Triggering of supraventricular premature beats. The impact of acute and chronic risk factors

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ARTICLE INFO

Article history:
Received 9 January 2012
Received in revised form 19 March 2012
Accepted 8 April 2012
Available online 15 May 2012

Keywords:
Circadian rhythm
Multiple regression analysis
Risk factors
Supraventricular arrhythmia
Trigger

Supraventricular premature beat (SPB) is usually considered a benign heart rhythm disturbance. However, an isolated SPB can trigger episodes of atrial fibrillation [1,2], supraventricular tachycardia [3] and malignant ventricular tachyarrhythmia [4,5]. A high frequency of SPB has been linked to the increased risk of death or stroke [6,7]. Circadian, weekly and annual variations in the occurrence of ventricular tachyarrhythmias and triggering by emotional and physical stress have been well-described [8–14]. Until now, factors that could be involved in the triggering of supraventricular arrhythmias have not been rigorously investigated.

Consecutive patients who underwent continuous 24-hour Holter monitoring between January and April 2001 in the Diagnostic Units of the Division of Cardiology, Department of Internal Medicine, University Hospital Split, Split, Croatia ($n=501$), were eligible for inclusion in the analysis. Patients who were unable to complete the diary, had atrial fibrillation, or their ECG recordings were inaccurate due to artifacts were excluded from the analysis ($n=63$). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of the University Hospital Split. All participants gave their informed consent. The authors of this article have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [15].

The identification of SPB was based on 3 criteria: prematurity, morphology, and postcontraction pause. An SPB was defined as a QRS of less than 0.12 seconds with a minimum shortening of 20% in the R-R interval. QRS complexes of duration of more than 0.12 seconds were considered SPB only if aberration was suspected. The postcontraction pause had to be noncompensatory. Differentiation from sinus arrhythmia was made according to the P-wave morphology, cyclic changes in preceding R-R intervals, or both.

Activity compatible with level 4 or more according to a metabolic equivalents scale from 1 to 8 was considered as exposure to physical activity. Exposure to emotional upset was defined as an emotional state compatible with level 3 or more according to the Onset Anger Scale [8,10,16]. Meteorologic parameters (atmospheric temperature and pressure, relative air moisture, wind speed and direction, rainfall and passages of cold or warm atmospheric fronts) were provided for every 3 hours (at 1, 4, 7 and 10 AM, and 1, 4, 7 and 10 PM). The frequency of SPB in an hour was expressed as a percentage of all episodes during recording which reduced the distribution of absolute number of SPB during monitoring and made the data normally distributed.

Linear regression analysis was used to investigate the direct impact of continuous meteorologic factors, repeated measures analysis of variance (ANOVA) to estimate whether the frequencies of SPB differed according to time of day, a two-way ANOVA to assess whether the circadian pattern of SPB occurrence depended on baseline characteristic and multi-way ANOVA was used to investigate the frequency of SPB according to physical, emotional and meteorologic stressors. A stepwise multiple regression analysis was used to simultaneously assess the independent predictive significance of both acute triggering and chronic (conventional) risk factors and medication.

Baseline characteristics of the 438 participants are given in Table 1 and preliminary models for multivariate analysis according to age and gender are given in Table 2. Physical activity, followed by the periods of increasing relative air moisture (Fig. 1), showed the strongest association with the occurrence of SPB and both remained significant predictors in all participant subgroups (Tables 3 and 4). The occurrence of SPB was somewhat higher during blowing of southerly and westerly winds (Fig. 2), but after adjustment for other external triggering factors the significance of this difference disappeared ($p=0.77$). Atmospheric pressure was a predictor of SPB in men, while lower levels of relative air moisture and passage of

Table 1
Baseline characteristics of the study participants ($n=438$).

Participants characteristics		
Age (mean years ± SD)	57.4 ± 15.1	
BMI (kg/m^2 ± SD)	26.9 ± 3.6	
	No	%
Patient characteristics		
Out-patients	404	92.2
Hypertension	259	59.1
Chest symptoms in previous 7 days	229	52.3
Familiy history of heart disease	152	34.7
Hypercholesterolemia	151	34.5
Smoking	73	16.7
Previous myocardial infarction	72	16.4
Diabetes mellitus	70	16
Medication used		
Aspirin	141	32.2
β-Blocker	137	31.3
Diuretic	129	29.5
ACE inhibitor	128	29.2
Anxiolytic	71	16.2
Nitrate	59	13.5
Hypolipemic	58	13.2
Calcium channel blocker	57	13
Digitalis	34	7.8
Propafenone	19	4.3
Amiodarone	9	2.1

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Table 2
Preliminary multivariate models for baseline characteristics, chronic risk factors and medication used independently predictive of SPB in participants according to gender and age.

