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Short communication

Seasonal trend of ventricular arrhythmias in a nationwide remote monitoring database of implantable defibrillators and cardiac resynchronization devices

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ABSTRACT

Background: The occurrence of sustained ventricular arrhythmias (SVA) may be influenced by environmental factors. We aimed to investigate annual periodic trends of SVA from the intracardiac electrograms (IEGMs) stored in the implantable defibrillators (ICDs) or cardiac resynchronization therapy (CRT-D) recipients.
Methods: Data from the Home Monitoring Expert Alliance project, a pooled repository of remote monitoring transmissions were analyzed. All IEGMs stored were independently adjudicated by three cardiac electrophysiologists. Periodicity of SVA was evaluated with Generalized Estimating Equations (GEE) models, including periodic terms depending on months in a year.
Results: A total of 2936 ICD/CRT-D patients (median age 70 years, 79.6% male) were followed for a median period of 25[13–44] months. Most prevalent structural heart diseases were ischemic (50.8%) and idiopathic dilated (30.6%) cardiomyopathies. Overall, 942 (32.1%) patients experienced a total of 4824 SVA. At GEE analysis, we found a significant periodic component ($p = 0.048$) when considering both shocked and non-shocked episodes. SVA less frequently occurred in Junes and Julies (3.7×1000 patient-month). No evidence of significant periodicity was collected in the subgroup of ischemic patients.
Conclusions: In this RM-based cohort of ICD/CRT-T patients, we observed an annual periodicity of SVA occurrence, with a lower incidence in summer months.

1. Introduction

The occurrence of sustained ventricular arrhythmias (SVA) may be influenced by environmental factors. Indeed, previous studies showed circadian variations of SVA with a peak in the morning hours [1]. Despite a well-known effect of meteorological triggers on major cardiovascular diseases [2], observations of periodic pattern over a longer time horizon are few and often limited to specific heart diseases, such as the arrhythmogenic right ventricular dysplasia [3] or the Brugada syndrome [4]. Daily remote monitoring (RM) of cardiac implantable electronic devices (CIEDs) reporting comprehensive information on arrhythmias may provide a unique opportunity to investigate this issue allowing large cohort observations. Recently, marked seasonal trends in atrial fibrillation have been demonstrated using daily RM technology [5]. The aim

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Table 1
Mean ventricular episode rate (no. of episodes × 1000 patient-months).

Month	Any SVA episode	VT	Fast VT	Self-ex. VF	VF
January	6.0	2.1	3.0	0.9	0.09
February	5.0	2.4	1.7	0.7	0.14
March	4.7	2.4	1.4	0.8	0.15
April	4.4	2.4	1.2	0.7	0.10
May	4.6	2.7	1.0	0.7	0.10
June	3.7	2.2	1.0	0.5	0.09
July	3.7	1.8	1.2	0.6	0.05
August	4.3	1.6	1.7	0.8	0.15
September	5.2	2.9	1.3	0.9	0.06
October	5.6	2.9	1.7	0.6	0.40
November	4.2	2.3	1.2	0.6	0.07
December	4.9	2.0	1.8	0.9	0.24
p^*	0.048	0.005	0.27	0.61	0.027

SVA: sustained ventricular arrhythmia; VT: ventricular tachycardia; self-ex. VF: self-extinguishing ventricular fibrillation; VF: ventricular fibrillation.
* Significance level associated to the periodic component of the GEE Poisson models.

of our analysis was to assess periodic trends over the year also in SVA using a nationwide RM database of implantable defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds).

2. Methods

This analysis was performed on the database of the Home Monitoring Expert Alliance (HMEA) project [6]. The HMEA is an independent initiative running in 41 Italian sites which provides a pooled repository of data transmitted during routine use of the Home Monitoring (BIOTRONIK SE KG & Co., Berlin, Germany) system. All patients registered in the HMEA project gave written informed consent to data processing for research purpose.

The Home Monitoring is a RM technology for CIEDs characterized by automatic and daily transmissions of device settings, diagnostics, and intracardiac electrogram (IEGM) registrations of arrhythmic episodes to a central Service Center for physician consultation.

