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Research Article





Influence of Meteorological Factors on Acute Type A Aortic Dissections in Kiel, Germany

Junghans S1, Scherff T2, Lutter C3, Pueschel A4, Donndorf P4, Gross J4*

¹Ferring Arzneimittel GmbH Kiel, Germany

²Berufsgenossenschaftliches Unfallkrankenhaus Boberg, Hamburg, Germany

³Department of Orthopaedic- Surgery, Rostock University Medical Centre, Rostock, Germany

⁴Department of General-, Viszeral-, Thoracic-, Vascular- and Transplantation- Surgery, Rostock University Medical Centre, Rostock, Germany

*Corresponding author: Justus Gross, Department of General-, Viszeral-, Thoracic-, Vascular- and Transplantation- Surgery, Rostock University Medical Centre, Rostock, Germany

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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 of northern Germany, the occurrence of acute TAAD is not related to temperature but does increase significantly on days with higher precipitation.

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Keywords: Aortic dissection; Cardiac surgery; Climate

List of Abbreviations: AD: Aortic Dissection; IRAD: International Register For Aortic Dissection; FET: Frozen Elephant Trunk; TAAD: Type A Aortic Dissection; TBAD: Type B Aortic Dissection; THW: Temperature Humidity Wind

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. A distinction is made in the Stanford classification between type A (TAAD) and type B (TBAD) dissection. If the intima tear is between the heart and the end of the aortic arch, it is classified as TAAD and considered a cardiac surgical emergency and must be treated as quick as possible. Several techniques are possible here to reconstruct the affected section of the aorta. In principle, the intima tear (also called the entry) must be repaired. In TBAD, the intimal tear is located distal to the aortic arch (and therefore typically in the domain of vascular surgery) and may or may not be an emergency depending on severity and clinical status at presentation: complicated (i.e. requiring immediate treatment) or uncomplicated. The more recent non A-non B classification is usually subject to an individual decision in the therapy. 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 dving before admission and one quarter who die during initial hospitalization.[1,2] One study in the UK estimated that the AD proportion of incident dissection events that occur over age 75 will reach 49.7% in 2030 and 57.3% by 2050. [3] A large systematic analysis by the International Registry of Aortic Dissection (IRAD) found that 67% of all dissections was TAAD; in-hospital mortality was 29.5% for TAAD (caused mainly by aortic rupture, pericardial tamponade), and 11.5% for TBAD (caused mainly by visceral ischemia). [4] With regard to treatment options and outcomes, TAAD mortality after surgical intervention (23.6%) is significantly lower than after drug therapy (60.2%) whereas drug therapy for TBAD has a better effect on mortality (9.1%)[4].

These devastating statistics show how important a quick and targeted diagnosis is to initiate the best possible therapy. 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 known which 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.[4,5] 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 pattern 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.). [6] Manfredini et al published a multifactorial model to explain the circadian occurrence with the activation of the sympathetic nervous system and associated with a higher coagulability of the blood. [7] The moment of intimal tear in AD may be precipitated by higher mean arterial blood pressure and changes in atmospheric pressure may be 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 which may influence the occurrence of TAAD. Kiel is a city of 235,782 inhabitants (census 2013) 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.

Material and Methods

All acute TAAD repairs from January 1st, 2012 to November 24th, 2017 at the Cardiac Surgical Center of the University Hospital Schleswig-Holstein Campus (UKSH) in 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 on the Kiel Fjord, 900 m from Kiel University Hospital. The weather station is 32 m above sea level and uses sensors 2-18 m higher again. The sensors measure the following weather data: 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 were carried out and circadian and seasonal anomalies were also analyzed. Descriptive statistics provide an overview of the data with frequency, incidence, age of

onset and gender distribution 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 can be derived from this. Even a seasonal accumulation in relation to the seasons does not show a statistically significant correlation (Figure 1).

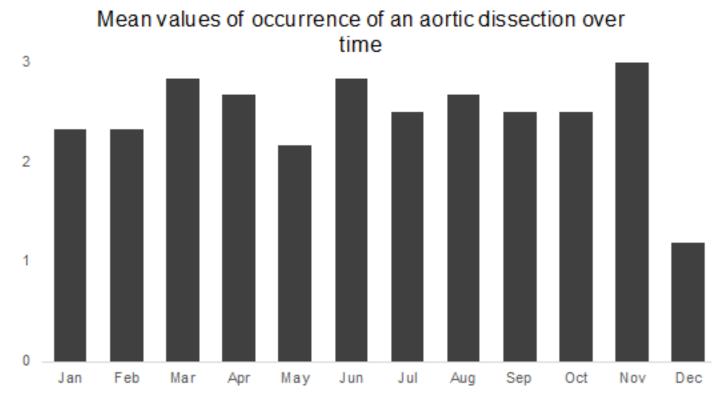


Figure 1: Mean values of the occurrence of an aortic dissection over time.