	β	p		β	p
Men			Women		
Model 1			Model 1		
Age	0.073	0.004	Previous chest symptoms	0.072	0.003
Previous chest symptoms	0.058	0.02	Previous myocardial infarction	−0.049	0.07
BMI	−0.047	0.051	BMI	−0.048	0.07
Hypertension	−0.031	0.21	Diabetes mellitus	−0.038	0.15
Hypercholesterolemia	−0.025	0.31	Current smoking	−0.034	0.17
Family history of heart disease	0.022	0.35	Age	−0.028	0.29
Previous myocardial infarction	−0.022	0.38	Family history of heart disease	0.019	0.42
Model 2			Model 2		
Digitalis	−0.088	0.0003	β-Blocker	−0.063	0.01
Amiodarone	0.060	0.02	Aspirin	−0.063	0.01
Propafenone	−0.054	0.03	Digitalis	−0.057	0.03
Diuretic	0.040	0.13	Amiodarone	−0.049	0.04
Anxiolytic	−0.028	0.24	Diuretic	−0.049	0.09
ACE inhibitor	0.024	0.36	Calcium channel blocker	0.048	0.06
			ACE inhibitor	0.043	0.11
			Propafenone	−0.022	0.37
Participants under 65 years			Participants over 64 years		
Model 1			Model 1		
Previous myocardial infarction	−0.096	<0.0001	Men	0.099	<0.0001
Current smoking	−0.065	0.004	Previous chest symptoms	0.091	0.0006
Previous chest symptoms	0.052	0.02	BMI	−0.082	0.002
Family history of heart disease	0.048	0.03	Diabetes mellitus	−0.077	0.004
Diabetes mellitus	0.041	0.08	Hypertension	−0.045	0.08
Hypercholesterolemia	−0.018	0.45	Previous myocardial infarction	0.032	0.27
Model 2			Model 2		
Digitalis	−0.100	<0.0001	Propafenone	−0.121	<0.0001
Calcium channel blocker	0.066	0.01	Digitalis	−0.064	0.02
Nitrate	0.064	0.01	ACE inhibitor	0.059	0.03
β-Blocker	−0.055	0.02	Aspirin	−0.052	0.07
Aspirin	−0.045	0.08	Amiodarone	−0.036	0.17
Diuretic	0.030	0.26	Anxiolytic	0.037	0.19
Anxiolytic	−0.025	0.27	Hypolipemic	0.035	0.19
Propafenone	0.021	0.36	Nitrate	−0.031	0.24

β and p values were obtained from the stepwise multiple regression analysis.
Model 1 includes participant characteristics and risk factors; Model 2 includes prehospital medication used.

a cold front were associated with a favorable effect in women (Table 3). The level of atmospheric temperature was a predictor of SPB in those aged less than 65 years (Table 4), with a similar trend in women (Table 3).

In those over 64 years of age, male gender, hypertension and lower BMI independently increased the likelihood of SPB. Taking digitalis reduced the likelihood of SPB in all participant subgroups. In women and younger participants, taking calcium channel blockers increased the likelihood of SPB as well as nitrates in younger participants only (Tables 3 and 4).

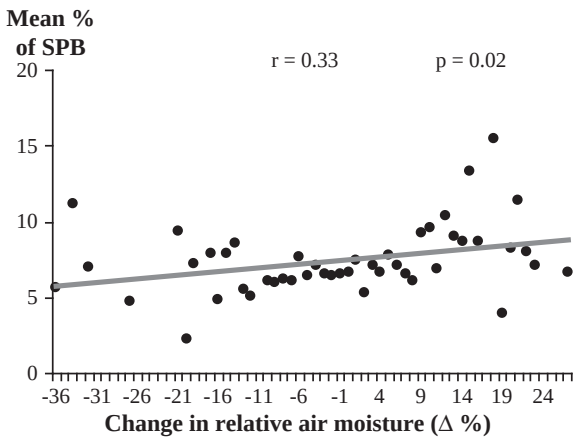

Fig. 1. Mean percentage of SPB per 3-hour daily intervals according to change in relative air moisture for all study participants (in Δ% of air saturation; linear regression equation: $y = 7.5 + 0.05\,X$).

A circadian variation in the occurrence of SPB with two peaks, late morning (6–11 AM) and afternoon (3–8 PM), was observed in all gender and age subgroups, even after adjustment for the external triggering factors (Table 5). The pattern of daily distribution significantly differed according to gender, presence of chest symptoms during the previous week or aspirin taking, and borderline significantly according to β-blocker taking (Table 6). A significantly greater occurrence of SPB was observed during the afternoon and evening in women with previous chest symptoms (Fig. 3), but not in men ($p = 0.31$ for variable; $p = 0.19$ for interaction). Digitalis taking reduced the overall daily frequency of SPB, particularly during the afternoon and night in men (Fig. 3).

To the best of our knowledge, this is the first study evaluating both acute triggering and chronic risk factors involved in the occurrence of SPB. Physical activity showed the strongest triggering potential in all participant subgroups, followed by the periods of raising air moisture, while lean hypertensive elderly men seem to be the most susceptible to the occurrence of SPB. This population could be generally at greater risk of atrial fibrillation, stroke or death associated with physical activity or unfavorable weather conditions. Meteorologic factors such as atmospheric pressure or wind were also associated with the increased frequency of SPB in some participant subgroups.