The effect of solar-geomagnetic activity during and after admission on survival in patients with acute coronary syndromes

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ORIGINAL PAPER

The effect of solar-geomagnetic activity during and after admission on survival in patients with acute coronary syndromes

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Abstract A number of studies have established the effects of solar-geomagnetic activity on the human cardio-vascular system. It is plausible that the heliophysical conditions existing during and after hospital admission may affect survival in patients with acute coronary syndromes (ACS). We analyzed data from 1,413 ACS patients who were admitted to the Hospital of Kaunas University of Medicine, Lithuania, and who survived for more than 4 days. We evaluated the associations between active-stormy geomagnetic activity (GMA), solar proton events (SPE), and solar flares (SF) that occurred 0–3 days before and after admission, and 2-year survival, based on Cox's proportional-hazards model, controlling for clinical data. After adjustment for clinical variables, active-stormy GMA on the 2nd day after admission was associated with an increased (by 1.58 times) hazard ratio (HR) of cardiovascular death (HR=1.58, 95 % CI 1.07–2.32). For women, geomagnetic storm (GS) 2 days after SPE occurred 1 day after admission increased the HR by 3.91 times (HR=3.91, 95 % CI 1.31–11.7); active-stormy GMA during the 2nd–3rd day after admission increased the HR by over 2.5 times (HR=2.66, 95 % CI 1.40–5.03). In patients aged over 70 years, GS occurring 1 day before or 2 days after admission, increased the HR by 2.5 times, compared to quiet days; GS in conjunction with SF on the previous day, nearly tripled the HR (HR=3.08, 95 % CI 1.32–7.20). These findings suggest that the heliophysical conditions before or after the admission affect the hazard ratio of lethal outcome; adjusting for clinical variables, these effects were stronger for women and older patients.

Keywords Geomagnetic activity · Solar flare · Solar proton event · Acute coronary syndromes · Survival

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Introduction

In recent years, a number of studies have reported the effects of environmental physical factors such as solar activity and space weather conditions on the timing of occurrence of some cardiovascular pathologies: myocardial infarction (MI), cardiovascular death, stroke, etc. Geomagnetic storms (GS) and Forbush decreases increase the rate of myocardial infarction, cardiovascular death, MI death, and stroke (Villoresi et al. 1998; Gurfinkel et al. 1998; Cornelissen et al. 2002; Mendoza and Diaz-Sandoval 2000, 2004; Dimitrova et al. 2009). A sharp increase in the negative Bz component of the interplanetary magnetic field and the presence of storms sudden commencements are associated with increase in MI rates (Cornelissen et al. 2002; Dorman et al. 2008). Solar proton events (SPE) increase the risk of emergency admission for MI, and the effect of GS on the risk of MI is stronger if GS occurs in conjunction with SPE (Vencloviene et al. 2013). Some evidence has been reported on the negative effect of increased geomagnetic activity (GMA) on many cardiovascular parameters associated with the risk of adverse cardiovascular events. Blood pressure and heart rate changes are synchronized selectively with one or other aspect of physical environment, namely the seasons (at ~1.0 year cycle), Earth magnetism (at ~0.5 year) and/or solar flares (at ~0.42 year) (Cornelissen et al. 2010). Geomagnetic storms are associated with a decrease in heart rate variability (Watanabe et al. 2001; Cornelissen et al. 2002), an increase in blood pressure (Ghione et al. 1998; Dimitrova et al. 2004), and a decrease in melatonin level (Burch et al. 1999; Weydahl et al. 2001). Increased GMA led to an increase in tissue perfusion, variability of blood flow, and growth of the amplitude of neurogenic and myogenic oscillations (Zenchenko et al. 2010). During GS, significantly increased platelet aggregation and blood coagulation (Pikin et al. 1998), increased blood viscosity, and decelerated blood flow (Oraevskiĭ et al. 1998; Gurfinkel et al. 1995) were seen in patients with ischemic heart disease; these factors increased the risk of myocardial ischemia and cardiomyocyte damage during acute coronary syndrome. Therefore, it is plausible that environmental heliophysical conditions, such as increased GMA, SPE, solar flares, and powerful heliophysical disturbances, such as GS in conjunction with solar flares or occurring after SPE during hospital admission or the first few days of hospitalization may be among the risk factors affecting the survival of patients with acute coronary syndromes.

The principal aim of many scientific clinical studies in the field of cardiovascular disease is the evaluation of patient survival function on the basis of patient clinical data (Van de Werf et al. 2008; Yan et al. 2007). The aim of this study was the analysis of 2-year survival in patients admitted with acute coronary syndromes (MI or unstable angina), depending on the patients' clinical variables and the heliophysical environment during and after admission, separately for men and women, and younger and older patients.