Table 1 shows the daily averages, minima and maxima of the various weather parameters analyzed. They were generated on the basis of the weather data, which existed with a resolution of 8 minutes. The data give an overview of the parameters used. The table is intended to give an impression of the magnitude of the average, but also maximum and minimum, behavior of weather parameters over the course of a year.

		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
Rei 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	85,44
	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

Table 1: Overview of the various weather parameters and display of the daily averages, minima and maxima.

Comparison of Aortic Dissection and Temperature over Time

Since the temperature on the day of dissection is discussed as a possible trigger in numerous publications, the following section shows the statistical analysis of the effects of temperature on aortic dissection over time. The absolute number of aortic dissections varies between 0 and 7 incidents per month, as there does not seem to be any significant accumulation of incidents even with the absolute number of TAADs per month. The correlation between the average temperature and the number of TAAD incidents is also close to zero (=0.06). The significance analysis also confirmed this assumption (p=0.595). In our data, there does not seem to be any correlation between the temperature and the occurrence of a dissection.

Effect of The Average Values of The Weather Parameters on The Occurrence of Aortic Dissection

The comparison shows that only precipitation on days with an acute TAAD is significantly higher than on days without (p-value of the two-tailed t-test, 2.93%), but the p-value of the Wilcoxon test is 14.55% (a lower level of significance). It suggests 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. In general, all p-values relate to tests on both sides. We therefore base the null hypothesis that the difference is equal to 0 (Table 2).

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	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 %
Windspeed	4.05	4.13	0.08	54.28 %	42.68 %
Precipitation	1.99	3.16	1.17	1.93 %	12.24 %

Table 2: 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.

Effect of The Mean Differences in Daily Averages on The Occurrence of Aortic Dissection

The evaluation shows the average differences between the daily averages of the weather parameters shown above, with the maxima being used in the calculation for precipitation. They are broken down into days with and without occurrence of acute TAAD. The statistical analysis shows that on days on which AD takes place, the difference in precipitation to the incident is significantly higher than on days without dissection. This means that on days with acute TAAD, the precipitation increases significantly more than the day before than on days without. The difference is close to zero on days without. Both the t-test and the Wilcoxon rank sum test are significant (Table 3).

	No acute AD	≥1 acute AD	Difference	p-Value (t-Test)	p-Value (Wilcoxon rank sum test)
Temperature	-0.02	0.18	0.20	21.60 %	13.64 %
Pressure	0.05	-0.55	-0.60	23.43 %	7.56 %
Relative Humidity	-0.04	0.59	0.63	35.35 %	29.33 %
Windspeed	0.02	-0.22	-0.24	8.12 %	10.93 %
Precipitation	-0.10	1.09	1.19	2.73 %	7.22 %

Table 3: Average values of the differences from the day before the weather data divided into days with and without acute type A aortic dissection.

Effect of The Absolute Differences in The Daily Averages on The Occurrence of an Aortic Dissection

Table 4 shows the average absolute differences between the daily averages. As with the analysis of the maxima of the precipitation are also used for the calculation here. The analysis shows that only the absolute difference in the THW index on days with acute TAAD compared to the previous day is higher than on days without. The p-value of the difference in the t-test is marginally significant (p = 8.39%). In contrast, it was significant in the Wilcoxon rank sum test (p = 2.76%). Derived from this, the THW index (the felt temperature) differs more than on the previous day than on days without acute TAAD.

	No acute AD	Acute AD	Difference	p-Value (t-Test)	p-Value (Wilcoxon rank sum test)
Temperature	1.41	1.48	0.07	48.48 %	62.71 %
Pressure	4.41	4.76	0.35	27.96 %	55.16 %
Relative humidity	6.73	6.27	-0.46	29.71 %	28.81 %
Windspeed	1.22	1.32	0.11	21.32 %	11.28 %
Precipition	2.55	3.18	0.63	19.02 %	78.32 %
THW- Index	0.98	1.09	0.10	8.39 %	2.76 %

Table 4: Average values of the absolute differences to the day before the weather data, divided into days with and without acute type A aortic dissection.

Temperature Development on the Days Before the Aortic Dissection

Figure 2 shows the average temperature on the days prior to the onset of acute TAAD. The time axis goes from the day of AD (t = 0) to two weeks before (t = -14). 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, which was calculated on the basis of all available days. The deviations of the temperature from the global mean temperature show that the differences in temperatures from the occurrence of an aortic dissection have no influence.

