

Influence of Meteorological Factors on the Incidence of Acute Type A Aortic Dissections in Northern Europe

Simon Junghans^{1#}, Peter Donndorf^{2*}, Thore Scherff³, Christoph Lutter⁴, Anja Pueschel² and Justus Groß¹

¹Department of Cardiovascular Surgery, University Hospital Schleswig Holstein, Kiel, Germany

²Department of General-, Viszeral-, Thoracic-, Vascular- and Transplantation- Surgery, Rostock University Medical Centre, Rostock, Germany

³Berufsgenossenschaftliches Unfallkrankenhaus Boberg, Hamburg, Germany

⁴Department of Orthopaedic- Surgery, Rostock University Medical Centre, Rostock, Germany

#-This author contributed equally to this work

Abstract

Background: Acute Type A Aortic Dissection (TAAD) is a life-threatening disease. Apart from the well-known atherosclerotic risk factor, circadian, seasonal and climate-related patterns are also factors with a significantly higher risk in winter, on the first day of the working week, and in the morning hours (between 6 a.m. and 12 p.m.). Acute TAAD can also be triggered by higher mean arterial blood pressure with corresponding blood pressure peaks, and changes in atmospheric pressure. The aim of this study is to analyze climatic parameters in the catchment area of Kiel in northern Germany which can influence the occurrence of acute TAAD.

Methods: All acute TAAD repairs from January 1st, 2012 to November 24th, 2017 in the University of Hospital Schleswig-Holstein Campus (UKSH) were evaluated. Traumatic aortic dissections were excluded. Statistics were performed regarding to R&R commander programs using Wilcoxon rank sum test for data correlation analyzes.

Results: A total of 181 acute TAAD repairs were identified. There were no significant correlation between the mean temperature and the number of acute TAAD incidents, the mean differences between the daily averages of the weather parameters or the mean temperature on the days (0-14) before the onset of acute TAAD. However, precipitation remains constant on the 3rd and 4th days before acute dissection and decreases the day before ($t=-1$). On the day of acute dissection ($t=0$), it increases significantly.

Conclusion: Relative climatic changes (rather than absolute values) may have a greater effect on the incidence of acute dissection. The effect of climatic variations appear to depend on the local context, such as the initial value at which the variation begins. Lower temperatures (from a higher baseline temperature) have a different effect than lowering it from an already low value. In the Kiel region in northern Europe, the occurrence of acute TAAD is not related to temperature but does increase significantly on days with higher precipitation.

Keywords: TAAD • Circadian • Seasonal • Blood pressure peaks

Introduction

Background

Aortic Dissection (AD) is a serious medical condition in which the inner layer of the aorta tears and an intimal flap separates the original into a true and the false lumen. The Stanford classification distinguishes between type A (TAAD) and type B (TBAD) dissection. The incidence of aortic dissection generally is reported between 2.9–6/100,000 per person-years and has major implications for both patients and healthcare providers with around one fifth of patients dying before admission and one quarter who die during initial hospitalization [1,2]. The risk factors for developing AD are divided into acquired and congenital risk factors. Naturally, both risk factors are mutually dependent in the course of a life. Various congenital connective tissue disorders are associated with an increased

risk of AD whereas acquired risk factors such as hypertension or atherosclerosis exist in up to 78% and up to 33%, respectively [3-6].

The pathophysiology of aortic dissection is still not completely understood although there is agreement that the development is multifactorial and combines acquired and innate risk factors. Circadian, seasonal, and climate-related patterns are also factors with significantly higher risk in winter, on the first day of the working week, and in morning hours (between 6 a.m. and 12 a.m.) Manfredini R, et al. [7] published a multifactorial model to explain the circadian occurrence with the activation of the sympathetic nervous system associated with a higher coagulability.

The moment of intimal tear in AD may be precipitated by higher mean arterial blood pressure and changes in atmospheric pressure are likely a contributing factor as there is seasonal variation in blood pressure [8]. Despite a large number of reports linking AD and circadian and seasonal conditions, the evidence is so far inconclusive in terms of causality or correlation [9-12]. The aim of this study is to analyze climatic parameters in the catchment area of the University Hospital Schleswig-Holstein Campus (UKSH) in Kiel, Germany potentially influencing the occurrence of TAAD. Kiel is a city of 235,782 inhabitants and of around 118.65 km², located on the Baltic coast in Northern Europe, in a temperate climate zone with direct exposure to the maritime climate. As a result, the summers are cool, and the winters are mild despite the northern location.

