Marfan syndrome (MFS) is an autosomal dominant disorder that affects many tissues and organs and is caused by mutations in FBN1, the gene that encodes the large glycoprotein fibrillin 1. Most people with MFS develop dilatation of the aortic root, often from an early age. The aortic wall histopathology shows medial degeneration, with fragmentation of elastic fibers and pools of proteoglycan. Acute aortic dissection (AAD), with either intramural hematoma, dissection flap, or aortic rupture, was recognized more than 4 decades ago as the leading cause of death in MFS. Since then, a variety of medical and surgical approaches have reduced the risk of AAD and prolonged life expectancy in MFS. Dissection of the thoracic aorta, especially the ascending portion, has an extremely high mortality, with a death rate of 1% to 2% per hour for the first 24 hours in patients who do not receive treatment. In recent years, for those patients who survive to reach care, the mean hospital mortality rate for AAD is still about 25%. Important in the recognition of AAD in the MFS population is understanding its epidemiology. Chronobiology is a field of medicine and biology that studies the presence of rhythms and their effects on physiology and pathophysiology. Many cardiovascular...
conditions exhibit rhythmic patterns, with notable peaks at certain points in the 24-hour day as well as weekly and seasonal variations. Previous studies have described these cycles in myocardial infarction (MI), stroke, pulmonary embolism, and, more recently, Takotsubo cardiomyopathy. Several studies examined the chronobiology of AAD in the general population of numerous countries. However, no studies have explored this phenomenon in patients with MFS. The goal of our study was to examine the chronobiologic patterns of AAD in MFS using 2 large international registries and examine what, if any, impact the co-morbid conditions have on the timing of AAD.

Methods

Two registries, International Registry of Acute Aortic Dissection (IRAD) and Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC), were queried regarding the timing of AAD in patients with MFS. The rationale, study design, and methods for both registries have been previously reported.

Briefly, IRAD enrolled 4,160 total patients with an AAD on arrival to the hospital. From 1996 to 2012, 37 institutions from 11 countries participated in IRAD and enrolled patients. GenTAC was comprised of 8 coordinating centers in the United States that prospectively enrolled 3,747 subjects from 2007 to 2013 with known thoracic aortic disease associated with 12 specific conditions. GenTAC centers collected biosamples, imaging data, medical history, and periodic follow-up medical history from all participants who consented to such activities.

Gender and date of birth were used to exclude duplicate data from subjects enrolled in both registries. Informed consent was given by all participants, and institutional review board approval was received by each institution. The study methods comply with the Declaration of Helsinki. For statistical analyses, hourly and monthly intervals for statistical analysis were defined according to previous work.

The hourly distribution of AAD was collected from the IRAD data set. We analyzed the likelihood of AAD during 6-hour segments of the day (morning: 6 A.M. to 12 P.M.; afternoon: 12 to 6 P.M.; evening: 6 P.M. to 12 A.M.; overnight: 12 to 6 A.M.). The 24-hour period was divided into daytime (6 A.M. to 6 P.M.) and nighttime (6 P.M. to 6 A.M.) for further analysis.

Monthly data from both the IRAD and GenTAC registries were combined to represent seasons in 3-month segments spanning November to January, February to April, May to July, and August to October. We also compared the distribution of AAD in the colder 6 months (November to April) compared to warmer 6 months of the year (May to October).

Queries of the GenTAC and IRAD databases were limited to participants with a known diagnosis of MFS according to the revised Ghent criteria and who had an aortic dissection with either a recorded time or month, or both. GenTAC patients with MFS had genotypes confirming MFS diagnosis, whereas IRAD patients with MFS were identified clinically and through history by each enrolling site according to the Ghent criteria. Patients in the GenTAC database did not have data on hour of AAD, whereas those included from the IRAD registry did have this data available and formed the basis for the hourly analysis. Subjects who had a previous history of aortic reconstruction/replacement in or adjacent to the section of the aorta that dissected were excluded as this subgroup may not accurately reflect the pathophysiology of MFS being investigated here.

IRAD enrolled 181 patients with MFS who suffered an AAD, 125 of whom had the date and time of their AAD reported. GenTAC enrolled 894 participants with MFS with 169 of those reporting any type of aortic dissection; a subset of these patients had the date of dissection reported. In total, 125 patients with MFS had reported data on the time of day of AAD and 244 patients had data regarding the month during which an AAD occurred, with a total of 257 patients with a combination of these data. Both registries recorded gender, age at time of dissection, date, and type of dissection (Stanford type A vs type B) for participants. The registries recorded information about co-morbid conditions such as hypertension (HTN), diabetes mellitus (DM), and tobacco use from some but not all participants.

The chi-square test was used to assess the unique incident-time profile of AAD in this population. We subdivided time into multiple components, including time of day, month, and season when AAD occurred. We also examined the interaction of possible contributing factors such as age, gender, and smoking history with the time variation in AAD presentation. Percent of patients within each category were reported after excluding those with no reported data.

Results

Subject characteristics are listed in Table 1. Mean subject age at time of AAD was 38 years, and 156 (61%) of subjects were men; 167 (65%) of patients suffered a type A dissection. Of the 168 patients who identified their race, 143 (85%) were Caucasian and 8 (5%) were black. Of the participants, 13% had previously used tobacco products, 35% patients reported having a history of HTN, whereas 3% had DM.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.7</td>
<td>+/- 12</td>
</tr>
<tr>
<td>Male</td>
<td>156</td>
<td>61%</td>
</tr>
<tr>
<td>Type A dissection</td>
<td>167</td>
<td>65%</td>
</tr>
<tr>
<td>White</td>
<td>143</td>
<td>85%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8</td>
<td>3%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>88</td>
<td>34%</td>
</tr>
</tbody>
</table>

Figure 1 illustrates the hourly distribution of AAD in patients with MFS. Significant differences were noted in the distribution of AAD based on 6-hour intervals (p = 0.001, Figure 1B) and 12-hour intervals (p = 0.001, Figure 1C). Specifically, dissections were significantly more likely to occur during the daytime hours, with 66% of dissections occurring from 6 A.M. to 6 P.M. (Figure 1C).

Gender and type of dissection both had a significant effect on the distribution of AAD throughout 24 hours (Table 2). Men were more likely to dissect during the daytime compared to nighttime (74% vs 26%, respectively), whereas women dissected more evenly throughout the
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات