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Extreme temperature and out-of-hospital cardiac arrest in Japan: A nationwide, retrospective, observational study

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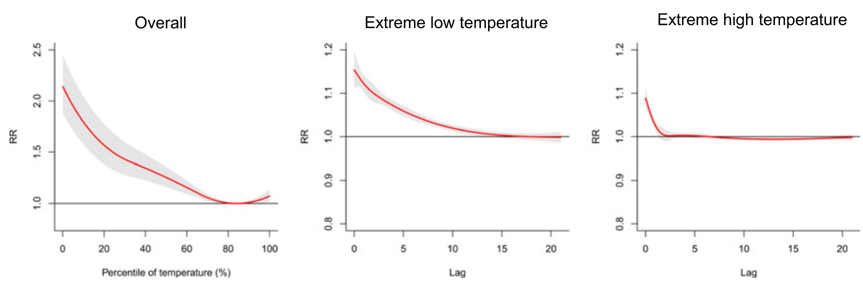
HIGHLIGHTS

- Low as well as high temperatures show effects on OHCA.
- Extremely high and low temperatures are associated with OHCA.
- Heat effects were acute and disappeared after a few days.
- Cold effects were also acute, but persisted for several days.
- There was no spatial heterogeneity among prefectures.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Although several studies have estimated the effect of extreme temperatures on out-of-hospital cardiac arrest (OHCA) in a single city or region, few have investigated variations in this association on a national level in Japan.
Methods: Daily data on OHCAs and weather variations were obtained from the 47 prefectures of Japan between 2005 and 2014. A time-series Poisson regression model with a distributed lag non-linear model was used to estimate the prefecture-specific effects. A multivariate meta-analysis was applied to pooled estimates on a national level.
Results: A total of 659,752 OHCA cases of presumed-cardiac origin met the inclusion criteria. The minimum morbidity percentile (MMP) was identified as the 84th percentile for temperature, ranging from 20.8 °C in Hokkaido to 28.8 °C in Okinawa. The overall pooled relative risk versus the MMP was 2.10 (95% CI: 1.84, 2.40) at extremely low temperatures (1st percentile) and 1.06 (95% CI: 1.01, 1.12) at extremely high temperatures (99th percentile). The effects of extremely high temperatures were acute and disappeared after a few days, while those of extremely low temperatures were also acute, but persisted for several days. The multivariate Cochran's Q test indicated no heterogeneity between prefectures ($p = 0.699$; $I^2 = 1.0\%$).
Conclusions: Extreme temperatures are associated with an increased risk of OHCA. Timely prevention strategies might reduce the risk of OHCA during extreme temperatures. Several days prevention should be also implemented for extremely low temperatures.

1. Introduction

Recent studies have provided evidence of an association between ambient temperature and morbidity or mortality (Basu and Samet, 2002; Ye et al., 2012). These weather-related outcomes are expected to increase commensurately as periods of extreme temperature

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increase in frequency, intensity, and duration due to climate change (Le Tertre et al., 2006; Semenza et al., 1996; Stocker et al., 2014). Although extremely high and low temperatures adversely affect the health of people in the affected area, there are inconsistencies in the direction and magnitude of non-linear lag effects (Basu and Samet, 2002; Le Tertre et al., 2006; Semenza et al., 1996; Stocker et al., 2014; Ye et al., 2012). A number of studies have investigated the impact of temperature on major health outcomes (Basu and Samet, 2002; Le Tertre et al., 2006; Semenza et al., 1996; Stocker et al., 2014; Ye et al., 2012). However, to our knowledge, few quantitative studies have investigated the risk of out-of-hospital cardiac arrest (OHCA) related to extreme temperatures.

Extremely hot and cold temperatures are reportedly associated with cardiovascular mortality and morbidity. Emerging evidence suggests that extreme temperatures might be an important risk factor for OHCA (Empana et al., 2009). In addition, previous studies have indicated that sudden cardiac death and out-of-hospital coronary death show remarkable seasonal variation, with a significant increase in winter (Arntz et al., 2000; Nakanishi et al., 2011; Toro et al., 2010). In the United States, cold temperatures were found to significantly increase the risk of out-of-hospital cardiac or sudden coronary mortality (Cagle and Hubbard, 2005; Gerber et al., 2006). Moreover, a recent multi-city study conducted in China suggested that extremely hot and cold temperatures significantly increased the risk of out-of-hospital coronary mortality (Chen et al., 2014). However, most studies have only examined the effects of temperature in a single city or region, and are therefore not necessarily extend to the national level. Further, previous studies have demonstrated distinct non-linear relationships between temperature and cardiovascular morbidity, in which the morbidity-modifying effects of temperature were spatially heterogeneous (Turner et al., 2012). To our knowledge, however, no study has assessed a diverse range of communities exposed to a variety of climatic conditions. Therefore, elucidating the complex, non-linear, and multi-parameter relationship between climate variation and OHCA on a national scale is essential.