Data and methods

The study was conducted in Kaunas city (geomagnetic latitude 52.38 N) during 2005. Information on hospital admissions due to acute coronary syndromes (ACS) was obtained from the Clinic of Cardiology, Hospital of Lithuanian University of Health Sciences (former Kaunas University of Medicine). We used data from 1,413 patients who were treated for ACS—MI (I21) with and without ST elevation or unstable angina (I20.0)—who survived after ACS for more than 4 days, and had survival data for over 2 years of follow-up. Myocardial infarction was diagnosed according to WHO guidelines: angina pain and equivalent, ischemic signs on ECG (Q wave, ST and T changes), and an increase in troponin I level (>0.5 μg/L). Coronary artery (CA) angiography was performed by applying the Judkins technique. Severe stenosis of 1, 2, or 3 vessels was defined as a narrowing of the coronary artery (>70 %). Patients with signs of acute MI and heart failure were ranked according to the Killip classification. Outcomes during 2 years were evaluated using the patients' records taken from the outpatients unit of Department of Cardiology, data of the standardized questionnaire (postal or via phone), and information from the Residents' Register Service under the Ministry of the Interior and the Civil Registry Office of Kaunas city. There were 115 (8.1 %) cardiovascular deaths during the follow-up period.

Data on solar flares, SPE, and GMA were used as environmental data. Daily Ap indexes were used as a measure of the level of GMA. The Ap index is defined as the geomagnetic disturbance index over 24-h intervals measured at the level of the surface of the Earth. According to NOAA (National Oceanic and Atmospheric Administration) classification, a GS occurs when $Ap \geq 30$. In the analysis, GMA was classified as quiet ($Ap<8$), unsettled ($8 \leq Ap<16$), active ($16 \leq Ap<30$), or stormy ($Ap \geq 30$). As a measure of the level of solar flares, north daily flare index was used as a continuous variable, or was considered as a binary value: no flare (north daily flare index=0); yes flare (north daily flare index>0). Ap and flare indexes were downloaded from the joint USA/European Solar and Heliospheric Observatory (web site ftp://ftp.ngdc.noaa.gov/STP/SOLAR_DATA/).

SPE were defined as integral 5-min averages of proton energies >10 MeV exceeding 10 pfu (http://www.swpc.noaa.gov/ftpdir/indices/SPE.txt); [1 pfu=1 proton/(cm^2-s-sr)]. Daily average of proton >10 MeV flux, which was downloaded from the National Geophysical Data Centers OMNIWeb data base (http://omniweb.gsfc.nasa.gov/) was used as a measure of the level of SPE. According to the specifications of our study, SPE was considered to have occurred if the daily average of proton MeV flux was >10.

We analyzed the effect of heliophysical variables (occurring 2 days before and 3 days after the hospital admission) on the hazard ratio of cardiovascular death for all patients, separately for men and women, and for patients younger or older than 70 years of age.

Statistical analysis

Survival times were calculated by counting the time (in days) from hospital admission to cardiovascular death or the last date the patient was known to be alive. Patient survival was evaluated using the Kaplan–Meyer curve. Survival curves were compared using the Log-rank test; the difference was considered statistically significant if $P<0.05$. To evaluate the risk of cardiovascular death, we used the multivariate proportional-hazards Cox model created by the backward stepwise method, using clinical variables. We calculated the total risk score (TRS) to assess the significance of the combination of informative clinical parameters for survival:

estimated adjusted hazard ratios of clinical variables in the final multivariate Cox regression model were transformed into integer values (risk scores): 1 point for HR <2; 2 for HR between 2 and 2.5; and 3 for HR ≥2.5; subsequently, TRS were calculated as a sum of these integer values. We assessed the effect of heliophysical variables by including them in the multivariate Cox model created by using clinical data. To evaluate the interaction between the heliophysical environment and the total cardiovascular risk, TRS, the most informative heliophysical indices, and their mathematical products were included in the Cox model as predictors.

An unfavorable environmental event such as GS can induce health effects not only on the day of the event but on subsequent days as well. We investigated the effect of heliophysical variables on the survival function on the day of admission (lag 0), and 1–2 days before (lag 1–2) and after [lag (−1)–(−2)] admission. To assess the impact of patients' characteristic and environmental variables during hospitalization on the risk of cardiovascular death, we presented the adjusted hazard ratio into the Cox model with 95 % confidence intervals. Statistical analysis was performed using SPSS 13 software.

