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The Chronobiology of Stanford Type A Aortic Dissections

A Comparison of Northern versus Southern Hemispheres

Abe DeAnda Jr., MD[7]*, Eugene A. Grossi, MD[1], Leora B. Balsam, MD[1], Marc R. Moon, MD[2], Clifford W. Barlow, MD[3], Daniel O. Navia, MD[4], Patricia Ursomanno, PhD[1], Bulat A. Ziganshin, MD[5], Annette E. Rabinovich, BA[1], John A. Elefteriades, MD[5], Julian A. Smith, MD[6]

[1] Department of Cardiothoracic Surgery, New York University, New York, New York, USA

[2] Division of Cardiothoracic Surgery, Washington University-St. Louis, St. Louis, Missouri, USA

[3] Department of Cardiothoracic Surgery, University Hospital Southampton, Southampton, UK

[4] Department of Cardiothoracic Surgery, Instituto Cardiovascular de Buenos Aires, Buenos Aires, Argentina

[5] Aortic Institute at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, Connecticut, USA

[6] Department of Cardiothoracic Surgery, Monash Medical Centre, and Department of Surgery (MMC), Monash University, Clayton, Victoria, Australia

[7] Division of Cardiothoracic Surgery, University of Texas Medical Branch - Galveston, Galveston, TX, USA

Abstract

Background: **Seasonal variations of Stanford Type A dissections (STADs) have been previously described in the Northern Hemisphere (NH). This study sought to determine if these variation are mirrored in the Southern Hemisphere (SH).**

Methods: **Data from patients treated surgically for STADs were retrospectively obtained from existing administrative and clinical databases from NH and SH sites. Data points of interest included age, sex, date of dissection, and 30-day mortality. The dates of dissections (independent of year) were then organized by season.**

Results: **A total of 1418 patients were identified (729 NH and 689 SH) with complete data available for 1415; 896 patients were male with a mean age was 61 ± 14 years, and the overall 30-day mortality was 17.3%. Comparison of NH and SH on a month-to-month basis demonstrated a 6-month phase shift and a significant difference by season, with STADs occurring predominantly in the winter and least in the summer. Decomposition of the monthly incidence using Fourier analysis revealed the phase shift of the primary harmonic to be –21.9 and 169.8 degrees (days), respectively, for NH and SH. The resultant 191.7 day difference did not exactly correspond to the anticipated 6-month difference but was compatible with the original hypothesis.**

Conclusion: **Chronobiology plays a role in the occurrence of STADs with the highest occurrence in the winter months independent of the hemisphere. Season is not the predominant reason why aortas dissect, but for patients at risk, the increase in systemic vascular resistance during the winter months may account for the seasonal variations seen.**

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Key Words

Aortic dissection • Chronobiology

Introduction

There is a growing body of evidence to suggest that cardiovascular events display both a seasonal and circadian variation in occurrence. For acute Stanford Type A aortic dissections (STADs), it is widely

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http://aorta.scienceinternational.org

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* Corresponding Author:
Abe DeAnda Jr., MD
Division of Cardiothoracic Surgery
University of Texas Medical Branch - Galveston
301 University Blvd. JS Annex 6-120, Galveston, TX 77555, United States
Tel. +1 409 772 1203; Fax +1 409 772 1420, E-Mail: abdeanda@UTMB.edu

observed and appreciated that the winter months tend to be the time when these dissections most often occur [1-3], possibly due to the cold weather having an impact on the systemic vascular resistance [4]. Other factors occur during these same months, which might also have an impact including the increased "stress" of holidays and year-end business events [5]. Interestingly, all studies (including the International Registry of Acute Aortic Dissection, IRAD) have relied on patient data from Northern Hemisphere (NH) sites. We were interested in whether or not Southern Hemisphere (SH) occurrences would mirror those of the NH, thereby lending more credence to the weather theory rather than to the time of year. Our hypothesis was that the season would have more of an impact than the time of year.

