Original article

Decrease in Environmental Temperature May Trigger the Onset of Acute Aortic Dissection

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Abstract

Aim: The most important risk factors for a Stanford type A acute aortic dissection (AAD) include arterial hypertension and connective tissue disorders, while numerous studies have identified meteorology factors, such as environmental temperature also play an important role. The aim of this study is to explore the relationship between environmental temperature and the frequency of AAD surgically threated over a 12-year period at a Croatian university hospital.

Methods: This is a retrospective, monocenter observational study conducted at the University Hospital Centre Zagreb. The study includes 134 patients who were threated surgically for Stanford type A AAD between January 2001 and December 2012. Temperature categories (low, moderate and high) were based on the calculated monthly average environmental temperature and standard deviation given from official daily environmental temperatures for the respective period.

Results: The results show a higher frequency of AAD in days of low temperature compared to days of moderate temperature or high temperature. The frequency of days with AAD was somewhat higher in moderate than high temperature category, but the difference is not statistically significant. The relative frequency of AAD for low, moderate and high temperature categories were 4.55, 2.96 and 1.93, respectively.

Conclusion: Environmental temperature drop induces stressful adaptive body response, including an additional hemodynamic load and increase in arterial blood pressure, strong enough to trigger the AAD-etiopathogenesis. Furthermore, our findings indicate that body response to environmental heat may differ from a response to reduced environmental temperature, due to observed small number of events in days of high temperature.

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Introduction

Among cardiovascular diseases, which are the leading cause of death in the developed countries, acute aortic dissection (AAD) stands out as one of the most lethal. With an in-hospital mortality rate of 22 % for Stanford type A (involving ascending aorta) and about 12 % for Stanford type B (no ascending aorta involvement), AAD represents an emergency case in the cardiovascular surgery (1). At a histological level, AAD is the tearing of the inner surface of the aortic layer known as intima, whereupon blood at high pressure splits or dissects the media to form a false channel or lumen that runs alongside the true lumen. A further re-entrance tear allows blood to circulate through the false lumen (2, 3). Retrograde spreading of this tear results in either the penetration of blood into the pericardium, causing hemopericardium and heart tamponade, or the rupturing of the aortic wall. Both of these scenarios are medical emergencies, as they lead to the rapid death of the patient if timely surgical intervention is not performed (2, 4).

AAD affects men at about twice the rate that it does women and it commonly occurs between 60 and 80 years of age (5). Besides age, other well-known risk factors are an arterial hypertension, an aortic aneurism, congenital diseases of connective tissue like Marfan syndrome or Elhers-Danlos syndrome, various types of vasculitis and a bicuspid aortic valve (6). Furthermore, a number of studies have revealed meteorology factors (e.g., environmental temperature) as potentially risk factors which increase the incidence and mortality of AAD during the cold months of the year (7-11). A number of published studies have compared AAD with the exact data on environmental temperature and interestingly, although all the studies were carried out in a moderate zone of Western Europe, the results of the studies are contradictory. In fact, one group of authors from the United Kingdom (12) showed that climate factors have no impact on the occurrence of AAD, whereas a group of authors from Germany failed to identify any relationship between air temperature and the incidence of AAD. However, the German authors did point out possible association which tended to be significant, explaining it as result of a small number of events (13). On another note, a group of authors from France (9) has reported that AAD has a higher incidence during colder months of year, and a research group in the Netherlands (14) noted that a higher incidence of AAD correlates to a lower air temperature (low minimal daily temperature). A second group from Germany (15) noted that changes in the air temperature and amount of cloudiness are the most representative weather predictors among the studied parameters.

The aim of this study is to explore the relationship between relative environmental temperature and the frequency of Stanford type A acute aortic dissection.

Materials and methods

This is a retrospective, monocenter observational study conducted in one university hospital located in Zagreb (Croatia). The study has been approved by the Ethical Committee of University Hospital Centre Zagreb. Information from hospital records were combined with data from local weather forecast archives. This approach assumes that all person in a specified geographic area experienced the same exposure conditions.

Clinical data

The medical records of the patients consecutively admitted to the Department of Cardiac Surgery at the University Hospital Centre Zagreb in the period between 1 January 2001 and 31 December 2012 were investigated. Inclusion criteria were diagnosis and surgically treatment of the patient with a Stanford Type A AAD. The baseline characteristics of patients (gender and age), diagnosis of arterial hypertension and/or connective tissue disorder, as well as precise date and time of the first AAD symptoms were recorded for each candidate.