Multivariate meta-regression analysis with distributed lag non-linear models helps to estimate and pool non-linear and delayed associations from multiple locations (Gasparrini and Armstrong, 2013; Gasparrini et al., 2012). This two-stage modeling approach reduces over-simplification of the exposure-response relationship or lag structure and can be applied to any context requiring assessment of non-linear and delayed relationships within different sub-groups or populations (Gasparrini and Armstrong, 2013; Guo et al., 2014). The majority of previous studies have been based on conventional linear or linear-threshold assumptions and univariate meta-analysis approaches, which cannot describe complex non-linear relationships and may exclude important variables. Thus, a more comprehensive understanding using the two-stage analysis of weather variables might help to facilitate the development of a reliable early warning system to predict OHCA.

Here, we used national OHCA data collected between 2005 and 2014 in Japan to investigate the associations between extreme temperatures and daily reports of OHCA throughout the 47 prefectures of Japan. To our knowledge, this is the first nationwide study to investigate the effects of temperature on the risk of OHCA using a two-stage time series analysis.

2. Methods

2.1. Study design and subjects

This retrospective observational study used national registry data. The patients were aged 18 to 110 years and had OHCA of presumed cardiac origin before the arrival of emergency medical service (EMS) personnel between January 1, 2005 and December 31, 2014 in Japan. Patients were treated by EMS personnel and were transported to medical institutions.

This study was approved by the ethics committee at Kyushu University Graduate School of Medical Sciences. The requirement for written informed consent was waived. Patient records and other patient information remained anonymous and de-identified prior to analysis. All methods were conducted in accordance with approved guidelines and regulations.

2.2. EMS and data collection

Detailed information on the EMS system in Japan is published elsewhere (Kitamura et al., 2010; Ogawa et al., 2011). Briefly, municipal governments provide EMS via approximately 800 fire stations with transportation centers under the 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 hospitals.(Council, 2007) Following the standardized Utstein-style reporting guidelines for cardiac arrest, the EMS personnel summarize each case of OHCA in cooperation with the physicians in charge (Cummins et al., 1991). Data from the 800 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. In a nationwide, and population-based manner, the FDMA has collected data regarding all OHCA cases using a standardized Utstein-style format. In Japan, registration of OHCA data is required under the Fire Service Act and is considered to have a same validity and completeness between prefectures and different years. We obtained data on daily minimum, mean and maximum temperatures, and relative humidity from 47 prefectures of Japan. Daily minimum, mean and maximum temperatures, and relative humidity were calculated as the 24-hour average based on hourly measurements, and obtained 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 because these were synoptic climatological stations and intended to capture macro-scale weather for each prefecture (Supplementary Fig. S1). Daily mean temperature was selected as the main exposure index, as it reflects exposure over 24 h and provides easy-to-interpret data for decision-making purposes (Guo et al., 2011; Guo et al., 2014; Guo et al., 2012).

2.3. Statistical analysis

2.3.1. First-stage time series model

A time series regression model based on a generalized linear model assuming a quasi-Poisson distribution was first applied to obtain prefecture-specific temperature-morbidity relationships. In this first-stage regression, the non-linear and delayed effect of temperature was modeled using distributed lag non-linear models for each prefecture (Gasparrini and Armstrong, 2013; Gasparrini et al., 2012). A natural cubic B-spline was used to define a cross basis function for temperature as well as for the lag space, with a maximum lag period of up to 21 days. The natural cubic B-spline basis was set using 4 degrees of freedom for temperature and lag. The choice of lag periods of up to 21 days was motivated by previous studies suggesting that effects of cold temperatures were more delayed and lasted for a few weeks, while the effects of high temperatures were more acute and possibly affected by harvesting effect (Gasparrini and Armstrong, 2013; Guo et al., 2014). A categorical variable for day of the week, and an indicator variable for public holidays, were included in the model because previous studies suggested that these are potential confounding factors for OHCA (Bagai et al., 2013; Kitamura et al., 2014; Wallace et al., 2013).

Prefecture-specific temperature-morbidity associations are generally evaluated using an absolute temperature scale. However, temperature ranges differ among Japan's 47 prefectures, hampering the combination of curves across prefectures using non-overlapping temperature ranges. In addition, due to adaptation to climate change