***Address for Correspondence:** Peter Donndorf, Department of General-, Viszeral-, Thoracic-, Vascular- and Transplantation- Surgery, Rostock University Medical Centre, Rostock, Germany, Tel- 0381-4946161, E-mail: donndorf@med.uni-rostock.de

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Materials and Methods

All acute surgical TAAD repairs from January 1st, 2012 to November 24th, 2017 at the Cardiovascular Center of the University Hospital Schleswig-Holstein

(UKSH), Campus Kiel, Germany were analyzed. Traumatic aortic dissections were excluded. Weather data in that time period were acquired from the GEOMAR-Helmholtz Center for Ocean Research Kiel, Germany, located 900 m from the University Hospital. The weather station is 32 m above sea level and uses sensors 2-18 m higher again. The sensors measure the following parameter: wind direction, wind speed (m/s), air temperature (°C), global radiation (W/m²), relative humidity (%), counter-radiation (W/m²), air pressure (hPa), accumulated precipitation (L/m²), THW index (temperature, humidity, and wind speed used to calculate perceived temperature), heat index and perceived temperature (°C). Using the high-resolution weather data (8-min), we created the respective daily averages as well as the minima and maxima of the individual weather parameters.

Clinical data comprised age, sex and intervention date from all acute TAAD procedures within the same time period were extracted from the prospective UKSH dissection registry. Due to urgent nature, the date of dissection was assumed to be the operative treatment day. Data were anonymized and transferred to an Excel spreadsheet. Duplicates were removed and the average age of onset and the gender distribution were calculated. With the help of the R and R-Commander programs, correlation analyzes according to Bravais- Pearson was carried out and circadian and seasonal anomalies were analyzed. Descriptive statistics provide an overview of the data with frequency, incidence, age of onset and gender distributions are displayed in tables and graphs. Exploratory statistics were used to analyze the data.

Results

A total of 181 acute TAAD repairs were analyzed. The mean age of the patients was 65.7 (22–90) years; on average, women developed acute TAAD at 71.8 years of age and men at 62.5 years. The average number of acute TAAD per month varies between 1.6 incidents in December and 3.3 in March. No significant monthly accumulation was found. Even a seasonal accumulation was not evident (Figure 1).

Mean values of the weather parameters collected in from January 1st, 2012 to November 24th, 2017. The results correspond with the estimated climatic changes over a year in a temperate climate zone with direct exposure to the maritime climate (Figure 2).

Comparison of aortic dissection and temperature over time

The absolute number of aortic dissections varies between 0 and 7 incidents per month and there is no significant accumulation of incidents in warmer or colder periods of the year (Figure 1). Hence, the correlation between the average temperature and the number of TAAD incidents is close to zero (=0.06). The significance analysis also confirmed this assumption (p=0.595).

Effect of the average values of the weather parameters on the occurrence of aortic dissection

Comparative analysis shows that only precipitation on days with an acute

TAAD is significantly higher than on days without (p=1.93%, t-test; p=12.24 Wilcoxon test). Results suggest that the difference is driven by a few days with extremely high precipitation. The statistical analysis of the other weather parameters did not reveal any statistically significant correlation. They show a large discrepancy in relation to the required level of significance (Table 1).

Effect of the mean differences in daily averages on the occurrence of aortic dissection

In a next step we evaluated the change between the daily averages of the incident day and the day before separately for all analyzed weather parameters. The results are shown in Table 2. For the change in precipitation between the incident day and the day before there was a significant difference between days with AD and days without AD (p=2.73%, t-test; p=7.22% Wilcoxon test (Table 2).

Temperature development on the days before the aortic dissection

The average temperature development on the days prior to the onset of an acute TAAD was analyzed for fourteen days prior the incident. There were no significant deviations of the temperature from the global mean temperature prior the occurrence of an acute TAAD (Figure 3).

Precipitation development on the days before the aortic dissection

The average development of precipitation on the days prior to the onset of an acute TAAD was analyzed for fourteen days prior the incident. There was a significant increase of the precipitation level on the day of acute TAAD compared with the global maximum value (Figure 4).

Discussion

Aortic morphology, a high mean arterial pressure, tobacco abuse, and female sex are all established risk factors for rupture; seasonal variation and a possible causative role of atmospheric pressure has also been studied widely. A correlation between meteorological factors and cardiovascular and cerebrovascular diseases has been suggested in several settings (both geographical and aortic condition) with cold temperature possibly causing increased sympathetic drive on blood pressure; other hemodynamic variables such as increased platelet and red blood cell counts and blood viscosity have been shown to be affected by weather [13-15].

