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Extent of Myocardial Damage in Patients after Emotional Stress-Induced Myocardial Infarction during Euro Cup Soccer 2008

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Abstract

Background: The World Cup soccer 2006 has been shown to provoke levels of stress sufficient to increase the incidence of acute coronary syndrome. However, the clinical outcome of these patients remains elusive. We sought to assess whether emotional stress-induced myocardial infarction might increase myocardial damage compared to non-stress-induced events. Design and Methods: We prospectively analysed the extent of left ventricular damage after emotional stress-induced myocardial infarction occurred during Euro Cup Soccer 2008 (study group, n = 51). Data were compared to a matched reference group (n = 55). The primary endpoint was a composite of cardiac troponin-T/I and the left ventricular ejection fraction at day 4th after the initial event. Results: Compared to standard values of troponin T and troponin I, concentrations were increased in both the study group and the reference group (troponin T: 4.7 ± 8.5 ng/ml vs. 2.4 ± 4.3 ng/ml; troponin I: 13.1 ± 16.5 ng/ml vs. 8.7 ± 13.9 ng/ml). The difference, adjusted for confounding variables, between both groups did not reach statistical significance (p = 0.33). Likewise, left ventricular ejection fraction (EF) was decreased in both the study patients and the reference group (51% ± 12% EF vs. 55% ± 10% EF), the difference between both groups was just not significant (p = 0.12). Discussion: In conclusion, because of the lack of significance, we cannot testify at present, weather emotional stress, e.g. induced by soccer matches of the national team, influences the extent of myocardial damage following myocardial infarction. However, a positive correlation can be assumed, because the troponin levels are considerably higher in the study group than in the control group.

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Keywords

Emotional Stress, Myocardial Infarction, Ventricular Damage, Troponin-T/I

1. Introduction

The interdependence of stress and cardiovascular disease is intuitive and well documented [1] [2]. The trigger of stress can differ, the way of the reaction in the organism always stays the same [3]. Stress can be physical but also emotional. The pathophysiologic processes underlying emotional stress are still unknown. The triggering hypothesis suggests that the emotional impact of challenging events results in plaque rupture with subsequent thrombosis [4].

Also watching soccer can result in emotional stress. The association between watching soccer matches and acute cardiovascular events has been the subject of several epidemiologic studies [5]-[10].

We have recently demonstrated a 2.7 fold increase in the incidence of acute cardiovascular events in association with World Cup soccer matches of the national team. Because of the close time relationship, it seems likely that these additional cardiac emergencies are triggered by emotional stress [11]. However, up to now, the clinical outcome of patients who suffered a stress-induced myocardial infarction compared to a non-stress-induced event still remained unknown.

Mercanoglou *et al*. discovered that rats, which were exposed to stress (for instance by isolation, changing hierarchy, lack of space and feeding), suffered a significant higher myocardial damage following surgically triggered myocardial infarction than rats which were not exposed to stress [12].

The aim of the present study was to assess whether emotional stress-induced myocardial infarction, occurred during Euro Cup Soccer (ECS) 2008, might be a trigger strong enough to cause an increase of myocardial damage when compared to the infarct size of patients who experienced a non-stress-induced myocardial infarction.

2. Methods

2.1. Acquisition of Data

The prospectively assessed study period was June 7 to June 29, 2008, the time the Euro Cup Soccer (ECS) 2008 took place in Austria and Switzerland. The study sites were in Bavaria and in the city of Berlin, 18 hospitals providing percutaneous coronary intervention (PCI) served as study centers.

We prospectively studied patients who experienced a myocardial infarction with ST-segment elevation (STEMI) or without ST-segment elevation (NSTEMI). In order to gain clinical information of the patients we designed a standardized questionnaire. Furthermore, patients were screened for accompanying emotional circumstances during the ECS 2008.

STEMI was defined by the presence of ST-segment elevation ≥ 0.1 mV in unipolar leads or elevation of ≥ 0.2 mV in anterior wall leads and confirmed by elevated cardiac troponin T or troponin I. NSTEMI was defined using the diagnostic criteria of the European Society of Cardiology.

We compared the extent of myocardial damage in two different groups:

1) The study group

Patients (n = 51) who experienced a stress-induced myocardial infarction due to observing Euro Cup soccer matches (TV, public viewing, stadium or radio).

2) The reference group:

Patients (n = 55) who reported no relevant emotional circumstances that may have provoked a considerable contribution to the myocardial infarction, matched for age, gender, and type of myocardial infarction.

The following data were collected:

The patient's sex, age, medical history (known coronary artery disease, hypertension, hypercholesterolemia, diabetes mellitus, abuse of nicotine), medication at the time of hospital admission (acetylsalicylic acid, beta-adrenergic blockers, ACE-blockers, statins), date of hospital admission and discharge, final clinical diagnosis (STEMI or NSTEMI), surrounding circumstances while onset of symptoms (consumption of drugs, alcohol), and creatinine level, routinely determined at the time of hospital admission (standard value: ≤ 1.0 mg/ml).

2.2. Quantification of Infarct Size

To distinguish the extent of myocardial damage, we analysed left ventricular function by echocardiography and cardiac troponin T or troponin I at day 4 after hospital admission. Sample collection and analyses were performed according to manufacturer's recommendations by investigators blinded to categorization into the two patient populations.

The time delay between the onset of symptoms, determination of serum Troponin T or troponin I and left ventricular function was comparable in all patient groups (study and reference).

2.3. Cardiac Troponin T (cTnT) Measurement

Serum cTnT levels (study group: n = 24, reference group: n = 22) were measured by a cTnT enzyme-linked immuno sorbent assay (ELISA), and performed 96 hours after myocardial infarction (MI) according to the manufacturer's instruction. An elevated cTnT was defined as a value ≥0.05 ng/ml or ≥0.03 ng/ml, dependent on the used analytical method of troponin T of the study centre.

2.4. Cardiac Troponin I (cTnI) Measurement

Serum cTnI levels (study group: n = 27, reference group: n = 33) were measured by a heterogeneous immunoassay module and performed 96 hours after myocardial infarction (MI) according to the manufacturer's instruction. An elevated cTnI was defined as a value ≥0.09 ng/ml, ≥0.05 ng/ml, or ≥0.032 ng/ml, dependent on the used analytical method of troponin I of the study centre.

2.5. Evaluation of Left Ventricular Function by Echocardiography

Left ventricular ejection fraction (LVEF) was assessed by the Simpson's method [13] and performed 96 hours after MI by the attending physicians of the participating study centres according to the guidelines of the European Society of Cardiology/American College of Cardiology, reduction in LVEF was defined as <60%.

2.6. Statistical Analysis

In order to analyse whether emotional stress through observing Euro Cup soccer matches induces myocardial infarction a linear regression model is calculated for the primary outcome variable troponin at day 4 after hospital admission on the scale of the common logarithm and the secondary outcome variable left ventricular ejection fraction. The troponin level of the patient with 0 ng/ml troponin is set to the minimum troponin concentration different from 0 ng/ml. A confounder model is established using stepwise linear regression with the Akaike information criterion. In addition to the fixed confounder variables age and the categorical troponin group (only in the models with the troponin as response variable), the stepwise forward procedure selects the relevant confounders from the following variables: sex, known hypertension, hypercholesterolemia, diabetes mellitus, coronary artery disease or abuse of nicotine, medication with beta-adrenergic blockers, ACE-blockers, statins and acetylsalicylic acid, consumption of alcohol, creatinine level.

Based on the confounder model, the impact of watching soccer is analysed.

The robustness of the resulting model is examined with a t-test for group differences and a linear regression model with random effects accounting for the unobserved heterogeneity of the included hospitals.

The study protocol was approved by the local ethical committee of the University of Munich (LMU), and all patients gave informed consent before the study enrollment.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

3. Results

The present study is based on comparative analysis in 2 different groups (study and reference group) (see **Table 1**).

All patients showed increased values of troponin as an expression of myocardial infarction compared to standard values. Patients in the study group presented higher concentrations of troponin I (study group: n = 27, reference group: n = 33) and troponin T (study group: n = 24, reference group: n = 22) compared to the reference

group (troponin I: 13.1 ± 16.5 ng/ml vs. 8.7 ± 13.9 ng/ml; troponin T: 4.7 ± 8.5 ng/ml vs. 2.4 ± 4.3 ng/ml; **Figure 1**).