Results

Among 1,413 patients with ACS, 928 (65.7 %) were men, and 488 (34.5 %) were older than 70 years of age. In total, 115 (8.1 %) patients died from cardiovascular causes. Myocardial infarction comprised almost 66.7 %, and unstable angina 33.3 % of total emergency admissions for heart attack; 29.8 % of the participants had a history of MI, and 81.5 % had a history arterial hypertension (Table 1). During hospitalization, 94.2 % of patients underwent coronary angiography. Table 1 lists significant univariate associations between individual clinical variables and the survival function.

Table 1 Patient baseline characteristics, medical history, presenting clinical features, and their univariate association with the survival function. *MI* Myocardial infarction, *ST* ST segment in ECG, *CA* coronary artery, *PTCA* percutaneous transluminal coronary angioplasty, *CABG* coronary artery bypass grafting

Clinical characteristic	All patients (n=1,413) N (%)	Death (n=115) N (%)	Log rank P
Men	928 (65.7)	67 (58.3)	0.077
Women	485 (34.3)	48 (41.7)	
Age >70	488 (34.5)	79 (68.7)	<0.001
Anamnesis:			
MI	421 (29.8)	44 (38.3)	0.058
Myocardial revascularization	218 (15.5)	10 (8.7)	0.033
Chronic obstructive pulmonary disease	72 (5.1)	10 (8.7)	0.067
Peripheral artery disease	31 (2.2)	7 (6.1)	0.001
Stroke	78 (5.5)	17 (14.8)	<0.001
Renal diseases	74 (5.23)	13 (11.3)	0.001
Arterial hypertension	1152 (81.5)	82 (71.3)	0.002
Diabetes	225 (15.9)	24 (20.9)	0.116
Diagnosis:			
MI with ST elevation	530 (37.5)	62 (53.9)	<0.001
MI without ST elevation	413 (29.2)	24 (20.9)	
Unstable angina	470 (33.3)	29 (25.2)	
Paroxysmal atrial fibrillation	82 (5.8)	19 (16.5)	<0.001
Paroxysmal ventricular tachycardia	33 (2.3)	6 (5.2)	0.030
Cardiac valvulopathy[a]	376 (26.6)	58 (50.4)	<0.001
Heart rate ≤50 beats per min	52 (3.8)	11 (9.6)	<0.001
(50–80]	951 (69.3)	54 (46.6)	
(80–90]	185 (13.5)	21 (18.4)	
>90	184 (13.4)	29 (25.4)	
Killip class III–IV	176 (12.5)	47 (40.9)	<0.001
Pulmonary hypertension	291 (20.6)	51 (44.3)	<0.001
CA stenosis >70 %:			
One–two	726 (51.4)	42 (36.5)	<0.001
Three	453 (32.1)	65 (56.5)	
PTCA during hospitalization	456 (32.3)	22 (19.1)	0.003
CABG during hospitalization	335 (23.7)	26 (22.6)	

[a] Tricuspid and mitral regurgitation

Table 2 Multivariate Cox model for the assessment of the hazard for cardiovascular death (adjusted HR, 95 % CI of HR). *HR* Hazard ratio, *MI* myocardial infarction, *CA* coronary artery, *PTCA* percutaneous transluminal coronary angioplasty

Variable	HR	95 % CI	*P*	Risk score
Age	1.06	1.04–1.08	<0.000	1[a]
Stroke in anamnesis	2.32	1.37–3.39	0.002	2
Arterial hypertension in anamnesis	0.41	0.27–0.63	<0.000	−2
Peripheral artery disease in anamnesis	2.22	1.01–4.87	0.047	2
MI with ST elevation in diagnosis	1.49	1.00–2.22	0.048	1
Paroxysmal ventricular tachycardia	2.20	0.94–5.12	0.069	2
Killip class III–IV	2.23	1.46–3.41	<0.001	2
Heart rate[b] ≤50 beats per min	2.65	1.37–5.16	0.004	3
(80–90]	1.48	0.88–2.47	0.139	1
>90	1.62	1.01–2.61	0.046	1
Pulmonary hypertension	1.89	1.27–2.81	0.002	1
Three CA stenosis >70 %	1.63	1.09–2.45	0.018	1
PTCA during hospitalization (CA stenosis >70 %)	0.63	0.38–1.05	0.077	−1

[a] Beginning with 60 years of age, 1 point is added every 5 years

[b] Reference category (50–80]

A higher mortality was associated most closely with patient age, a history of stroke, MI with ST elevation in the diagnosis, paroxysmal atrial fibrillation, heart rate, heart failure during admission, cardiac valvulopathy, and pulmonary hypertension. By applying the informative variables, a multivariate Cox model for the assessment of the complex hazard for cardiovascular death was created (Table 2).