Methods

Institutional Review Board exemption for de-identified patient outcome data analysis was obtained, and the requirement for written informed consent was waived. Patient information was retrospectively collected from six sites (Table 1) with 729 patients in the NH and 689 patients in the SH for a total of 1418 patients; three patients were excluded from the analysis because of missing data. Specific data points queried were age, sex, date of operation, and 30-day mortality. Patients were assigned a hemispheric location based on study site and results were aggregated based on hemisphere. An assumption was made that the date of operation was associated with the date of clinical presentation; that date was then converted to a season with the seasons in the NH being defined as Winter (December 21–March 20), Spring March 21–June 20), Summer (June 21–September 20), and Fall (September 21–December 20). SH seasons were offset by 6 months. Nonparametric comparisons were performed using the Pearson Chi-square test (SPSS Version 22, IBM, Armonk, New York, USA) and temporal variation analyzed with Fourier analysis (Matlab R2010B, Mathworks, Natick, Massachusetts, USA).

Results

A total of 1418 patients were identified (729 NH and 689 SH) with complete data available for 1415; 896 patients were male (63%) with a mean age of 61 ± 14 years (range 18–92), the overall 30-day mortality was 17.3%. Comparison of NH and SH on a month-to-month basis demonstrated a 6-month phase shift (Pearson-χ^2 26.7, p=0.005) and a significant difference by season, with STADs occurring predominantly in the winter and least in the summer (Pearson-χ^2 11.6, p=0.009) (Figure 1). Decomposition of the monthly incidence using Fourier analysis revealed the phase shift of the primary harmonic to be –21.9 and 169.8 degrees (days), respectively, for NH and SH. This corresponds to peak incidences in the NH in early December and in the SH in late May. The resultant 191.7-day difference did not exactly correspond to the anticipated 6-month difference but was compatible with the original hypothesis. All dissections (both hemispheres) were combined with the day of year calculated with respect to the associated winter solstice. Using this combined data set, when harmonic analysis was performed the phase shift of the primary harmonic occurred 20 days prior to the winter solstice. Thus, the actual peak event occurs *prior* to the calendar winter season (i.e., late November in the NH) but the seasonal variation persists. Using the peak as the actual starting point and distributing

Table 1. Sites of patient enrollment for study.

Site	Country	Principal investigator	n	Time interval
New York University	USA	DeAnda	71	2003–2011
Yale University	USA	Elefteriades	181	1981–2012
Washington University	USA	Moon	252	1984–2009
Southampton	England	Barlow	225	2000–2012
ANZSCTS*	Australia/New Zealand	Smith	583	2001–2012
Buenos Aires	Argentina	Navia	106	2001–2011

*The Australian and New Zealand Society of Cardiac and Thoracic Surgeons National Cardiac Surgery Database.

the data in six month blocks, the mirror image results are strikingly seen (Figure 2).

Discussion

This study confirms the seasonal association of aortic dissection, with an increase in incidence during the winter months. The impact of weather on cardiovascular disease has been investigated previously. Verberkmoes et al. [6] looked at the incidence of STADs, acute myocardial infarctions (AMI), and abdominal aortic aneurysms in the Dutch population and found a positive correlation with temperature (and no correlation with atmospheric pressure) for STAD and AMI, but did not see a similar correlation

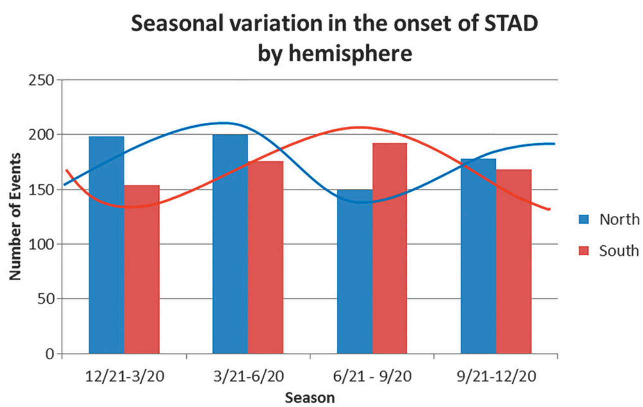

Figure 1. Seasonal variation in the onset of Stanford Type A dissection by hemisphere.