Besides age and troponin group, the medication of acetylsalicylic acid was detected as relevant confounding variables.

In summary, watching Euro Cup soccer increases the troponin level by 42.7% (**Table 2**). However, the difference

Table 1. Patient's characteristics.

	Total No. of patients	
Characteristics	study group	reference group
Male sex	40 (78.4%)	37 (67.3%)
Female sex	11 (21.6%)	18 (32.7%)
Age-yr	65.7 ± 12.2	65.3 ± 12.6
Coronary artery disease		
Known	15 (29.4%)	11 (20.0%)
No	35 (68.6%)	40 (72.7%)
Unknown	1 (2.0%)	4 (7.3%)
Hypertension		
Known	34 (66.7%)	32 (58.2%)
No	15 (29.4%)	20 (36.4%)
Unknown	2 (3.9%)	3 (5.5%)
Hypercholesterolemia		
Known	29 (56.9%)	28 (50.9%)
No	14 (27.5%)	22 (40.0%)
Unknown	8 (15.7%)	5 (9.1%)
Diabetes mellitus		
Known	11 (21.6%)	13 (23.6%)
No	35 (68.6%)	40 (72.7%)
Unknown	5 (9.8%)	2 (3.6%)
Nicotine abuse		
Yes	27 (52.9%)	23 (41.8%)
No	21 (41.2%)	30 (54.5%)
Unknown	3 (5.9%)	2 (3.6%)
Acetylsalicylic acid		
Use	18 (35.3%)	21 (38.2%)
No use	30 (58.8%)	33 (60.0%)
Unknown use	3 (5.9%)	1 (1.8%)
Beta-adrenergic blockers		
Use	16 (31.4%)	18 (32.7%)
No use	31 (60.8%)	35 (63.6%)
Unknown use	4 (7.8%)	2 (3.6%)
ACE-blockers		
Use	20 (39.2%)	16 (29.1%)
No use	27 (52.9%)	36 (65.5%)
Unknown use	4 (7.8%)	3 (5.5%)
Statin		
Use	15 (29.4%)	17 (30.9%)
No use	32 (62.7%)	36 (65.5%)
Unknown use	4 (7.8%)	2 (3.6%)

Table 2. Multiplicative effects of watching soccer and confounding variables on troponin levels.

	effect	standard error	confidence interval		p-value
			lower	upper	
watching soccer	1.427	0.521	0.405	2.449	0.333
age	1.019	0.016	0.989	1.050	0.210
troponin group: T	0.427	0.161	0.112	0.742	0.026
ASS medication	0.319	0.125	0.074	0.563	0.004
ASS medication unknown	2.569	2.588	−2.503	7.641	0.351

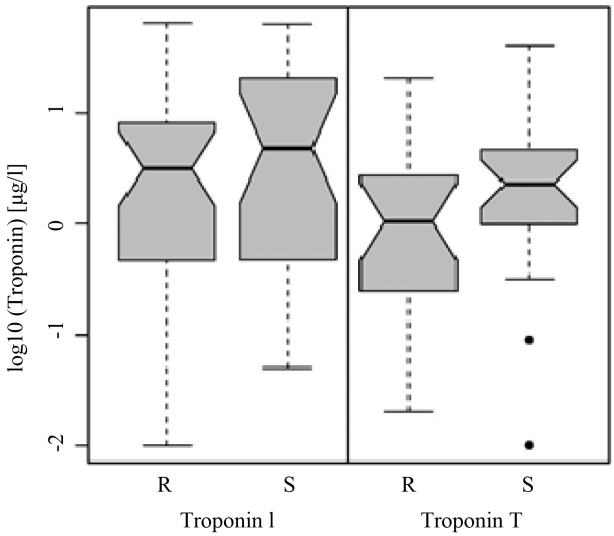

Figure 1. Common logarithm of the troponin values for the two troponin groups I and T separately for the reference group (R) and the study group (S).

between both groups did not reach statistical significance (p = 0.33). ASS medication yields to a significant decrease of 68.1% in troponin value. Furthermore, the troponin level increases with rising age (not significant).