One study of 19,599 fatal ruptured aneurysms in the northern hemisphere showed peak incidence in December and January and a trough in June and July. Low temperatures are associated with an increase in atmospheric pressure, and high temperatures with a decrease which may explain-at least in part-seasonal variations in the incidence of aortic aneurysm ruptures which has been shown in some studies to be influenced by atmospheric pressure [16-21]. Others have failed to establish such a link because of the inherent variability of vascular events and the climatic differences themselves [22-25]. In addition, correlation

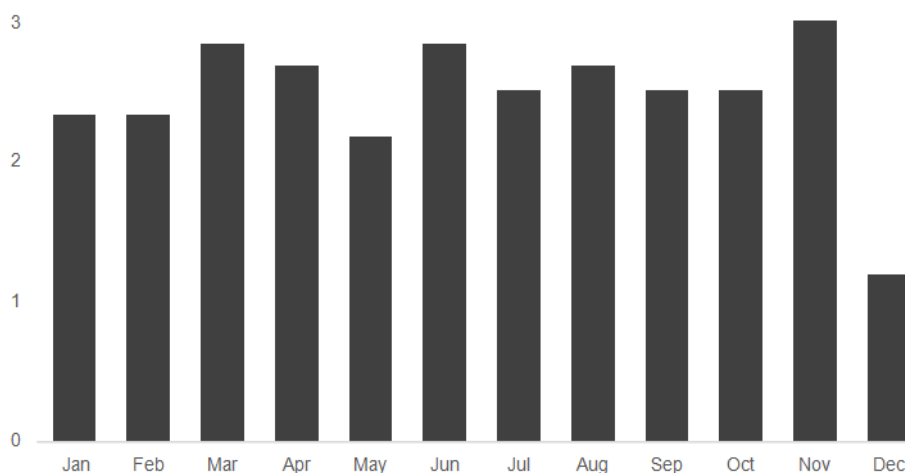


Figure 1. Mean values of the occurrence of an aortic dissection over time.

| | | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|-------------|---------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Temp (°C) | Minimum | 0,42 | 0,7 | 2,78 | 4,98 | 9,4 | 12,17 | 14,73 | 14,42 | 12,32 | 9,17 | 4,95 | 2,89 |
| | Average | 2,27 | 2,77 | 5,45 | 8,17 | 12,97 | 15,8 | 18,26 | 17,95 | 15,24 | 11,35 | 6,95 | 4,9 |
| | Maximum | 4,08 | 4,86 | 8,61 | 11,72 | 16,75 | 19,51 | 22,03 | 21,87 | 18,53 | 13,78 | 8,97 | 6,76 |
| | Range | 3,66 | 4,17 | 5,83 | 6,74 | 7,35 | 7,34 | 7,31 | 7,45 | 6,21 | 4,61 | 4,02 | 3,86 |
| Press (hPa) | Minimum | 1009,2 | 1010,5 | 1013,8 | 1011,3 | 1012,3 | 1012,6 | 1012,7 | 1013,5 | 1013,7 | 1013 | 1008,7 | 1012,2 |
| | Average | 1013,2 | 1014,4 | 1017,2 | 1014,4 | 1015,1 | 1015,2 | 1015 | 1015,9 | 1016,1 | 1016,2 | 1012,4 | 1016,4 |
| | Maximum | 1017,2 | 1018,3 | 1020,6 | 1017,6 | 1017,8 | 1017,7 | 1017,3 | 1018,3 | 1018,6 | 1019,3 | 1016,2 | 1020,4 |
| | Range | 8,04 | 7,79 | 6,74 | 6,23 | 5,5 | 5,14 | 4,6 | 4,83 | 4,95 | 6,29 | 7,46 | 8,2 |
| Rel hum (%) | Minimum | 74,96 | 69,28 | 59,72 | 53,62 | 52,69 | 53,38 | 53,66 | 54,18 | 61,26 | 70,11 | 74,68 | 75,87 |
| | Average | 84,87 | 82,62 | 77,39 | 73,5 | 72,28 | 73,33 | 74,06 | 75,15 | 79,84 | 84,51 | 86,55 | 86,44 |
| | Maximum | 92,51 | 92,3 | 90,83 | 90,27 | 89,92 | 91,44 | 92,38 | 92,2 | 93,57 | 94,14 | 94,74 | 94,45 |
| | Range | 17,55 | 23,02 | 31,11 | 36,64 | 37,23 | 38,06 | 38,72 | 38,02 | 32,3 | 24,02 | 20,06 | 18,58 |
| Wind (m/s) | Minimum | 2,21 | 2,05 | 1,82 | 1,29 | 1,24 | 1,03 | 0,94 | 0,94 | 1,24 | 1,67 | 1,75 | 2,07 |
| | Average | 4,78 | 4,59 | 4,4 | 4,02 | 4,03 | 3,63 | 3,47 | 3,37 | 3,57 | 4,06 | 4,12 | 4,7 |
| | Maximum | 7,83 | 7,71 | 7,6 | 7,41 | 7,45 | 6,96 | 6,88 | 6,55 | 6,66 | 7,08 | 7,05 | 7,72 |
| | Range | 5,62 | 5,66 | 5,78 | 6,11 | 6,2 | 5,93 | 5,93 | 5,61 | 5,42 | 5,4 | 5,31 | 5,64 |
| Prec (mm) | Average | 2,04 | 1,44 | 1,05 | 1,51 | 2,08 | 2,85 | 2,69 | 2,07 | 2,04 | 2,51 | 2,11 | 2,56 |