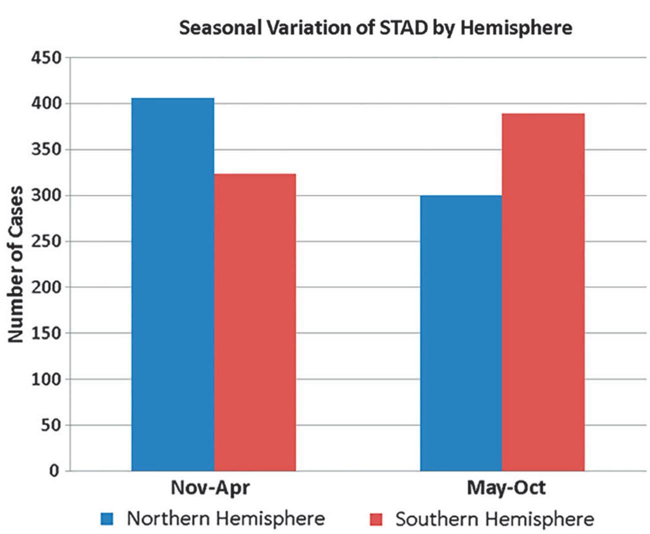

Figure 2. Seasonal variation of Stanford Type A dissection by hemisphere.

with abdominal aortic aneurysms. As suggested by Edwin et al. [7], Verberkmoes proposed that the pathogenesis of STAD was a balance between three factors: an underlying abnormality of the aortic media (either genetic or acquired), intimal injury, and hemodynamic factors, which would propagate the dissection once the tear was initiated. In this framework it would appear that cold weather would impact the third of these factors due to an increase in systemic vascular resistance. The work of Benouaich et al. [8], like the Dutch study, correlated the incidence of STAD with atmospheric temperature; and like our study, they found the incidence of dissection to be higher in the winter months than in the summer (p=0.018). Using data from the French national meteorological office (MétéoFrance) the authors further showed that within the same season, days with aortic dissection were colder than those without (p=0.017).

Weather is not the primary reason aortas dissect, and as already noted there is interplay between at least three factors. Other hemodynamic factors would include underlying chronic hypertension, acute hypertensive episodes as well as other extrinsic events. Ryu et al. [9], in their small series of 166 patients with STADs, found that 72% of the STAD episodes were associated with either physical (53%) or mental (19%) activities. Hatzaras et al. [10] documented 31 patients with an acute STAD associated with intense physical exertion, predominantly weightlifting. Based on their analysis, they concluded that "…moderate aortic dilatation confers vulnerability to exertion-related aortic dissection" (mean aortic diameter in this series was 4.63 cm). Thus we could speculate that colder weather, in the context of moderate aortic dilatation, could increase the systemic vascular resistance, resulting in a higher risk for dissection. In addition, colder temperatures also have systemic effects on hematologic, hemostatic, and rheological factors which may produce local effects on the intima which may further increase the risk of dissection [11].

Other chronobiological themes have been examined in STADs. Recently, Shuhaiber et al. [12] examined the impact of the lunar cycle on mortality and length of stay following surgical repair of STAD. Season did not have a significant impact on survival, but the lunar cycle, specifically the Full moon, impacted mortality. It remains unclear why the lunar cycle would influence survival.

A large retrospective administrative database study by Kumar et al. [13] examined over 89,000 hospitalizations for acute aortic dissections (both Stanford Type A and B) from 2004–2011. This study was limited to the United States and showed significant seasonal variability with peaks in January. This analysis utilized a time-series analysis (cosinor model) and the results were similar to the analysis by Mehta et al. [1]. Interestingly, while these authors also saw the peak in January for combined Type A and B dissections, when subgroup analysis was performed the peak for Type B was in February while the peak for Type A was in December.