After searching operating protocols 212 patients were identified as fitting the given criteria, but 35 were excluded due to onset of iatrogenic AAD (2 patients) and incomplete or unclear data (33 patients). Upon consultation with Croatian Meteorological and Hydrological Service (CMHS), the geographic area of the specific climate type was determined, meaning a CfB climate type according to the Köppen classification. It is a temperate oceanic climate (C) without dry season (f) but with warm summers (B) (16). The geographic area of interest is a circular area with a diameter of 195 km (with Zagreb as the center) and includes nine Croatian counties inhabited by approximately 2.1 million inhabitants. Accordingly, another 43 of the remaining 177 patients were excluded given that they reside outside of the determined geographic area at the moment of onset of AAD. Hence, a total of 134 patients with surgically treated Stanford type A AAD were included in the study.

Meteorological data

Exact data on environmental temperatures for the determined area and timeframe were collected from the official weather database provided by CMHS. All average daily temperatures of twelve-years studied period were categorized in one of the three relative temperature categories: low, moderate or high. Relative temperature categories, for each month separately, were determined from the calculated average monthly temperature and standard deviation of these months (e.g. all Januaries, Februaries etc.) during the studied period. Hence, the moderate category of each month is defined as the interval between the value of average monthly temperature plus and value of average monthly temperature minus one standard deviation. At the same way, the high and low categories of each month are defined as one standard deviation higher or lower than the average monthly temperature of these months. Consequently, daily average temperatures of the studied twelve-year period which were between the monthly average temperature and one standard deviation interval in which the average daily temperature belongs to, were placed in the moderate category. Daily average temperatures higher than the average monthly temperature plus one standard deviation for the month they belong to were placed in the high category, whereas average daily temperatures lower than the average monthly temperature minus one standard deviation were placed into low category (Figure 1).

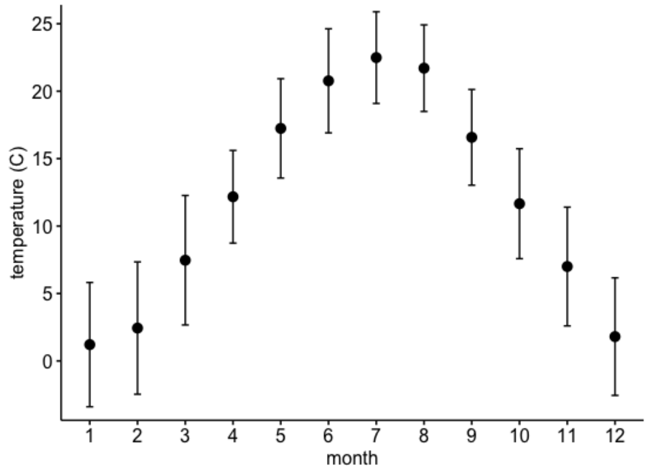

Figure 1. Categorization of average daily temperatures of the studied twelve-year period in respect to the average monthly temperature and standard deviation of each month

The figure shows average monthly temperature (black dots) with one standard deviation interval for each month. Average monthly temperatures plus the respective standard deviation are linked together with a red line and all average monthly temperatures minus the respective standard deviation are linked together with a blue line in order to get the boundaries of relative temperature categories. All average daily temperatures which were fallen above the red line are categorized as a high temperature and those below the blue line as a low temperature. Average daily temperatures which were within one standard deviation interval are categorized as a moderate temperatures.

Furthermore, temperature categories were divided into two groups, one for days when AAD occurred and the other without AAD occurrence. Finally, the same categories from all months were summarized in order to obtain the final table for analysis.

Statistical analysis

Descriptive statistics and statistical analysis were performed using statistical software program R (17). The normality distribution of average monthly temperatures for each month was tested using the Kolmogorov-Smirnov test. Differences in the frequency of days with and without occurrence of AAD between temperature categories was tested using the chi-square test. P-values < 0.05 were considered to be statistically significant.

Results

According to the clinical and geographic criteria given in this study (see the Materials and methods section), a total of 134 patients who were threated surgically for Stanford type A AAD at the Department of Cardiac Surgery, University Hospital Center Zagreb, between January 2001 and December 2012, were included in the data analysis. A descriptive analysis by gender shows that 89 (66.4%) of cases were men and 45 (33.6%) were women. The average age of the patients was 57.8 years with a standard deviation (SD) of 12.8, ranging from 18 to 82 years. Arterial hypertension was noticed in 91 (67.9 %) patients while 25 of them (18.7 %) did not have arterial hypertension, whereas data were missing for 18 patients (13.4%). Furthermore, the Marfan syndrome, one of the most common connective tissue disorder, was detected in one case (0.7 %) (Table 1)..

