World Journal of Cardiology

Online Submissions: http://www.wjgnet.com/esps/
wjc@wjgnet.com
doi:10.4330/wjc.v5.i3.60

World J Cardiol 2013 March 26; 5(3): 60-64
ISSN 1949-8462 (online)

BRIEF ARTICLE

Electrocardiographic features of patients with earthquake related posttraumatic stress disorder

Erkan İlhan, Abdullah Kaplan, Tolga Sinan Güvenç, Murat Biteker, Evindar Karabulut, Serhan Işıklı

Erkan İlhan, Abdullah Kaplan, Department of Cardiology, Van Erciş State Hospital, 65400 Van, Turkey
Tolga Sinan Güvenç, Department of Cardiology, Kafkas University School of Medicine, 36000 Kars, Turkey
Murat Biteker, Department of Cardiology, Haydarpaşa Numune Education and Research Hospital, 64668 Istanbul, Turkey
Evindar Karabulut, Serhan Işıklı, Department of Psychiatry, Van Erciş State Hospital, 65400 Van, Turkey
Author contributions: Ilhan E, Kaplan A and Işıklı S designed and performed the research; Karabulut E, Güvenç TS and Biteker M supervised the research design and manuscript preparation; all authors approved the manuscript.
Correspondence to: Dr. Erkan Ilhan, Department of Cardiology, Van Ercis State Hospital, 65400 Van, Turkey. erkan.ilhan@yahoo.com.tr
Telephone: +90-505-4365384 Fax: +90-216-4183317
Received: October 11, 2012 Revised: October 25, 2012
Accepted: January 17, 2013
Published online: March 26, 2013

Abstract

AIM: To analyze electrocardiographic features of patients diagnosed with posttraumatic stress disorder (PTSD) after the Van-Erciş earthquake, with a shock measuring 7.2 on the Richter scale that took place in Turkey in October 2011.

METHODS: Surface electrocardiograms of 12 patients with PTSD admitted to Van Erciş State Hospital (Van, Turkey) from February 2012 to May 2012 were examined. Psychiatric interviews of the sex and age matched control subjects, who had experienced the earthquake, confirmed the absence of any known diagnosable psychiatric conditions in the control group.

RESULTS: A wide range of electrocardiogram (ECG) parameters, such as P-wave dispersion, QT dispersion, QT interval, Tpeak to Tend interval, intrinsicoid deflection durations and other traditional parameters were similar in both groups. There was no one with an abnormal P wave axis, short or long PR interval, long or short QT interval, negative T wave in lateral leads, abnormal T wave axis, abnormal left or right intrinsicoid deflection duration, low voltage, left bundle branch block, right bundle branch block, left posterior hemiblock, left or right axis deviation, left ventricular hypertrophy, right or left atrial enlargement and pathological q(Q) wave in either group.

CONCLUSION: The study showed no direct effect of earthquake related PTSD on surface ECG in young patients. So, we propose that PTSD has no direct effect on surface ECG but may cause electrocardiographic changes indirectly by triggering atherosclerosis and/or contributing to the ongoing atherosclerotic process.

Key words: Earthquake; Posttraumatic stress disorder; Cardiovascular disease; Electrocardiogram

İlhan E, Kaplan A, Güvenç TS, Biteker M, Karabulut E, Işıklı S. Electrocardiographic features of patients with earthquake related posttraumatic stress disorder. *World J Cardiol* 2013; 5(3): 60-64 Available from: URL: http://www.wjgnet.com/1949-8462/full/v5/i3/60.htm DOI: http://dx.doi.org/10.4330/wjc.v5.i3.60

INTRODUCTION

Posttraumatic stress disorder (PTSD) is a psychiatric disease that is characterized by recurrent symptoms of stress and anxiety that develop after exposure to an extreme psychological trauma, such as earthquake, war or accidents[1]. Although acute cardiovascular events, such as sudden death, myocardial infarction and Takotsubo cardiomyopathy, are frequently reported, especially during the early phases of these mental stressors[2-5], cardiovascular effects of PTSD are not well known. While there are a few studies examining electrocardiographic features of veterans with PTSD[6,7], we did not encounter any study examining electrocardiographic features of patients with PTSD re-

lated to an earthquake. In this study, we aimed to analyze electrocardiographic features of patients diagnosed with PTSD after the Van-Erciş earthquake, with a shock measuring 7.2 on the Richter scale that took place in Turkey in October 2011.