Considering the influence of other informative factors, it can be stated that the HR of death in patients with prior stroke, prior peripheral artery disease, paroxysmal ventricular tachycardia,

Table 3 Adjusted HR for heliophysical variables. *GMA* Geomagnetic activity, *GS* geomagnetic storm, *SPE* solar particle event, *SF* solar flare

Variable	Lag	HR[a] (95 % CI) All patients	*P*	HR[a] (95 % CI) Women	*P*	HR[a] (95 % CI) Age >70	*P*
GMA: quiet	1	1		1		1	
Unsettled-active		1.31 (0.88–1.97)	0.188	1.40 (0.73–2.66)	0.314	1.35 (0.84–2.22)	0.239
Stormy		1.76 (0.95–3.26)	0.075	2.09 (0.87–5.00)	0.100	2.54 (1.26–5.15)	0.010
GMA: quiet-unsettled	−2	1		1		1	
Active		1.50 (0.95–2.38)	0.084	1.59 (0.75–3.38)	0.230	1.93 (1.11–3.35)	0.019
Stormy		1.71 (1.00–2.93)	0.050	2.74 (1.27–5.92)	0.010	2.48 (1.34–4.59)	0.004
GMA: stormy	−1	1.17 (0.68–2.01)	0.562	2.30 (1.07–4.94)	0.034	1.33 (0.69–2.56)	0.399
	−2	1.56 (0.92–2.64)	0.097	2.44 (1.16–5.13)	0.017	2.13 (1.18–3.85)	0.012
	−3	1.24 (0.73–2.13)	0.427	2.13 (1.01–4.50)	0.047	1.34 (0.71–2.52)	0.370
GMA: active-stormy	−2	1.58 (1.07–2.32)	0.021	2.01 (1.09–3.69)	0.024	2.13 (1.35–3.38)	0.001
	−2 & (−3)	1.74 (1.12–2.70)	0.014	2.66 (1.40–5.03)	0.003	2.51 (1.52–4.15)	0.001
GS 2 days after SPE	−1	2.16 (0.97–4.82)	0.067	3.91 (1.31–11.7)	0.015	2.45 (0.96–6.26)	0.060
GS with SF	1	1.73 (0.82–3.64)	0.148	2.94 (0.97–8.89)	0.057	3.08 (1.32–7.20)	0.009
SPE	2	1.67 (0.92–3.01)	0.091	2.50 (1.11–5.63)	0.028	1.60 (0.81–3.20)	0.179
	0	1.25 (0.69–2.25)	0.458	2.33 (1.05–5.19)	0.039	1.28 (0.64–2.56)	0.481
	−1	1.11 (0.59–2.09)	0.748	2.39 (1.09–5.28)	0.032	1.03 (0.49–2.19)	0.937
SF>0	2	1.37 (0.89–2.10)	0.153	1.87 (1.00–3.49)	0.051	1.71 (1.03–2.83)	0.037
	1	1.54 (1.01–2.35)	0.045	2.41 (1.32–4.39)	0.004	2.11 (1.29–3.44)	0.003
SF index=0	1	1		1		1	
0<SF index≤1		1.46 (0.85–2.50)	0.170	1.96 (0.89–4.35)	0.101	2.18 (1.15–4.14)	0.017
SF index>1		1.64 (0.93–2.90)	0.088	2.99 (1.40–6.38)	0.005	2.04 (1.06–3.91)	0.032
SF index continuous	1	1.03 (1.00–1.05)	0.062	1.05 (1.02–1.09)	0.001	1.04 (1.00–1.07)	0.027

[a] Adjusting for age, prior stroke, prior peripheral artery disease, prior arterial hypertension, heart rate, paroxysmal ventricular tachycardia, Killip class, myocardial infarction with ST elevation in diagnosis, pulmonary hypertension, three coronary artery stenosis, and percutaneous transluminal coronary angioplasty during hospitalization

and Killip class III–IV was over 2 (risk score 2). If patients with impaired coronary arteries underwent PTCA during hospitalization, the hazard ratio dropped by about 1.5 times [risk score (−1)]. Low heart rate (≤50 bpm) increased the HR by about 2.65 times (risk score 3), compared to 51–80 bpm; pulmonary hypertension increased the HR by over 1.8 times, and CA stenosis of three vessels over 70 %—by more than 1.6 times, compared to HR in other patients. The TRS (the sum of risk scores in Table 3) ranged from −3 to 13, the mean value was 1.6, the standard error was 0.08, and the percentiles were following: 75th—3, and 90th—6.