Figure 2. Overview of the various weather parameters and display of the daily averages, minima and maxima for every month.

Table 1. The table shows the mean values (arithmetic mean) of the daily averages (or maxima in the case of precipitation) of the weather parameters broken down into days, with and without occurrence of acute type A aortic dissection.

| | No acute AD | ≥1 acute AD | Difference | p-value (t-test) | p-value (Wilcoxon rank sum test) |
|-------------------|-------------|-------------|------------|------------------|----------------------------------|
| Temperature | 10.27 | 10.22 | -0.05 | 91.84% | 98.35% |
| Pressure | 1015.15 | 1014.49 | -0.66 | 42.80% | 19.67% |
| Relative Humidity | 79.09 | 79.17 | 0.08 | 92.17% | 80.40% |
| Wind speed | 4.05 | 4.13 | 0.08 | 54.28% | 42.68% |
| Precipitation | 1.99 | 3.16 | 1.17 | 1.93% | 12.24% |

Table 2. Average values of the differences between the incident day and the day before for all analyzed weather parameters divided into days with and without acute type A aortic dissection.

| | No acute AD | ≥1 acute AD | Difference | p-value (t-Test) | p-value (Wilcoxon rank sum test) |
|-------------------|-------------|-------------|------------|------------------|----------------------------------|
| Temperature | -0.02 | 0.18 | 0.2 | 21.60% | 13.64% |
| Pressure | 0.05 | -0.55 | -0.6 | 23.43% | 7.56% |
| Relative Humidity | -0.04 | 0.59 | 0.63 | 35.35% | 29.33% |
| Wind speed | 0.02 | -0.22 | -0.24 | 8.12% | 10.93% |
| Precipitation | -0.1 | 1.09 | 1.19 | 2.73% | 7.22% |