MATERIALS AND METHODS

Patients

Twelve patients with PTSD admitted to Van Erciş State Hospital (Van, Turkey) from February 2012 to May 2012 were included in the study. Anyone in the study population with a rhythm other than sinus rhythm, a history of cardiovascular or other chronic medical disorders, or using beta-blockers, tricyclic antidepressants or other medications that affect autonomic function and electrocardiogram (ECG) patterns was excluded from the study. Transthoracic echocardiography was performed in all subjects of the study and subjects with any chamber enlargement, systolic or diastolic dysfunction, valvular heart disease, pulmonary hypertension or any other detectable heart disease were excluded from the study. Psychiatric interviews of the sex and age matched control subjects who had experienced the earthquake confirmed the absence of any known diagnosable psychiatric conditions.

Analysis of electrocardiograms and definitions

Recording of a 12-lead ECG was performed after 10 min of supine rest at standard sensitivity (10 mm = 1 mV) and a paper speed of 50 mm/s. ECG was obtained at the same time of the day (between 09:00 AM and 11:00 AM) for all participants and in a quiet room to minimize external noise. ECGs were scanned to digital media in 300 dpi. Then they were transferred to high-resolution computer screens and evaluated by two of the investigators who were blind to clinical and patient information. Three consecutive beats were used for analysis.

PR interval, R wave amplitude and QRS duration were calculated in lead V5. A PR interval longer than 200 ms was defined as long PR and shorter than 120 ms was defined as short PR. A QRS duration longer than 120 ms was defined as long QRS. The presence and site of pathological Q waves were recorded. A Q wave in any leads longer than 40 ms was defined as pathological q(Q) wave. Abnormal P wave axis was defined as P axis < 0 degrees or > 75 degrees[8]. Intrinsicoid deflection is the duration of the earliest appearing Q or R wave to the peak of the R wave. It was calculated in V2 for the right ventricle and V5 for the left ventricle. Abnormal intrinsicoid deflection was defined > 35 ms and > 45 ms for right and left ventricle respectively.

P wave duration was defined as the time measured from the onset to the end of the P wave deflection. The onset of the P wave was considered as the junction between the isoelectric line and first visible upward or downward slope of the trace. The return of the trace to the isoelectric line was considered to be the end of the P wave. P wave dispersion (Pd) was defined as the difference between maximum and minimum P wave durations (Pmax and Pmin, respectively) occurring in any of the 12 leads[9]. QT interval was defined as the interval from the beginning of the QRS complex to the end of the T wave. The end of the T wave was defined as intersection of the terminal limb of the T wave with the isoelectric baseline[10]. The longest and shortest QT intervals across 12 leads were defined as the maximum QT (QTmax) and the minimum QT (QTmin) intervals, respectively. They were corrected according to heart rate by using the Bazett formula and were defined as corrected QTmax (cQTmax) and corrected QTmin (cQTmin), respectively. cQT dispersion (cQTd) was defined as the difference between cQTmax and cQTmin. For the Tpeak to Tend interval (TpTe) measurement, time interval between the peak of T wave, *i.e.*, the time point in which T wave had highest amplitude and end of the T wave which also was defined as the crossing point of the T wave and isoelectric line, was noted as a function of time. TpTe was also corrected according to heart rate and referred to as cTpTe. Abnormal ECG recordings with ambiguous T-waves, distorted, flat or with high noise levels by any means were excluded.

Left atrial enlargement was defined as a P wave with a broad and negative (> 1 mm) terminal part in lead V1 and/or P wave duration ⩾ 120 ms in leads I or II. Right atrial enlargement was defined as P wave amplitude > 0.2 mV in leads II and aVF and/or > 0.1 mV in lead V1 and V2. Supraventricular or ventricular ectopic beats were defined as one or more supraventricular or ventricular extrasystoles in 10 s. A QRS duration ⩾ 120 ms was defined as prolonged QRS. Ventricular conduction abnormalities were classified as right bundle branch block (RBBB), left bundle branch block (LBBB), left anterior hemiblock (LAH) or left posterior hemiblock (LPHB). Deviation of the QRS or T wave axis to the left (-30 <) or to the right (> 90) was defined as an abnormal QRS axis. The QT interval was corrected using the Bazett formula ($QTc = QT/\sqrt{RR}$). Left ventricular hypertrophy was defined by the Sokolow-Lyon criterion (S in V1 + R in V5 or V6 ⩾ 3.5 mV). Low voltage was diagnosed when the amplitude of the QRS complex in each of the three limb leads (I, II, III) was < 5 mm. Repolarization abnormalities included ST segment elevation, ST segment depression and T-wave inversion.