Effect of heliophysical conditions during and after admission on survival of patients with ACS

During the period of the study (365 days), minor ($30 \leq Ap < 50$) storms were observed on 20 (5.5 %) days, and major GS ($Ap \geq 50$) on 15 (4.1 %) days. On 71 (19.5 %) days, the north solar flare (SF) index was over 0. The SPE was observed on 28 (7.7 %) days. On 15 (20.8 %) days, SPE occurred or continued 1 day after the SF, whereas on 13 (4.4 %) days, this event occurred at other times. Geomagnetic storms occurred on 15 (21.3 %) days in conjunction with SF; regarding days without SF, GS occurred on 20 (6.8 %) days. On 13 (46.4 %) days, GS occurred 1 day after SPE; on 22 (6.5 %) days, GS occurred at other times. In total, 44.2 % of patients were admitted during days of quiet geomagnetic field (GMF), and 45.6 % of patients during days of unsettled-active GMF. A total of 143 (10.1 %) patients were admitted during stormy days ($Ap \geq 30$); 278 (19.7 %) patients were hospitalized during days with north SF index>0, and 125 (8.8 %) patients during days with SPE.

Survival was worse for patients for whom GS occurred on day 1–2 after hospital admission, or when SF occurred 1 day before admission (Fig. 1); survival functions did not differ significantly for patients for whom GS occurred 1 day before hospitalization and for whom it did not occur. After adjustment for clinical variables, the effect of heliophysical events (elevated GMA, SF, or SPE) was observed on the day before and on the 2nd day after hospital admission (Table 3). Active-stormy GMA level during the 2nd day after admission increased the HR compared to the quiet-unsettled level registered on the same day. For all patients, the active-stormy GMA on the 2nd day after admission increased HR by 1.58 times (HR=1.58, 95 % CI 1.07–2.32). For patients admitted 1 day after SF, HR increased by over 1.5 times (HR=1.54, 95 % CI 1.01–2.35).

No significant association was established between heliophysical variables and survival for men. For women, the strongest association was seen between GS, SPE, and SF occurring 1–3 days before–after admission. GS occurring on the 1st–3rd day after hospital admission increased the HR by over 2 times; GS 2 days after SPE, occurring 1 day after admission increased the HR by 3.91 times (HR=3.91, 95 % CI 1.31–11.7). The active-stormy GMA on days 2–3 after the admission increased the HR over 2.5 times (HR=2.66, 95 % CI 1.40–5.03). SPE increased HR for women by over 2 (lag 2; 0; −1) times. After days with SF index>0, the HR increased by 2.41 times (HR=2.41, 95 % CI 1.32–4.39); in women, a dose–response relationship was observed between the SF index level (0; 0.01–1; >1) 1 day prior to admission and HR (1; 1.96 (0.89–4.35); 2.99 (1.40–6.38)).

In patients aged ≤70 years, heliophysical variables did not affect HR for cardiovascular death. In patients aged over 70 years, GS occurring 1 day before admission increased the HR by 2.5 times compared to quiet days. The active GMA level on the 2nd day after admission significantly increased the HR by over 1.9 times, compared to the quiet-unsettled GMA level. GS in conjunction with SF that occurred the day before admission increased the HR by over 3 times (HR=3.08, 95 % CI 1.32–7.20). SF occurring 1–2 days before admission increased the HR by over 1.7 times.

The inclusion of heliophysical indices in the multivariate Cox model did not induce any significant changes in the coefficients at clinical markers, and thus the addition of the heliophysical variable to the complex risk model did not change the risk scores. Since SF index>0 on the day before hospital admission and GMA level on the 2nd day after admission