Multiplicative effects of watching Euro Cup soccer and of the confounding variables on myocardial infarction-measured through the troponin level-are summarized in **Table 2**.

The simple comparison of the study and the reference group with the unadjusted t-test also does not show significant differences (troponin I: p-value = 0.690, troponin T: p-value = 0.162). The inclusion of a random hospital effect reveals only little variability between the hospitals and the effects only change marginally.

Likewise, left ventricular ejection fraction (EF) was decreased in the study patients compared to the reference group (51% ± 12% EF vs. 55% ± 10% EF), as shown in **Figure 2**.

Hypercholesterolemia, hypertension and the creatinine level are identified as relevant and significant confounding variables for the left ventricular ejection fraction. Observing the soccer games of the Euro Cup also negatively affects the ejection fraction by decrease of 3.48 (**Table 3**); but the effect is not significantly different from zero (p = 0.12).

4. Discussion

In the present study, we tested the hypothesis whether the extent of a stress-induced myocardial damage is increased compared to a non-stress-induced infarct size in humans.

Pathophysiological we expected that stress results in an increase of sympathetic nervous system activation and by this in higher concentration of circulation catecholamines and other stress hormons like cortisol or CRH. The resulting changes of circulation like increase of heart rate and blood pressure may trigger acute cardiovascular events on the one hand [14]. On the other hand effects of stress can also be activation of platelets,

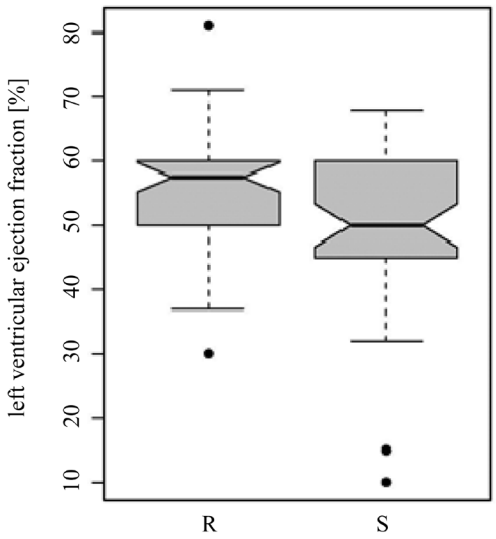

Figure 2. Left ventricular ejection fraction separately for the reference group (R) and the study group (S).

Table 3. Multiplicative effects of watching soccer and confounding variables on left ventricular ejection fraction.

	effect	standard error	confidence interval		p-value
			lower	upper	
watching soccer	−3.478	2.222	−7.893	0.938	0.121
age	0.013	0.097	−0.179	0.206	0.890
hyperchol	−4.836	2.452	−9.709	0.036	0.052
hyperchol unknown	−2.794	3.771	−10.286	4.698	0.461
creatinine level	−2.883	1.699	−6.259	0.493	0.093
hypertension	0.020	2.655	−5.255	5.295	0.994
hypertension unknown	−12.306	5.621	−23.475	−1.137	0.031

changes in coronary vascular tone due to stimulation of α sympathetic receptors [14] and by this changing the oxygen supply of myocardium during stress resulting in bigger damage caused by myocardial infarction. Because of the non-significant results we cannot testify at present whether watching soccer games before onset of myocardial infarction influences the myocardial damage.

In all cases, infarct size was quantified by determination of serum cardiac troponin and two-dimensional echocardiographic measurement of left ventricular ejection fraction on the day 4 after hospital admission.

Infarct size, strongly determined by the extent of myocardial damage [15], is a major prognostic factor for cardiovascular death, re-infarction, and congestive heart failure [16]. The assessment of infarct size can be achieved by biochemical methods or by imaging modalities such as two-dimensional echocardiography [17] or contrast-enhanced magnetic resonance imaging (MRI) [18].

Troponin is normally not detectable in serum; elevated levels were found in all patients with Q wave and non-Q wave myocardial infarction during a period of 124 hours, caused by severe ischemic cell damage [19]. According to previous studies, we could also demonstrate that troponin levels were significantly increased in both patients who experienced a myocardial infarction induced by emotional stress and patients with a non-stress induced MI when compared to the standard value [19].