Statistical analysis

Statistical analysis was performed with SPSS 16.0 (IBM Inc., New Orchard Road, Armonk, NY, United States). Continuous variables were given as mean ± SD and categorical variables were given as percentages. Due to small sample size, comparisons between groups were performed with nonparametric tests. For continuous parameters, Mann-Whitney *U* test was used, while χ^2 or Fisher's exact test was used as appropriate for categorical variables. All statistical comparisons were made within 95%CI. A *P* value of less than 0.05 was accepted as statistically significant.

RESULTS

Except for diastolic blood pressure, demographic fea-

Table 1 Demographic and clinical features of the groups (mean ± SD)

	PTSD (n = 12)	Controls (n = 12)	P value
Age (yr)	28.4 ± 7.5	28.5 ± 7.2	NS
Gender (%female)	91.6	83.30	NS
Body mass index (kg/m^2)	23.8 ± 4.3	24.3 ± 3.1	NS
Creatinine Clearance (mL/min)	99.4 ± 26	99.8 ± 16	NS
Current smoker (%)	16.6	16.6	NS
Family history of coronary artery disease (%)	0	8.3	NS
Systolic blood pressure (mmHg)	103.5 ± 8.8	110.4 ± 11.4	NS
Diastolic blood pressure (mmHg)	64.5 ± 6	71.9 ± 7	0.03
Heart rate (beat/min)	78.7 ± 18.6	78.8 ± 13.5	NS

PTSD: Posttraumatic stress disorder; NS: Not significant.

tures of the groups were comparable (Table 1). There was no one with a history of hypertension, hyperlipidemia or diabetes mellitus in either group. Transthoracic echocardiography was available in all patients and control subjects. Basic echocardiographic measurements of the groups were also similar (Table 2).

Electrocardiographic features of the groups are presented in Table 3. There was no difference between ECG parameters of the groups. There was no one with abnormal P wave axis, short or long PR interval, long or short QT interval, negative T wave in lateral leads, abnormal T wave axis, abnormal left or right intrinsicoid deflection duration, low voltage, left bundle branch block, right bundle branch block, left posterior hemiblock, left or right axis deviation, left ventricular hypertrophy, right or left atrial enlargement and pathological q(Q) wave in either group.

DISCUSSION

Unanticipated catastrophic events resulting in acute psychological stress have been extensively reported as a cause of cardiovascular events and mortality[1]. Kim *et al*[4] reported the relationship between severe emotional stress and vasospastic angina in patients without organic coronary heart disease. Meisel *et al*[11] documented an increase in the incidence of acute MI and sudden death in the Tel Aviv area during the initial phases of the Gulf War in 1991. An increase in hospital admissions for acute MI in England on the day of the 1998 World Cup match against Argentina has also been reported[12]. There is also extensive literature demonstrating increased cardiovascular events and mortality after earthquakes which are good examples of unique unpredictable disasters resulting in severe mental stress. Tsuchida *et al*[13] demonstrated that severe earthquakes result in an increased incidence of acute coronary syndromes and cerebral hemorrhage. Increased cerebrovascular events were also reported after the Hanshin-Awaji earthquake[14,15]. Although the precise pathophysiological mechanism of the cardiovascular consequences of acute mental stressors are not well known, some physiological responses have been proposed to be potential triggers of myocardial supply-demand and by atherosclerotic plaque disruption, thrombus formation and eventually ischemia-arrhythmia[16,17]. Increase in heart

Table 2 Transthoracic echocardiographic features of the groups (mean ± SD)

	PTSD (n = 12)	Controls (n = 12)	P value
Left ventricular end diastolic diameter (mm)	42.8 ± 2.6	43.1 ± 3.4	NS
Left ventricular end systolic diameter (mm)	23.3 ± 1.7	24.9 ± 3.8	NS
Left ventricular ejection fraction (%)	63.3 ± 2.3	63.7 ± 1.8	NS
Interventricular septum thickness (mm)	8 ± 0.6	8.3 ± 0.7	NS
Left ventricular posterior wall thickness (mm)	7.8 ± 0.4	8.2 ± 0.6	NS
Left atrial anteroposterior diameter (mm)	31.5 ± 4.8	29.2 ± 4.1	NS

PTSD: Posttraumatic stress disorder; NS: Not significant.