Table 1. Patient characteristics (SD – standard deviation)

		Patients (n = 134)
Gender	Female	45 (33.6 %)
	Male	89 (66.4 %)
Age (years)	Youngest	18
	Oldest	82
	Mean/SD	57.8/12.8
Hypertension[1]	With	91 (67.9 %)
	Without	25 (18.7 %)
Connective tissue disorder	With[2]	1 (0.7 %)
	Without	133 (99.3 %)

[1]Missing values for 18 patients; [2] Marfan Syndrome

The difference in the frequencies of AAD between the defined relative temperature categories was statistically significant (χ^2 = 8.65, df = 2, p = 0.01). Further analysis shows a higher frequency of AAD in low temperature days compared to moderate temperature days (χ^2 = 4.12, df = 1, p-value < 0.05) or high temperature days (χ^2 = 7.12, df = 1, p < 0.01) (Table 2)..

Table 2. Relative temperature categories including frequencies of days (n) with and without occurrence of AAD (n (%))

	Low	Moderate	High	Total
Days with AAD	33 (0,75)	87 (2)	14 (0,32)	134 (3,1)
Days without AAD	692 (15,8)	2846 (64,9)	711 (16,23)	4249 (96,9)
Total	725 (16,55)	2933 (66,9)	725 (16,55)	4383 (100)

The difference in the frequencies of days with and without AAD between the defined relative temperature categories was statistically significant (χ^2 = 8.65, df = 2, p = 0.01). There is a higher frequency of AAD on low temperature days compared to moderate temperature days (χ^2 = 4.12, df = 1, p-value < 0.05) or high temperature days (χ^2 = 7.12, df = 1, p < 0.01**), while the difference between moderate and high temperature categories is not statistically significant (χ^2 = 1.95, df = 1, p = 0.16).*

Although the frequency of days with AAD is somewhat higher in the moderate than high temperature category, this difference is not statistically significant (χ^2 = 1.95, df = 1, p = 0.16). To get a more comparable and evident relationship, the given results were transformed into a relative frequency of AAD for each temperature category using a particular method. The number of days with AAD in each temperature category were divided by all days (with and without AAD) of the same category and then multiplied by 100. Hence, the relative frequency of AAD for low, moderate and high categories were 4.55, 2.96 and 1.93, respectively (Figure 2)..

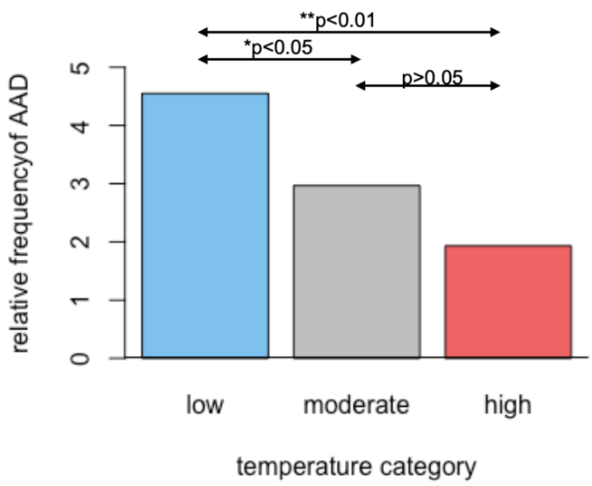

Figure 2. Relative frequency of AAD occurrence between temperature categories

There is a higher relative frequency of AAD occurrence for the low temperature category (4.55) compared to the moderate (2.96) and high (1.93) temperature category, while difference in frequency of AAD between the moderate and high temperature is not statistically significant. The specified P-values between categories correspond with those calculated from Table 2.

Discussion

This study reports a connection between variation of environmental temperature and occurrence of AAD. More than 60 percent of patients included in the present study were men, which correlates to the relevant literature (1, 10).

The average age of patients is 58 years with the number of patients aged 70-79 decreasing, which deviates from previously mentioned literature (5). This may be attributed to limitations of the methodology used in the study, meaning patients who died were not included, given that had not undergone surgery and consequently had not been recorded in the surgical operation protocol.