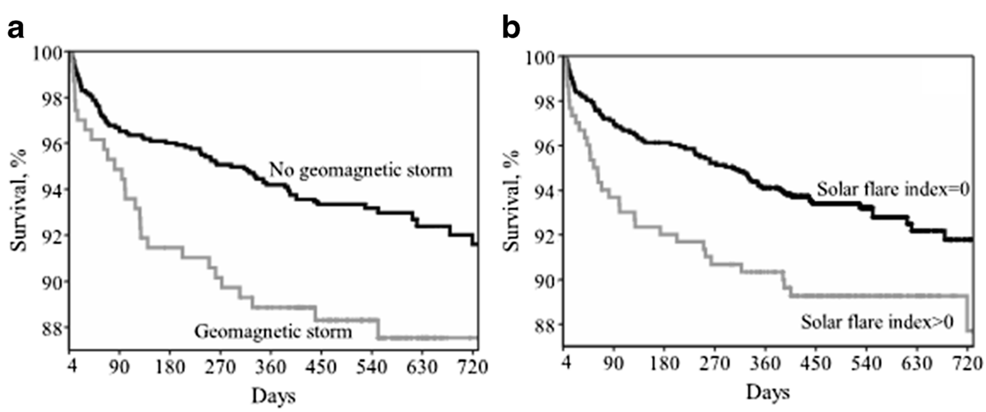

Fig. 1 Kaplan–Meyer curve for patients after acute coronary syndromes (ACS) depending on **a** the occurrence of geomagnetic storms (GS) during the first 2 days after admission ($P=0.021$), or **b** the solar flare (SF) index 1 day before admission ($P=0.045$)

Table 4 Multivariate Cox models created using total risk score (TRS), the heliophysical variable, and its products

Heliophysical variable and its product with TRS				Total risk score			χ^2 statistic
All patients	Beta (SE)	HR	95 % CI	Beta (SE)	HR	95 % CI	
Ap≥16 lag (−2)	0.48 (0.19)	1.61	1.10–2.36	0.40 (0.03)	1.49	1.41–1.58	221
(Ap≥16 lag (−2))*TRS	0.09 (0.03)	1.09	1.03–1.16	0.37 (0.03)	1.44	1.36–1.54	243
SF index>0 lag 1	0.47 (0.21)	1.60	1.07–2.42	0.40 (0.03)	1.49	1.41–158	220
(SF index>0 lag 1)*TRS	0.09 (0.03)	1.10	1.03–1.17	0.38 (0.03)	1.46	1.37–1.55	237
Women							
Ap≥30 lag (−2)	0.90 (0.36)	2.46	1.22–4.95	0.40 (0.05)	1.49	1.35–1.63	87
(Ap≥30 lag (−2))*TRS	0.14 (0.05)	1.15	1.04–1.27	0.37 (0.05)	1.45	1.31–1.60	108
Ap≥16 lag (−2)	0.79 (0.30)	2.20	1.23–3.94	0.41 (0.05)	1.51	1.37–1.66	84
(Ap≥16 lag (−2))*TRS	0.14 (0.05)	1.15	1.06–1.26	0.35 (0.05)	1.42	1.28–1.58	108
SF index>0 lag 1	0.80 (0.30)	2.23	1.24–4.02	0.40 (0.05)	1.49	1.36–1.64	86
SPE lag (−1)	0.97 (0.39)	2.64	1.22–5.71	0.41 (0.05)	1.51	1.37–1.67	83
[SPE lag (−1)]*TRS	0.20 (0.06)	1.22	1.08–1.39	0.39 (0.05)	1.48	1.34–1.64	98
Age >70 years							
Ap≥30 lag 1	0.75 (0.32)	2.11	1.13–3.93	0.38 (0.04)	1.47	1.35–1.60	87
Ap≥16 lag (−2)	0.71 (0.23)	2.04	1.30–3.20	0.38 (0.04)	1.46	1.34–1.58	91
SF index>0 lag 1	0.76 (0.24)	2.13	1.32–3.44	0.39 (0.04)	1.47	1.35–1.60	90

(additional, SPE lag 1 for women) were most informative for survival, we used these heliophysial variables and TRS for creating the prognostic models (Table 4). The prognostic models also included the products of TRS and heliophysical variables. According to the models, the presence of the active-stormy GMA level on the 2nd day after hospital admission or SF index>0 on the day before admission increased the HR by 1.6 times—as much as an increase in the patients' TRS by 1 point. The inclusion of the product of TRS and these heliophysical variables into the model instead of a single heliophysical variable significantly increased the value of χ^2 of the Cox model. Thus, it can be concluded that if the higher TRS of the patients is, then stronger the effect of (Ap≥16 lag (−2)) (Fig. 2) and (SF index>0 lag 1). For women, the presence of the active-stormy GMA level on the 2nd day after hospitalization, or SF index>0 on the day before hospital admission, or SPE on the 2nd day of hospitalization increased the HR by as much as did the increase in patients' TRS by 1 point.

Discussion

The significant risk factors identified in our study corresponded to those reported most commonly in studies by other authors. The significance of clinical factors in the survival of patients with ACS has been analyzed in a number of scientific studies, while evaluation of the effect of environmental factors on the survival function are significantly less common. The results of our study showed that further survival of ACS patients is affected not only by such patients' clinical conditions, but also by the heliophysical environment during hospital admission and on the first days of hospitalization.