Table 3 Electrocardiographic features of the groups (mean ± SD)

	PTSD (n = 12)	Control (n = 12)	P value
P wave parameters			
Pmax (ms)	96 ± 15	96.6 ± 11.5	NS
Pmin (ms)	67.7 ± 14.4	72.5 ± 8.6	NS
Pd (ms)	27.7 ± 11.3	24.2 ± 11.6	NS
QT parameters			
QT V5 (ms)	361 ± 41.3	350 ± 37.7	NS
cQT V5 (ms)	403.4 ± 35.1	401.2 ± 20.2	NS
Qtmax (ms)	373.3 ± 44.6	358.3 ± 32.4	NS
Qtmin (ms)	340 ± 36.2	325.8 ± 36.3	NS
QTd (ms)	33.3 ± 26.1	32.5 ± 17.6	NS
cQTmax (ms)	415.5 ± 27.5	411.5 ± 23.2	NS
cQTmin (ms)	380 ± 37.5	373.8 ± 30.3	NS
cQTd (ms)	35.5 ± 26.8	37.7 ± 19.5	NS
T wave parameters			
TpTe V5 (ms)	80.4 ± 17.4	83.3 ± 12.3	NS
cTpTe V5 (ms)	89.3 ± 15.2	95.4 ± 10.9	NS
Presence of negative T wave (anterior leads) (%)	66.6	58.3	NS
Presence of negative T wave (inferior leads) (%)	16.6	0	NS
Presence of U wave (%)	8.3	8.3	NS
PR interval (ms)	145.83 ± 23.53	143.33 ± 16.70	NS
QRS duration (ms)	73.3 ± 9.6	82.5 ± 11.4	NS
Right ventricle intrinsicoid deflection (ms)	26.6 ± 6.8	28.9 ± 4.9	NS
Left ventricle intrinsicoid deflection (ms)	34.5 ± 4	34.4 ± 5.1	NS
R wave amplitude	0.9 ± 0.3	1.2 ± 0.5	NS
Infra HIS conduction abnormalities			
Left anterior hemiblock (%)	0	8.3	NS
Left axis deviation (%)	0	8.3	NS
ST segment elevation (%)	0	16.6	NS

PTSD: Posttraumatic stress disorder; NS: Not significant; Pmax: Maximum P wave duration; Pmin: Minimum P wave duration; Pd: P wave dispersion; cQT: Corrected QT interval; QTd: QT dispersion; cQTd: Corrected QT dispersion; QTmax: Maximum QT interval; cQTmax: Corrected maximum QT interval; QTmin: Minimum QT interval; cQTmin: Corrected minimum QT interval; TpTe: Tpeak to Tend interval; cTpTe: Corrected Tpeak to Tend interval.

rate and blood pressure[18], rising sympathetic activation, decreased parasympathetic tone[1] and sudden catecholamine discharge[19] are some of the blamed psychobiological triggers of cardiovascular events during these catastrophes. All these factors along with vasoconstriction may result in increased shear stress on the vasculature, causing endothelial damage with the potential to disrupt vulnerable plaque[16]. On the other hand, activation of the inflammatory process seems to be most important contributor. Steptoe *et al*[17] showed increased interleukin-6 and tumor necrosis factor alpha following emotional stress, which are stimulators of macrophages/T-lymphocytes, leading to matrix metalloproteinases secretion and atherosclerotic fibrous cap degradation[1,20]. Diminished fibrinolytic activity and increased fibrinogen, von Willebrand factor, Factors VII and VIII could lead to a prothrombotic imbalance during acute mental stress[21,22]. Platelet activation was also shown to be increased during emotional stress secondary to sympathetic activity in plasma, caused by platelet-derived growth factors[23,24]. In addition, in some animal models, phenylephrine or electric shock and noise induced stress gave rise to increased blood pressure, heart rate, ejection fraction, maximal systolic flow velocity, norepinephrine and fibrinogen levels and eventually plaque rupture[25,26].