A human physiological, and possible pathological, outcome is strongly connected to numerous internal and external factors and their interplay which is a well-known fact. Hence, arterial hypertension, as one of the most common cardiovascular diseases and a predisposing factor for blood vessel rupture, was also noted within the study and which indicates a more frequent occurrence of AAD in patients with arterial hypertension (68 %), which correlates to the data in the literature (1, 18, 19). The significance of high arterial pressure in the onset of AAD may be attributed to its contribution to damaging the aortic inner layer (intima) which may be the first step in the onset of AAD (2, 3, 20). Due to Laplace's law, a sudden increase in arterial pressure inside the aortic lumen leads to an increase in aortic wall tension, consequently increasing the risk of aortic wall rupture (6). Environmental temperature is an important, but not always perceptible external factor affecting arterial pressure. Hintsala et al. showed that short-term cold exposure increases central aortic blood pressure and cardiac overload, which may contribute to the observed increased winter mortality (21). A similar result is that outdoor temperature and blood pressure are strongly correlated whereby systolic blood pressure decreases with increasing temperature, but only in the elderly population (those over than 80 years of age) as reported by Alperovitch et al. (22). To reduce the well-known influence of a climate type on environmental temperatures, we included 134 patients from only a single climate type (the Cfb type according to the Köppen classification). There has been only one study from France with a similar approach (23). Our results show a higher frequency of AAD for low temperatures regardless of the season and the month(s) of year. On another note, groups of authors from UK (7), former Serbia and Montenegro (8), Korea (10) and Japan (11) have reported that the frequency of AAD is significantly higher in winter and peaking in January. Similar results indicate that cold weather is correlates to a higher incidence of AAD as reported by Verberkmoes et al. from the Netherlands (14). Moreover, Li et al. reported that the onset of Stanford type B AAD was higher in winter than in summer and autumn, and that a low maximal daily temperature is associated with occurrence of the Stanford type B AAD (24), while Xie et al. noted that cold atmospheric temperature and larger daily temperature changes correlated to a higher incidence of AAD (25). Both of these studies were from China.

In our opinion, a relative drop in environmental temperature might be more important risk factor than absolute temperature value, given the highest frequency of AAD when the average daily temperature was categorized as low. This hypothesis was first mentioned in 2005, when Mehta et al. reported that the winter peak for AAD was evident in both cold and temperate climate settings, suggesting that the relative change in temperature, rather than absolute temperature, may be a mechanistic factor (26). Benouaich et al. showed that the incidence of aortic dissection was higher in a winter time than in summer, but also that the days with occurrences of AAD were colder than those without AAD, concluding that a relative change in temperature may be a triggering factor in onset of AAD (9). The results conform with a study by a group of authors from Nantes (France) who arrived to the same conclusion, but using different methodology. They reported that, regardless of the season, a decrease in average daily temperature of more than 5˚C, between days 0-7, significantly increases the risk of acute aortic syndrome at day 0 (23). Finally, a group from China which tried to predict AAD occurrence in respect to environmental temperature changes, concluded that for every 10 ˚C increase, the incidence drops by 0.21 units (27).

An explanation of the possible pathophysiologic mechanism for AAD occurrence regarding temperature changes may be activation of body temperature regulators such as thermogenesis, cytokine response, hemodynamic adaptation and hypermetabolism (6). The human organism retains the heat by decreasing the release of heat (i.e. vasoconstriction) and increasing heat generation (i.e. increased metabolism) what attribute to sympathetic activity increase. (6, 9, 14, 21). Consequently, vasoconstriction and an increased metabolism (including a higher cardiac work load) increases mean arterial pressure, which is inversely proportional to changes in body temperature, and in fact environmental temperature (6, 9, 14, 21).

Edwin et al. reported that the pathogenesis of AAD may result from the interaction of three factors: 1) an existing pathological condition of the aortic media, 2) any agent of intimal injury or tear, and 3) hemodynamic factors that propagate the dissection once it has been initiated (28). Hence, a possible explanation of the connection between a drop in environmental temperature and AAD occurrence is attributed to an increase in arterial pressure leading to a critical level when intimal injury occurs and consequently propagation to AAD caused by the same factor. This value of critical level of arterial pressure is unique for each person individually, while increasing in arterial pressure is generated by the activation of above-mentioned defense (sympathetic) mechanisms. The assumption is that a drop in environmental temperature induces a stressful, adaptive response from the body, including an additional hemodynamic load (and consequently increasing arterial pressure), which is strong enough to trigger and propagate the AAD etiopathogenesis. Also, our findings indicate that body response to an environmental heat may differ from the response to reduction in environmental temperature, given the big difference in AAD occurrence between low and high temperature categories.

These results suggest that a change in environmental temperature does not necessarily lead to a higher frequency of AAD. Instead the temperature must decrease. Moreover, the increase in environmental temperature may have a "protective" effect, given that the lowest frequency of AAD occurs for high temperatures what conforms with results reported by Law et al. (27). However, the difference between the moderate and high temperature category is not significant, and it may be due to the fact that the vast majority of average daily environmental temperatures during the year fall into the category of moderate temperatures (~66%) and as a consequence, AAD as a multifactorial disease, occurs just below these conditions. Consequently, this relationship may be confirmed using a larger number of events. Another limitation of the study should be pointed out. The University Hospital Centre Zagreb is not the only institution where AAD is surgically threated, hence an unknown number of events in the investigated area and period were not included in this study.

Conclusion

Present qualitative retrospective study highlights a dependence between changing of environmental temperatures and AAD occurrence, thus indicating a possible causative correlation, what provides the basis for further thesis research in a future multicenter study.

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