Our results showed that the heliophysical conditions before and after hospital admission affect the HR of lethal outcome, adjusting for clinical variables. GS occurring 1 day before admission adversely affected survival; this effect was stronger for older (age >70 years) patients and in cases when GS occurred in conjunction with SF or SPE. Increased GMA during

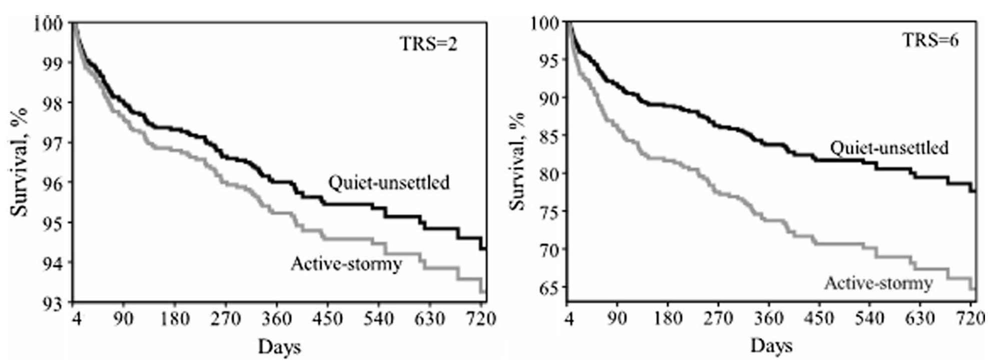

Fig. 2 Survival function for low [total risk score (TRS)=2)] and high (TRS=6) cardiovascular risk at the quiet-unsettled and active-stormy geomagnetic activity (GMA) level during the 2nd day after hospitalization

the first days of hospitalization also adversely affected further survival. Active-stormy GMA level on the 2nd day after hospitalization also worsened further survival. Women were particularly sensitive to the increased GMA on days 1–3 of hospitalization. The effect of heliophysical variables was stronger for patients with higher total risk score. The influence of elevated GMA on further survival might be explained by its impact on the cardiovascular system, resulting in an increased incidence of heart failure, rhythm disorder, and other pathologies.

Among the mechanisms whereby geomagnetic activity influences human health, the one mentioned most frequently is that involving melatonin and the Schumann resonance (Cherry 2002; Palmer et al. 2006). In a number of studies, the effect of GMA was associated with a drop in melatonin levels: GMA significantly reduced melatonin levels in a dose–response manner (Burch et al. 1999; Weydahl et al. 2001). Also, GS sharply disturbs the rhythm of the external synchronizer of biological rhythms (Oraevskiĭ et al. 1998; Breus et al. 1998), and is therefore accompanied by an adaptation stress reaction of the organism (Breus et al. 2012). Melatonin plays a central role in the regulation of diurnal variation of many human systems. Many cardiovascular variables associated with prognosis after ACS—such as heart rate, blood pressure, and platelet and endothelial function—exhibit diurnal variation; a circadian clock also exists in cardiomyocytes (Durgan et al. 2005; Dominguez-Rodriguez et al. 2010). Specific links between melatonin and cardiovascular disease have been indicated (Dominguez-Rodriguez et al. 2010); human melatonin production decreases in the presence of coronary artery disease (Yaprak et al. 2003) and during acute MI (Dominguez-Rodriguez et al. 2002). Melatonin acts as a potent antioxidant agent, reducing myocardial damage induced by ischemia reperfusion (Dominguez-Rodriguez et al. 2007). It has been found that greater reductions in melatonin production are observed in patients with a higher risk of MI or sudden death (Tengattini et al. 2008). Results obtained by other researchers suggest that the GS (1) disturbs the circadian clock of the human organism; (2) increases platelet aggregation and blood coagulation; and (3) decreases melatonin level, which increases myocardial damage induced by ischemia. These factors (1–3) in the pre-infarction condition or 1–2 days after ACS possibly increased myocardial damage and impaired its regeneration, which might have increased the risk of heart failure and arrhythmias during the later period, and might have adversely affected further survival. The effect of GS might have been stronger in higher-risk patients because they had reduced melatonin production.