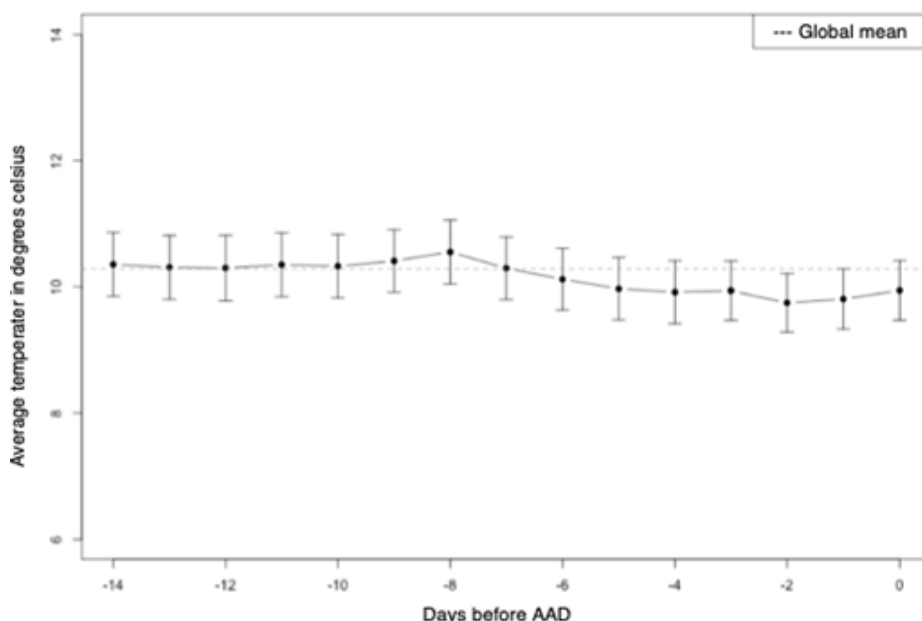


Figure 3. Temperature development from 0-14 days before acute aortic dissection. The error bars show the standard error, which is the estimator for the standard deviation of the mean values. The dashed line indicates the global mean value of the temperature, calculated on the basis of all available days.

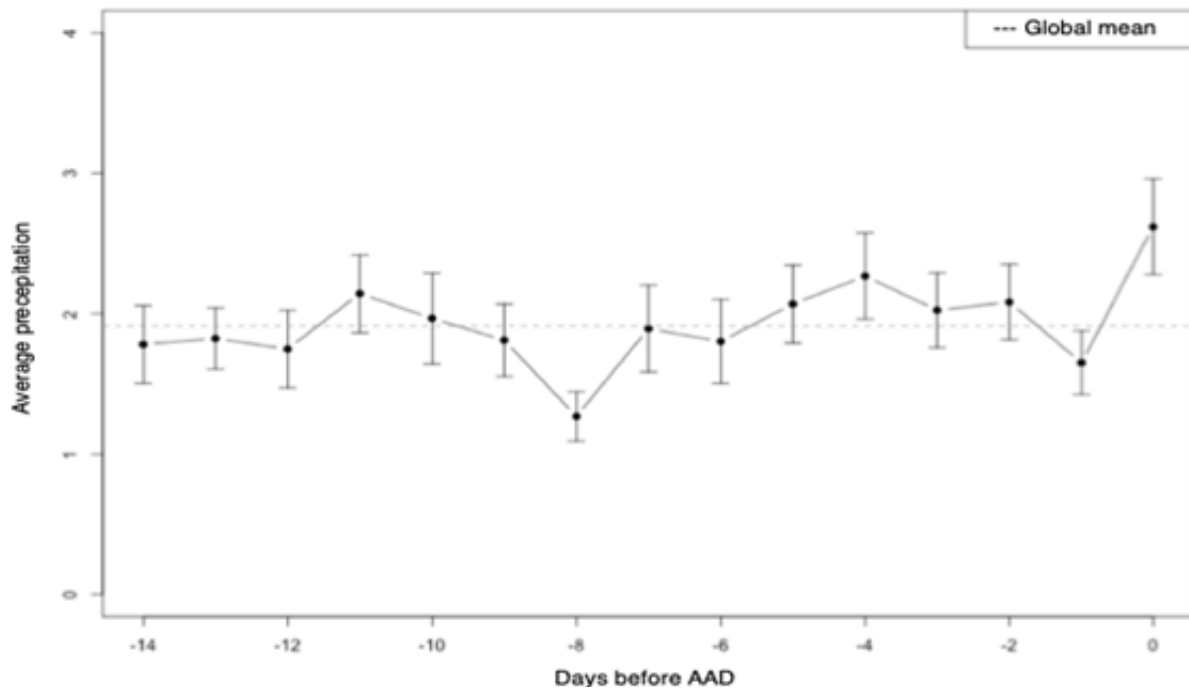


Figure 4. Development of precipitation 0-14 days before the onset of acute type A aortic dissection. The error bars show the standard error, which is the estimator for the standard deviation of the mean values. The dashed line represents the global maximum precipitation for the recording period.

and causality have been impossible to confirm as atmospheric conditions are also linked to the frequency, duration, and intensity of physical activities.

In 2002, Mehta RH, et al. [26] analyzed the IRAD database and reported for the first time in large cohort a high circadian variation and a frequency of acute aortic syndromes significantly higher during winter in the northern hemisphere with a peak in January. Another study from Bosnia and Herzegovina of 41 acute ADs and 40 aortic aneurysm ruptures found a link between atmospheric pressure and incidence on seasonal and monthly basis [27]. In a French study of 140 acute aortic syndromes, a $>5^{\circ}\text{C}$ decrease in temperature within the previous week was significantly associated with increased risk but especially in normotensive patients without blood pressure lowering medication and not in hypertensive individuals in treatment with blood pressure lowering medication [28-30].