Recent studies have shown that cardio specific antigens such as troponin T (cTNT) or troponin I (cTnI) possess better sensitivity and specificity and are therefore the preferred marker for diagnosis and risk stratification of patients with acute myocardial infarction [19], compared to creatine kinase MB fraction (CK MB).

Serial sampling of cTNT demonstrated that cTnT levels at 96 hours after primary percutaneous coronary in-

tervention (PCI) correlated comparably well with the infarct size, determined by MRI. Thus, the authors suggest that the 96h value of cardiac troponin T is convenient to use clinically [20] [21].

Accordingly, we determined the 96 h serum value of troponin patients who were treated by PCI due to a myocardial infarction with (STEMI) or without ST-segment elevation (NSTEMI).

Up to now, there is no evidence that troponin I correlates less than troponin T with infarct size [22]. However, concerning troponin I, the determination at 72 h after MI onset seems to reflect the infarct size more precisely [23]. On account of this the measurement of troponin I 24 h earlier might have led to more accurate results.

Our results demonstrate a high standard deviation that may in part be responsible for the lack of significance. First, the sample size of both the study and reference group may be too small to detect meaningful differences. Second, the high standard deviation may be caused by the inhomogeneous patient groups (STEMI and NSTEMI). Generally, infarct size and median troponin values were larger in STEMI than in NSTEMI [21]. As a consequence, troponin levels are spread out over a large range of values, resulting in a high standard deviation. Furthermore, in contrast to several previous reports [20] [21] one report has indicated that sampling at 96 hours may not be the optimal time point for single measurement due to heterogeneous time release curves of troponin in NSTEMI compared to STEMI [24].

Finally, the high standard deviation may be caused by different analytical methods of both cardiac troponin T and troponin I. In the management of acute coronary syndromes, cTnT is comparable in diagnostic and prognostic efficacy to cTnI [25]. However, a previous population-based study has shown different results (higher sensitivity, specificity and negative predictive value of the troponin I assay compared to a conventional troponin T assay) in the early diagnosis of acute myocardial infarction. However, the troponin T assay was used only for the diagnosis and not for comparisons with the troponin I assay (troponin T vs. troponin I value) [26].

In the primary analysis troponin I and troponin T were simultaneously considered (watching Euro Cup soccer increases the troponin level by 42.7%, p-value = 0.33), but a categorical variable indicating the troponin type is included in the model. A sensitivity analysis with separate models for troponin I and troponin T shows also increased, but also not significant, effects of observing the soccer games: watching soccer increases troponin I by 26.4% (p-value = 0.672) and troponin T by 64.7% (0.264).

In addition, the evaluation of left ventricular function by two-dimensional echocardiographic analysis is well established, and concentration of cTnT has a strong negative correlation with left ventricular ejection fraction assessed by echocardiography [27].

Our study shows a negative correlation between cTnT concentrations measured 96 hours post-myocardial infarction and echocardiographic left ventricular ejection fraction. Thus, we confirm with other investigators [27] [28].

In a former study, we analysed mortality rates due to myocardial infarction in the Bavarian population during World Cup Soccer. The number of deaths due to stress-induced myocardial infarction was not measurably increased compared to a non-stressed matched control group [29]. In the present study, we found no significant increase of myocardial damage in patients with stress-induced myocardial infarction, thus, the results may confirm our previous findings [29].

5. Conclusions

In conclusion, at present we cannot state an influence of soccer consumption on myocardial damage. Anyhow, a positive correlation can be assumed, because the troponin levels were considerably higher in the study group than in the control group.

Due to the mentioned limitations, further studies might be wise. A more detailed questionnaire, to find out the exact circumstances before onset of the first symptoms, could reduce recall bias, observer bias etc. However, a totally objective data acquisition cannot be achieved because stress is considered as a very subjective phenomenon. Furthermore, future studies should pay attention to more homogeneously patient groups (for instance only one method of troponin determination, only one hospital included etc.). In addition, a longer follow-up of patients including rates of re-infarctions, cardiac deaths etc. might cause more valuable results. Future studies are needed to analyse the efficacy of medical treatment, non-medical treatment, or both in reducing cardiac adverse events.

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Declaration of Conflicting Interests

All authors have no conflicts of interest to disclose.

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