For the purpose of this analysis we selected all ICD and CRT-D devices. Programming of detection zones, counters, and discrimination algorithms were set as per normal practice of each participating site. Ventricular detections, both in ventricular tachycardia (VT) and ventricular fibrillation (VF) zones were adjudicated as true or false ventricular arrhythmias (VAs) by a three cardiac electrophysiologists through IEGM visual inspection. A two-stage adjudication process was applied: in a first stage, objective criteria were applied, including presence of non-physiological signals, ventricular and atrial cycle length comparison; atrio-ventricular decoupling; unstable ventricular rhythm during supraventricular tachyarrhythmia. Whenever objective criteria were not possible or uncertain, adjudication was reached by majority vote. Adjudicated SVA were then classified as follows: (i) VT if detected in any VT zone; (ii) Fast VT if detected in the VF zone with regular cycles; (iii) self-extinguishing VF (Self-ex VF) if detected in the VF zone and terminated without any delivered therapy; (iv) VF if detected in the VF zone with irregular cycle and delivered shocks. The monthly rate was calculated as the mean number of events occurring in a month divided by the number of observed patient-month. Periodicity of SVA was evaluated with Generalized Estimating Equations (GEE). Episode count was modelled with a Poisson distribution as the dependent variable. The model included periodic terms (linear combination of oscillating functions) depending on months as covariates. Statistical significance level was set at $p = 0.05$. Continuous variables were reported as median (interquartile range) and binary variables as percentages. Analysis was performed with Stata software version 11.1SE (StataCorp, Texas, US).

3. Results

A total of 2936 ICD/CRT-D patients followed for a median period of 25 [13–44] months were included in the analysis. The median age was 70 years and the majority were male (79.6%). CRT-D patients were 39.7% and the median left ventricle ejection fraction was 30% [27%–35%]. The etiologies of the heart diseases were ischemic (50.8%), idiopathic dilated (30.6%), valvular (7.6%), hypertrophic (3.8%), Brugada syndrome (1.8%), arrhythmogenic right ventricular dysplasia (1.3%) and long QT syndrome (0.8%). In addition, a subset of patients (3.2%) was implanted for idiopathic ventricular tachycardia or fibrillation. At baseline history of SVA and atrial fibrillation was present in 21.4% and 21.0% of patients, respectively.

Device settings were not uniformly programmed in all patients. A VT zone was programmed in 95.6% of patients with a median detection cut-off of 158 (150–171) beats/min and a counter of 28 (26–40) beats. The VF zone was set at 200 (200–207) beats/min with a 12 (8–18) of 16 (12–14) counter.

Overall, 942 (32.1%) patients experienced a total of 4824 SVAs: 2275 (47.2%) VTs, 1571 (32.5%) Fast VTs, 864 (17.9%) Self-ex VFs and 114 (2.4%) VFs.

The monthly average episode rates are summarized in Table 1. At GEE analysis, a significant seasonal pattern was found for VT ($p = 0.005$) and VF ($p = 0.027$) episodes. VTs and VFs were less frequent in Julies/Augusts (1.7 × 1000 patient-month) and in Junes/Julies (0.07 × 1000 patient-month), respectively. Fig. 1 shows the bar graphs and the model-predicted trends of event rate over the year.