However, short or long term impact of repetitive mental stress on cardiovascular system in patients with PTSD is much less known. Weiss *et al*[27] found an association between increased rates of metabolic syndrome and PTSD. In another study, PTSD patients were found to have diminished levels of high-density lipoprotein cholesterol and elevated levels of serum cholesterol, triglycerides and low-density lipoprotein cholesterol[28]. One of the few studies examining the long-term mortality risk of patients with PTSD has been published recently[29]. In that study, PTSD was found to be an independent predictor of mortality in multivariate analysis for their study population, 891 military veterans (HR: 1.79, 95%CI: 1.15-2.79, $P = 0.001$). In addition, patients with PTSD ($n = 91$, 98% male) had a trend toward worse survival on Kaplan-Meier analysis ($P = 0.057$). Heart failure, increased end-systolic left ventricular diameter, left ventricular systolic dysfunction and arrhythmia were more frequent in patients with PTSD. In another study, PTSD was prospectively associated with heart disease mortality among veterans free of cardiac disease at baseline[30].

There are few studies comparing ECGs of patients with PTSD and healthy controls[6,7]. Boscarino *et al*[6] showed increased signs of atrioventricular conduction abnormalities and myocardial infarction in male veterans with PTSD. In the other study, Kazaie *et al*[7] examined ECGs of patients with post-war PTSD and detected more ECG abnormalities (abnormal QT interval, inverted T waves, ST segment depression, low voltage QRS complex, sinus tachycardia) in PTSD patients than in controls. However, the patients were older, mostly male and had the disease much longer in those studies than in ours. Therefore, ECG abnormalities found in those studies seem to be a consequence of ischemic heart disease caused by traditional risk factors with a probable contribution of PTSD. On the contrary, in our study, which is the first one comparing the ECGs of patients with earthquake related PTSD and healthy subjects, we could not find any electrocardiographic difference between groups.

In conclusion, our study showed no direct effect of earthquake related PTSD on surface ECG, at least not in short term follow up. Although long term follow up may disclose some ECG changes, most probably these changes will be due to atherosclerotic coronary artery disease. Therefore, we propose that PTSD has no direct effect on surface ECG but may cause electrocardiographic changes indirectly by triggering and/or contributing to the ongoing atherosclerotic process.

COMMENTS

Background

Acute mental stress is a well known trigger of myocardial infarction and anxiety has been recently found to be an independent risk factor for incident coronary heart disease. However, the effects of repetitive anxiety on electrocardiography are not well known.

Research frontiers

This study aimed to analyze electrocardiographic features of patients diagnosed with posttraumatic stress disorder, a psychiatric disease that is characterized by recurrent symptoms of stress and anxiety.

Innovations and breakthroughs

That study is the first one comparing the electrocardiograms (ECGs) of patients with earthquake related posttraumatic stress disorder (PTSD) and healthy subjects in an early period after the disaster.

Applications

The study's results showed no direct effect of earthquake related PTSD on surface ECG in young patients.

Peer review

The article is short, concise and the authors found no ECG abnormalities (such as P-wave dispersion, QT dispersion, QT interval, Tpeak to Tend interval, intrinsicoid deflection durations and other traditional parameters) in victims of an earthquake who developed PTSD compared to control subjects exposed to the same trauma (earthquake) but who did not develop PTSD.

REFERENCES

1 **Steptoe A**, Brydon L. Emotional triggering of cardiac events. *Neurosci Biobehav Rev* 2009; **33**: 63-70 [PMID: 18534677 DOI: 10.1016/j.neubiorev.2008.04.010]

2 **Sato M**, Fujita S, Saito A, Ikeda Y, Kitazawa H, Takahashi M, Ishiguro J, Okabe M, Nakamura Y, Nagai T, Watanabe H, Kodama M, Aizawa Y. Increased incidence of transient left ventricular apical ballooning (so-called 'Takotsubo' cardiomyopathy) after the mid-Niigata Prefecture earthquake. *Circ J* 2006; **70**: 947-953 [PMID: 16864923 DOI: 10.1253/circj.70.947]

3 **Yeung AC**, Vekshtein VI, Krantz DS, Vita JA, Ryan TJ, Ganz P, Selwyn AP. The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. *N Engl J Med* 1991; **325**: 1551-1556 [PMID: 1944439 DOI: 10.1056/NEJM199111283252205]