A meta-analysis by Vitale et al. [14] considered forty-two studies with more than 80,000 patients and once again showed an increase in aortic dissection and rupture in winter, with a relative risk of 1.171 in December ($p < 0.001$). The analysis also found a significant increase in relative risk on Monday, and in the morning from 6 am to noon. As with Shuhaiber [12] the weekly and circadian variation was not easily explainable but serves to emphasize that such variations can be observed.

Limitations

As is common with retrospective database analyses, the data analyzed were heterogeneous in the time-frame of data collection between institutions. We attempted to maximize the number of patients included by pooling the site data without regard to time of collection with the underlying assumption that there would not be a historical difference in occurrence. Additionally, as noted previously, we assumed that the onset of the STADs coincided with the time of surgery, which would mean that chronic STADs are likely to be included in the analysis. Without censoring of chronic STADs, we analyzed the data under the assumption that each site had the same proportion of chronic STADs, and that the incidental finding of a chronic STAD would be randomly distributed through the calendar year. Likewise, since acute STADs are traditionally defined as occurring within 2 weeks of the onset of symptoms, the possibility that the actual acute event could straddle the defined cutoff of seasons might erroneously place the onset in the wrong season. Finally, this analysis was based only on patients undergoing surgical repair, and thus conclusions cannot be drawn regarding the effect of season on populations with dissection who expired without antemortem diagnosis or who were excluded from surgical consideration.

Conclusion

Our study confirms the seasonal variation associated with aortic dissection and presents the added finding that this variation is independent of hemisphere, that is, calendar month. As proposed by others, this variation is multifaceted and may reflect seasonal changes in sympathetic activity, including changes in blood pressure and heart rate in colder months. Season alone is not the primary driver for aortic dissection, but this and other studies promote the idea that for patients deemed at risk, attention to amelioration of co-factors (i.e., hypertension) becomes especially pertinent during the winter season.

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ANZSCTS DATA MANAGEMENT CENTRE, CCRE, Monash University: Prof. Chris Reid, Dr. Lavinia Tran, and Mrs. Angela Brennan.

ANZSCTS DATABASE PROGRAM STEERING COMMITTEE: Mr. Gil Shardey (Chair), Mr. Peter Skillington, Prof. Julian Smith, Mr. Andrew Newcomb, Mr. Siven Seevanayagam, Mr. Bo Zhang, Mr. Hugh Wolfenden, Mr. Adrian Pick, Mr. Jurgen Passage, A/Prof Rob Baker, Prof Chris Reid, Dr Lavinia Tran, and Mr. Andrew Clarke.

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Scaybrook S; Lake Macquarie Hospital: Dennett B, Mills M; Liverpool Hospital: French B, Hewitt N; Mater Health Services: Diqer AM, Curtis L; Monash Medical Centre: Smith J, Baxter H; Prince of Wales Hospital: Wolfenden H, Weerasinge D; Royal Melbourne Hospital: Skillington P, Wynne R; Royal North Shore Hospital :Sze D; Royal Perth Hospital: Edwards M, Wright M, Le V. Royal Prince Alfred Hospital: Wilson M, Turner L; Powell, C; Sir Charles Gairdner: Kolybaba M; St George Hospital: Fermanis G, Newbon P; St Vincent's Hospital, VIC: Yii M, Newcomb A, Mack J, Duve K; St Vincent's Hospital, NSW: Spratt P, Hunter T; The Canberra Hospital: Bissaker P, Dean A; Townsville Hospital: Tam R, Farley A; Westmead Hospital: Costa R, Halaka M.

Conflict of Interest

The authors have no conflicts of interest relevant to this publication.

Comment on this Article or Ask a Question

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