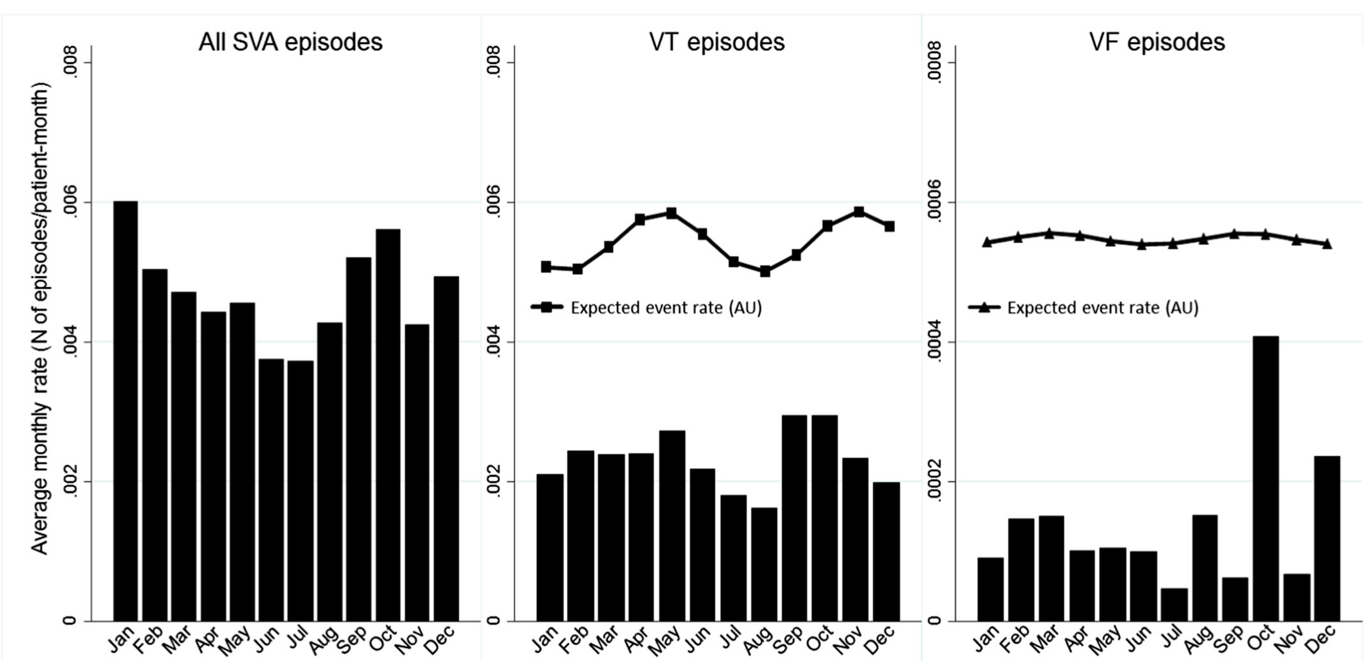

Fig. 1. Average monthly rate of all sustained ventricular arrhythmia (SVA), ventricular tachycardia (VT) and ventricular fibrillation (VF) episodes over the year. For the VT and VF class of episodes showing statistically significant periodic trends, the model predicted annual trend of event rate was added to the relative panel. AU: arbitrary units.

A subgroup analysis performed in patients with ischemic cardiomyopathy, did not show a significant seasonal variability. However a trend toward a higher prevalence of SVA in Decembers/Februaries (6.9 vs. 4.4×1000 patient-month, $p < 0.05$) was detected.

4. Discussion

In this analysis a significant annual periodicity of SVA occurrence was reported in a large cohort of ICD/CRT-D patients followed with a daily RM system. The observed pattern showed a lower occurrence of sustained episodes in the summer months, when considering both shocked and non-shocked arrhythmias. This finding suggested a possible role of environmental and meteorological factors in the triggering of VAs.

Although this analysis is not conclusive, potential mechanisms may be proposed. The first mechanism may be related to weather condition and temperature. Previous studies reported an increase of risk of sudden cardiac death associated with low temperature [2,7]. Heart rate and systemic blood pressure have been reported to rise in cold environments, thus increasing cardiac oxygen consumption and cardiac afterload [8,9]. More recently the results of the TEMPEST study have knotted the onset of electric storms, defined as the occurrence of ≥3 arrhythmic episodes with delivered shock, not with absolute temperature values, but with an increase in monthly temperature fluctuations [10].

Indeed, some studies reported an association between air temperature and blood markers of inflammation or electrocardiographic markers of ventricular repolarization [11,12]. These changes may increase the ventricular vulnerability to ischemic stressors. However, in a recent large database analysis high hospitalization rates were found at both temperature extremes [13].

A second mechanism may be related to a decrease in physical activity in cold months. An inverse relation between atrial arrhythmia incidence and level of activity has been already shown [5]. Heart rate variability generally decreases in winters. This may contribute to worse prognosis as low heart rate variability is associated to new-onset cardiovascular events [14].

In our analysis we did not detect significant seasonal effects on SVA incidence in the subgroup of ischemic patients. This may be explained by reduced statistical power in the ischemic subgroup. Nevertheless, the influence of temperature and seasonality on coronary events is still unclear and was found to be not consistent between types of myocardial infarction, populations and geographic regions. Previous studies reported peak for sudden cardiac death and myocardial infarction in winter [7]. In contrast, similar seasonal pattern was not observed for ST-segment elevation myocardial infarction admissions in a US national registry (ACTION Registry –GWTG, Acute Coronary Treatment Intervention Outcomes Network Registry-Get With the Guidelines) [15], while a peak of myocardial infarction in summer and fall was reported in patients with non-obstructive coronary [16].

5. Conclusions

In a RM-based cohort of CIED patients, an annual periodicity in SVA occurrence was detected with the highest incidence in winter months. The identification of periodic patterns of SVA distribution may not only provide pathological insights in the complex understanding of arrhythmias onset, but it may also paved the way to new approaches in the management of patients with cardiac devices.

Declarations of interest

D.G. and A.G. are employees of Biotronik Italia; the remaining authors have no conflict of interest to declare.

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