4 **Kim PJ**, Seung KB, Kim DB, Her SH, Shin DI, Jang SW, Park CS, Park HJ, Jung HO, Baek SH, Kim JH, Choi KB. Clinical and angiographic characteristics of acute myocardial infarction caused by vasospastic angina without organic coronary heart disease. *Circ J* 2007; **71**: 1383-1386 [PMID: 17721015 DOI: 10.1253/circj.71.1383]

5 **Leor J**, Kloner RA. The Northridge earthquake as a trigger for

acute myocardial infarction. *Am J Cardiol* 1996; **77**: 1230-1232 [PMID: 8651102 DOI: 10.1016/S0002-9149(96)00169-5]
6 **Boscarino JA**, Chang J. Electrocardiogram abnormalities among men with stress-related psychiatric disorders: implications for coronary heart disease and clinical research. *Ann Behav Med* 1999; **21**: 227-234 [PMID: 10626030 DOI: 10.1007/BF02884839]
7 **Khazaie H**, Saidi MR, Sepehry AA, Knight DC, Ahmadi M, Najafi F, Parvizi AA, Samadzadeh S, Tahmasian M. Abnormal ECG Patterns in Chronic Post-War PTSD Patients: A Pilot Study. *Int J Behav Med* 2013; **20**: 1-6 [PMID: 21960258 DOI: 10.1007/s12529-011-9197-y]
8 **Grant RP**. Clinical Electrocardiography: The Spatial Vector Approach. New York: McGraw-Hill, 1957
9 **Dilaveris PE**, Gialafos EJ, Sideris SK, Theopistou AM, Andrikopoulos GK, Kyriakidis M, Gialafos JE, Toutouzas PK. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. *Am Heart J* 1998; **135**: 733-738 [PMID: 9588401 DOI: 10.1016/S0002-8703(98)70030-4]
10 **Couderc J**, Zareba W. Assessment of ventricular repolarization from bodysurface ECGs in humans. In: Morganroth J, Gussak I, editors. Cardiac safety of noncardiac drugs: practical guidelines for clinical research and drug development. Totowa, NJ: Humana Press, 2005
11 **Meisel SR**, Kutz I, Dayan KI, Pauzner H, Chetboun I, Arbel Y, David D. Effect of Iraqi missile war on incidence of acute myocardial infarction and sudden death in Israeli civilians. *Lancet* 1991; **338**: 660-661 [PMID: 1679475 DOI: 10.1016/0140-6736(91)91234-L]
12 **Carroll D**, Ebrahim S, Tilling K, Macleod J, Smith GD. Admissions for myocardial infarction and World Cup football: database survey. *BMJ* 2002; **325**: 1439-1442 [PMID: 12493655 DOI: 10.1136/bmj.325.7378.1439]
13 **Tsuchida M**, Kawashiri MA, Teramoto R, Takata M, Sakata K, Omi W, Okajima M, Takamura M, Ino H, Kita Y, Takegoshi T, Inaba H, Yamagishi M. Impact of severe earthquake on the occurrence of acute coronary syndrome and stroke in a rural area of Japan. *Circ J* 2009; **73**: 1243-1247 [PMID: 19436118 DOI: 10.1253/circj.CJ-08-0812]
14 **Suzuki S**, Sakamoto S, Koide M, Fujita H, Sakuramoto H, Kuroda T, Kintaka T, Matsuo T. Hanshin-Awaji earthquake as a trigger for acute myocardial infarction. *Am Heart J* 1997; **134**: 974-977 [PMID: 9398112 DOI: 10.1016/S0002-8703(97)80023-3]
15 **Kario K**, Matsuo T. Increased incidence of cardiovascular attacks in the epicenter just after the Hanshin-Awaji earthquake. *Thromb Haemost* 1995; **74**: 1207 [PMID: 8560444]
16 **Schwartz BG**, French WJ, Mayeda GS, Burstein S, Economides C, Bhandari AK, Cannom DS, Kloner RA. Emotional stressors trigger cardiovascular events. *Int J Clin Pract* 2012; **66**: 631-639 [PMID: 22698415 DOI: 10.1111/j.1742-1241.2012.02920.x]
17 **Steptoe A**, Hamer M, Chida Y. The effects of acute psychological stress on circulating inflammatory factors in humans: a review and meta-analysis. *Brain Behav Immun* 2007; **21**: 901-912 [PMID: 17475444 DOI: 10.1016/j.bbi.2007.03.011]