Several authors have indicated the impact of GS on cardiovascular systems, the impairment of which possibly increased the risk of heart failure and arrhythmia, which possibly worsened survival. Chibisov et al. (1995) indicated that, during the main phase of severe GS, destruction and degradation of cardiomyocytes were observed in rabbit. On the 1st day of GS, pathological changes of capillary flow were detected in 71 % of patients with acute MI; similar changes were detected in over 60 % of patients with angina pectoris (Gurfinkel et al. 1995). The reaction of astronauts to GS involves a mobilization and activation of all centers of the sympathetic link, and—as a result—a significant increase and stabilization of the heart rate, and a decrease in the heart rhythm variability and the power of respiratory waves (Oraevskiĭ et al. 1998). During magnetic storms, patients with impaired functions of the cardiovascular system demonstrate a reaction of certain regions of the peripheral blood circulation system—in particular, a deterioration in capillary blood flow (Gurfinkel et al. 1995; Oraevskiĭ et al. 1998; Zenchenko et al. 2010).

It is noteworthy that, according to our study, not only GS, but also active GMA level on the 2nd day after hospitalization increased HR for cardiovascular death, compare to quiet-unsettled level. The majority of the aforementioned studies most frequently indicate only the health risk of GS alone.

As yet, no studies have used heliophysical variables as predictors in survival models for patients with ACS. However, many authors have stated that geomagnetic and other solar storms increase the risk of cardiovascular death. A higher incidence of death from MI was observed during periods of high GMA (Stoupel et al. 2002); as well as during Forbush decreases and severe GS (Mendoza and Diaz-Sandoval 2004). During high GMA, more sudden cardiac death with agony time of >1–24 h occurred, when the element of arrhythmic death is mostly excluded (Stoupel et al. 2002).

According to the findings of our study, SF occurring 1–2 days before admission worsened survival, and this effect was more evident in older patients (>70 years), high-risk patients, and women. Solar proton events occurring 2 days before and 1 day after hospital admission increased the HR for women by over 2 times; this effect was stronger in higher-risk patients. According to the literature, monthly proton >90 MeV energy flux correlated positively with monthly sudden death (Stoupel et al. 2002) and sudden cardiac death rates (Stoupel et al. 2000).

The effect on subsequent prognosis of heliophysical conditions during the occurrence and the treatment period of MI has been indicated in studies by other authors. It is evident that MI location and the culprit artery in MI were associated with GMA level during the onset of MI (Stoupel et al. 1988, 2008). Increased GMA was related more to anterior wall MI (Stoupel et al. 1988); anterior wall MI is more dangerous for further prognosis than is inferior wall MI. The complications of MI—cardiogenic shock—were associated with higher cosmic rays activity during days of PTCA (Stoupel et al. 2009).

The fact that SF and SPE occurring 1–2 days before admission worsen survival might be explained by the fact that flares produce high energy protons and ions within SPE and short wavelength radiation, ionizing the high atmosphere; SFs are followed by coronal mass ejection (CME), and GS are mostly the result of the arrival of CME on the Earth. These heliophysical conditions may affect human health.

According to our results, heliophysical events have a stronger effect on older patients. The fact that the effect of GMA is stronger in older patients has also been noted by other authors. Mendoza and Diaz-Sandoval (2004) found that MI rates on days of Forbush decrease and severe storms were higher for individuals aged ≥65 years. Human melatonin production decreases with age (Sack et al. 1986), which may explain why the effect of GS is stronger in the elderly population.

According to our results, heliophysical events were stronger in women than in men. Some authors have indicated a stronger effect of GMA in men: Mendoza and Diaz-Sandoval (2004) stated that MI rates on days of Forbush decrease and severe storms were higher for men. The analysis of monthly data showed that, in women, the occurrence of MI was related much more strongly to heliophysical parameters (Stoupel et al. 2005), but the correlation between the monthly number of cases of unstable angina and Ap indices was stronger for men (Stoupel et al. 2010). By analyzing the influence of daily changes in GMA on systolic and diastolic blood pressure, Dimitrova and Stoilova (2003) established that females are more sensitive to GMA disturbances compared to males, which corresponds to our results. Our findings indicating that women are more sensitive to heliophysical effects may be explained by the fact that they were older and that we excluded patients who died on the first 4 days and focused on long-term survival. Increased GMA affects the sympathetic nervous system, and the sympathetic nervous system is predominant in women (Raps et al. 1992).

On the basis of the results obtained, we can conclude that in patients with ACS:

(1) Geomagnetic storms on the day before hospital admission and on days 1–3 after hospitalization impair further survival;
(2) Solar flares and solar proton events occurring 1–2 days before admission further worsen survival;
(3) Heliophysical effects were stronger for the survival of elderly patients, high risk patients, and women.

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