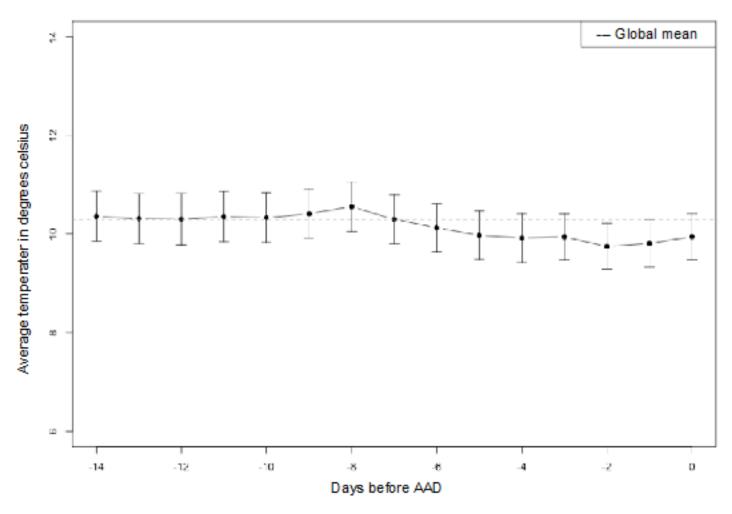


Figure 2: Temperature development from 0-14 days before acute aortic dissection.

Precipitation Development on The Days Before The Aortic Dissection

Figure 3 shows the development of precipitation before acute TAAD. The time axis represents from right to left the day of AD (t = 0) up to two weeks before (t = -14). 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. It can be clearly seen that the precipitation remains at a constant level on the 3rd and 4th day before AD. The day before AD (t = -1) the precipitation level drops. On the day of AD (t = 0), it increases significantly.

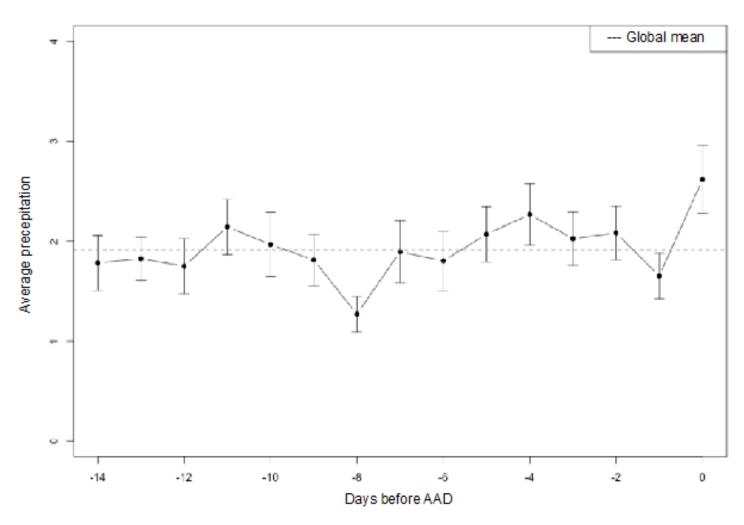


Figure 3: Development of precipitation 0-14 days before the onset of acute type A aortic dissection.

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. [16] Low temperatures are associated with an increase in atmospheric pressure, and high temperatures with a decrease which may explainat 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. [17-22] Others have failed to establish such a link because of the inherent variability of vascular events and the climatic differences themselves. [23-26] In addition, correlation 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 et al 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.[27] 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. [28] In a French study of 140 acute aortic syndromes, a >5 °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. [29] 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. [30] In the subtropical climate of Hong Kong, a large study of 3878 acute aortic dissections and 1174 and aortic aneurysm ruptures confirmed that meteorological variables were important factors influencing acute aortic events. [31] A linear regression analysis was performed in a pan-territory epidemiological survey for a period of 10 years on the impacts of meteorological factors. Both high atmospheric pressure and absence of thunderstorm warning were positively associated with more aortic dissections; furthermore, the incidences of aortic dissection and ruptured aortic aneurysm in a day could be predicted by ambient temperature in degrees Celsius using the following linear regression models:

- (1) incidence of a ortic dissection = $1.548 0.021 \times \text{temperature}$
- (2) incidence of ruptured aortic aneurysm = 0.564 0.010 \times 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). [32] Interestingly, this study demonstrated a correlation between acute AD incidence 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] Based on our results, we can confirm this statement (Table 1 and 2). 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. [33] (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. [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 locoregional 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 Kiel region 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. Based on these data, we cannot derive any pathophysiological correlation to the occurrence of dissections. 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 up to now.

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