrest, the EMS personnel summarize each case of OHCA in cooperation with the physician in charge [11]. Data from all fire stations with dispatch centers in the 47 prefectures are then sent to the Fire and Disaster Management Agency (FDMA) and integrated into the national registry system on the FDMA database server. Reporting of the registration of OHCA episodes is required under the Fire Service Act, and registration of OHCA data is considered complete across the country. Detailed information on the EMS system in Japan has been published elsewhere [12].

We collected data on OHCA cases occurring between January 1, 2005 and December 31, 2014 in the 47 Japanese prefectures from the FDMA. The patients were 18 to 110 years of age and had OHCA of presumed cardiac origin. The cause of cardiac arrest (i.e., presumed cardiac or non-cardiac) was determined clinically by the physician in charge, in cooperation with the EMS personnel. The arrest was considered to be of cardiac origin unless it was caused by drowning, trauma, drug overdose, exsanguination, asphyxia, or any other obvious non-cardiac cause.

We also obtained data on the daily mean duration of sunshine hours, temperature, and relative humidity collected from the Japan Meteorological Agency. A single weather station located within the urban area of the capital city was selected as a representative of the region for each prefecture. The daily mean sunshine hours, temperatures, and relative humidity levels were calculated as 24-h averages based on hourly measurements. Daily sunshine hours were recorded with rotating mirror sunshine recorders and were defined as the period when the direct solar irradiance was higher than 120 W/m^2. To focus on the within-summer variation in the effect of extremely long sunshine duration on OHCA, the study period was restricted to the summer season (June to September), identified as the four warmest months of the year according to the average monthly temperatures.

2.2. Ethical approval

This study was approved by the ethics committee of the Kyushu University Graduate School of Medical Sciences. Because this was a retrospective observational study conducted using national registry data and because the enrolled individuals were deidentified by the FDMA, the requirement for written informed consent was waived.

2.3. Statistical analysis

2.3.1. First-stage time series model

For the first stage, we used a distributed lag non-linear model combined with a quasi-Poisson regression model to examine the prefecture-specific non-linear lag effects of daily sunshine hours on OHCA [10]. To describe relationships with spatial sunshine data and with the lags simultaneously, the cross-basis function was defined using a natural cubic spline. A cross-basis matrix was obtained by estimation of the exposure–response function modeled with quadratic B-splines, with 1 internal knot at the 75th percentiles of the prefecture-specific summer sunshine distributions, and the lag-response function modeled with natural cubic B-splines, with an intercept and 2 internal knots at equally spaced values on the log scale. The maximum lags were set to 10 days to examine the delayed effects of extremely long sunshine duration on OHCA and to exclude the harvesting effect. A natural cubic B-spline with equally spaced knots and 4 degrees of freedom (df) for the day of the season was used to control for seasonality. A natural cubic B-spline with equally spaced knots and 1 degree of freedom for the year was used to adjust for long-term trends. Indicator variables for the day of the week and daily mean temperature were also included in the model.

Although sunshine–OHCA associations for each prefecture could be evaluated using absolute sunshine duration scales, the distributions and ranges of sunshine duration differed among the 47 prefectures. Additionally, the overall effects of sunshine duration on OHCA may be more meaningful on a relative sunshine duration scale than on an absolute sunshine duration scale due to climate change adaptation. Thus, the association of sunshine duration with OHCA was assessed by standardizing the prefecture-specific absolute sunshine durations to the prefecture-specific sunshine duration percentiles [10].

2.3.2. Second-stage meta-analysis

For the second stage, a multivariate random-effects meta-regression model was applied to obtain pooled effect estimates at the national level and then to estimate the best linear unbiased prediction of pooled associations of sunshine duration with OHCA for all 47 prefectures [13]. As meta-predictors, the mean absolute sunshine duration and absolute sunshine duration range in each prefecture were adjusted to account for residual heterogeneity between prefectures. Multivariate extension of the Cochran Q test and the I^2 index were used to assess residual heterogeneity among prefectures [10].

The minimum morbidity sunshine duration was derived from the weakest point of the overall cumulative association between sunshine duration and OHCA, and this value was interpreted as the optimum sunshine duration corresponding to the minimum morbidity risk. It represented the minimum morbidity percentile (MMP) of sunshine duration and was estimated using the best linear unbiased prediction of the pooled relationships between sunshine duration and OHCA in each prefecture, and these values were used as references to estimate the risk of OHCA by recentering the quadratic B-spline, which models the prefecture-specific overall cumulative sunshine–OHCA association. We defined extremely long sunshine duration as sunshine duration above the 99th percentile of sunshine duration, and the results were summarized by calculating overall cumulative relative risk (RR) at the 90th and 99th percentiles for whole summer, early summer (corresponding to first 2 summer months), and late summer (corresponding to last 2 summer months). Within-summer variation in extremely long sunshine duration-related OHCA was examined using the multivariate Wald test to assess the pooled prefecture-specific interaction terms at the national level. This method is described in detail elsewhere [10].

Sensitivity analyses were performed to examine the robustness of our results by controlling for df to account for seasonality, long-term trends (6 and 8 df per year) and relative humidity. All analyses were performed using the *dlnm* and *mvmeta* packages of R software (version 3.3.0, R Development Core Team, 2016). The significance level for all tests was set at $P < 0.05$ (two-sided).

3. Results

A total of 1,176,351 OHCA cases were registered between 1 January 2005 and 31 December 2014 in the 47 prefectures of Japan. We analyzed 166,496 OHCAs of presumed cardiac origin that occurred during the summer (June to September) and met the inclusion criteria (Table 1). The daily mean summer sunshine duration was 5.5 h, ranging from 4.2 h in Tochigi to 6.4 h in Okinawa (Table 1 and Supplementary Table S1).

The overall cumulative associations between summer sunshine duration and OHCA for whole, early, and late summer are shown in Fig. 1 and Table 2. The corresponding relationships in each prefecture are also shown in Supplementary Fig. S1. The MMP was the 0th percentile of the summer sunshine duration at the national level. The overall RR at the 99th percentile vs. the MMP was 1.15 (95% CI: 1.05–1.27). The estimated pooled RR for extremely long sunshine duration in early summer was 1.08 (95% CI: 0.91–1.28), whereas that in late summer was 1.31 (95% CI: 1.03–1.67). The multivariate Wald test showed no significant temporal variation in the effects of extremely long sunshine duration on OHCA ($p = 0.074$; Table 2). Multivariate random-effects meta-analysis indicated that there was no geographical heterogeneity among the prefectures (Cochran Q test, $p = 0.729$; $I^2 = 1.0\%$).

The pooled lag-response relationships between extremely long sunshine duration and OHCA at the 99th percentile for early and late summer are shown in Fig. 2. In early summer, an effect of extremely long sunshine duration was detected immediately and lasted for 1 or 2 days. An identical effect was observed in late summer; however, its appearance was delayed, and it lasted for several days.

To investigate whether the results were sensitive to the modeling choices, we also performed sensitivity analysis by using different degrees of freedom for seasonality or by including relative humidity to assess the robustness of our model. Sensitivity analysis showed that the results were broadly similar when we used 6 and 8 df per year for seasonality (Supplementary Figs. S2–S3) and relative humidity did not show any confounding effect (Supplementary Fig. S4). These results suggested that our findings were robust.

4. Discussion

In this study, we examined within-summer variation in the effects of extremely long sunshine duration on OHCA in all 47 prefectures of Japan. Most importantly, a significant association between extremely long sunshine duration and OHCA was observed during the summer periods, after adjusting for potential confounders including temperature, seasonality, and long-term trends. An effect of extremely long