In a study from Japan, days with cerebral infarction onset correlated with fewer sunshine hours, fewer solar radiation factors, greater precipitation, and more humidity, but found no relation between acute coronary syndrome, aortic dissection or aortic aneurysm rupture and climatic parameters [31]. In the subtropical climate of Hong Kong, a large study of 3878 acute aortic dissections and 1174 aortic aneurysm ruptures confirmed that meteorological variables were important factors influencing acute aortic events [32]. Both high atmospheric pressure and absence of thunderstorm warning were positively associated with more aortic dissections; furthermore, daily incidence could be predicted by ambient temperature using the following linear regression models:

$$\text{Incidence of aortic dissection} = 1.548 - 0.021 \times \text{temperature}$$

$$\text{Incidence of ruptured aortic aneurysm} = 0.564 - 0.010 \times \text{temperature}$$

In another French study of 206 TAADs, incidence was higher in winter time than in summer ($P=0.018$), days with AD were colder than those without ($P=0.017$), and lower atmospheric temperature in the three days preceding onset of symptoms ($P=0.0009$) [30]. Interestingly, this study demonstrated a correlation between acute AD incidences and decreased atmospheric temperatures, regardless of the time of the year; relative change in temperature is a mechanistic factor rather than absolute temperature, which is consistent with Mehta's IRAD study. However, another study did not find a statistically significant relationship between ADs and atmospheric pressure and temperature (although it did see a trend towards the standard deviation of ABP in the 48 hour period prior to dissection being greater than the standard deviation of pressure for that whole month [2.73 vs. 2.22 millibars]) [8]. In a similar study, acute AD frequency was 15 times higher on Mondays than Saturdays and 3.75 times higher than Sundays but was not associated with changes in atmospheric pressure, temperature, humidity, and wind [29]. (Although this finding in itself may be an artefact of some patients ignoring symptoms and delaying action on a holiday).

In a very large study involving 1,642 patients in two continents (China and United States), the authors concluded that AD occurred primarily on Wednesdays in winter, and on Sundays in summer, with the onset of the disease being related to temperature as well atmospheric pressure as well as the full moon phase. However, it must be taken into account that transcontinental weather data was combined in this study and that a loco-regional correlation of the weather data to the local occurrence of an aortic dissection was not the focus of the study [33,34].

Our findings suggest that temperature is not related to incidence of TAAD, but that the incidence is significantly higher on days with higher precipitation. This study has limitations including the assumption that dissection onset date is the same as dissection intervention date: although this is not an unreasonable assumption, it is known that some patients may have begun aortic dissection some time prior to symptoms with and a tamponading effect slowing the progression of collapse. In addition, only patients who had surgery were included in this study and there may be others who either did not survive until intervention. Finally, the chosen weather parameters themselves may be a confounding factor as characteristics and effect appear to vary depending on geography and how human activity is affected by climate changes. The at times large differences in the p-values between the t-test and Wilcoxon can be due to the different variance of the weather parameters on days with and without acute TAAD (the t-test assumes the same variance).

The impact of variations in climatic conditions may depend on local context such as the initial value at which the variation starts. A decrease in temperature starting from a high temperature could indeed have a different effect compared to a decrease from a low value. Therefore, rather than absolute climatic conditions, their relative changes may be of interest.

Conclusion

In our work we deliberately focused on the correlation of loco regional weather parameters to the occurrence of local aortic dissections. Contrary to many other publications, most of which concerned larger geographical areas, we were unable to determine a correlation with different air pressures or with temperature fluctuations. Our results indicate that in the analyzed region in northern Europe during the observation period the temperature is not related to the occurrence of TAAD, but the incidence of events was significantly increased on days with higher precipitation. If one summarizes the previously determined results of a connection between environmental influences and the occurrence of aortic dissection, one arrives at a very heterogeneous result. The effects of variations in climatic conditions may depend on the local context, such as the initial value at which the variation begins. Lowering the temperature from a high

temperature could in fact have a different effect than lowering it from a low value. Hence, their relative changes, rather than absolute climatic conditions, may be of interest. When assessing the determined correlations, it must be critically stated that from a climatic point of view, we are in a state of upheaval and that global warming is currently already revealing apparent changes in the climatic conditions we have been used to.

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