18 **Muller JE**, Abela GS, Nesto RW, Tofler GH. Triggers, acute risk factors and vulnerable plaques: the lexicon of a new frontier. *J Am Coll Cardiol* 1994; **23**: 809-813 [PMID: 8113568]
19 **Esler M**, Jennings G, Lambert G. Measurement of overall and cardiac norepinephrine release into plasma during cognitive challenge. *Psychoneuroendocrinology* 1989; **14**: 477-481 [PMID: 2623135]
20 **Ogawa H**, Mukai K, Kawano Y, Minegishi Y, Karasuyama H. Th2-inducing cytokines IL-4 and IL-33 synergistically elicit the expression of transmembrane TNF-α on macrophages through the autocrine action of IL-6. *Biochem Biophys Res Commun* 2012; **420**: 114-118 [PMID: 22405769 DOI: 10.1016/j.bbrc.2012.02.124]
21 **von Känel R**, Mills PJ, Fainman C, Dimsdale JE. Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: a biobehavioral pathway to coronary artery disease? *Psychosom Med* 2001; **63**: 531-544 [PMID: 11485106]
22 **Thrall G**, Lane D, Carroll D, Lip GY. A systematic review of the effects of acute psychological stress and physical activity on haemorheology, coagulation, fibrinolysis and platelet reactivity: Implications for the pathogenesis of acute coronary syndromes. *Thromb Res* 2007; **120**: 819-847 [PMID: 17321571 DOI: 10.1016/j.thromres.2007.01.004]
23 **Strike PC**, Magid K, Brydon L, Edwards S, McEwan JR, Steptoe A. Exaggerated platelet and hemodynamic reactivity to mental stress in men with coronary artery disease. *Psychosom Med* 2004; **66**: 492-500 [PMID: 15272093 DOI: 10.1097/01.psy.0000130492.03488.e7]
24 **Falk E**. Why do plaques rupture? *Circulation* 1992; **86**: III30-III42 [PMID: 1424049]
25 **von der Thüsen JH**, van Vlijmen BJ, Hoeben RC, Kockx MM, Havekes LM, van Berkel TJ, Biessen EA. Induction of atherosclerotic plaque rupture in apolipoprotein E-/- mice after adenovirus-mediated transfer of p53. *Circulation* 2002; **105**: 2064-2070 [PMID: 11980686 DOI: 10.1161/01.CIR.0000015502.97828.93]
26 **Ni M**, Wang Y, Zhang M, Zhang PF, Ding SF, Liu CX, Liu XL, Zhao YX, Zhang Y. Atherosclerotic plaque disruption induced by stress and lipopolysaccharide in apolipoprotein E knockout mice. *Am J Physiol Heart Circ Physiol* 2009; **296**: H1598-H1606 [PMID: 19286965 DOI: 10.1152/ajpheart.01202.2008]
27 **Weiss T**, Skelton K, Phifer J, Jovanovic T, Gillespie CF, Smith A, Umpierrez G, Bradley B, Ressler KJ. Posttraumatic stress disorder is a risk factor for metabolic syndrome in an impoverished urban population. *Gen Hosp Psychiatry* 2011; **33**: 135-142 [PMID: 21596206 DOI: 10.1016/j.genhosppsych.2011.01.002]
28 **Karlović D**, Buljan D, Martinac M, Marcinko D. Serum lipid concentrations in Croatian veterans with post-traumatic stress disorder,post-traumatic stress disorder comorbid with major depressive disorder,or major depressive disorder. *J Korean Med Sci* 2004; **19**: 431-436 [PMID: 15201512 DOI: 10.3346/jkms.2004.19.3.431]
29 **Xue Y**, Taub PR, Iqbal N, Fard A, Wentworth B, Redwine L, Clopton P, Stein M, Maisel A. Cardiac biomarkers, mortality, and post-traumatic stress disorder in military veterans. *Am J Cardiol* 2012; **109**: 1215-1218 [PMID: 22305506 DOI: 10.1016/j.amjcard.2011.11.063]
30 **Boscarino JA**. A prospective study of PTSD and early-age heart disease mortality among Vietnam veterans: implications for surveillance and prevention. *Psychosom Med* 2008; **70**: 668-676 [PMID: 18596248 DOI: 10.1097/PSY.0b013e31817bccaf]

P- Reviewers Vidovic A, Pivac N **S- Editor** Song XX
L- Editor Roemmele A **E- Editor** Zhang DN