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Short communications

Long lasting effect of physical stress on the LVEF

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Abstract

BACKGROUND: Animal and clinical studies have shown that exercise can deteriorate myocardial contractile function. The aim of this study was to examine whether the decrease of LVEF measured with gated SPECT lasts as long as 3 hours after exercise.
MATERIAL AND METHODS: 46 patients with CAD and a control group comprising 10 healthy subjects were studied. All patients underwent myocardial perfusion gated SPECT with 99mTc-tetrofosmin at rest and during stress. SPECT was started 1 hour p.i. at rest and twice — 1 hour and 3 hours after injection at stress. LVEF values were calculated by the method of Germano, using QGS software.
RESULTS: LVEF values measured at all time points were significantly lower in CAD patients than in control group. In normals mean LVEF values 1h after rest injection were similar to those obtained 1 and 3 hours after stress injection (59.0 ± 4.1 v. 60.0 ± 5.9 v. 58.0 ± 4.6 respectively; $p > 0.05$). One hour post exercise a decrease of LVEF was observed in 2 patients and 3 hours after injection also in 2 patients. CAD subjects showed slightly lower LVEF values determined 1h after stress than 1 hour after rest injection (50.8 ± 13.6 v. 49.3 ± 12.8; $p < 0.05$). More expressed reduction of LVEF was observed 3 hours after stress injection as compared to both rest and stress study (50.8 ± 13.6 v. 46.0 ± 12.2; $p < 0.001$ and 49.3 ± 12.8 v. 6.0 ± 12.2; $p < 0.001$ respectively). One hour post exercise, a decrease of LVEF values was observed in 18 patients and 3 hours after injection in 36 patients out of 46.
CONCLUSIONS: In the majority of patients with CAD physical stress applied for the purposes of myocardial perfusion SPECT study results in an impairment of the LV function. The impairment of the LVEF caused by physical stress is observed 1 hour after exercise, but it increases markedly in frequency and grows stronger during the next 2 hours. Patients with CAD who underwent cardiac examination connected with physical stress should remain under observation for several hours after termination of exercise.
Key words: gatedSPECT, LVEF, myocardial stunning

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Introduction

Gated single photon emission computed tomography is currently used for simultaneous assessment of left ventricular myocardial perfusion and function [1].

The observations on the biokinetics of sestamibi or tetrofosmin have shown that these tracers are trapped into the myocardium in the first minutes following injection and present a kind of steady state concentration in the organ during the next hours. In view of these data, the perfusion image derived from gated SPECT reflects myocardial tracer uptake at the injection time. On the other hand, the left ventricular function during such study is assessed at the time of acquisition, which is delayed in comparison with the time point of tracer administration.

Animal studies as well as some clinical studies have shown that exercise may deteriorate myocardial contractile function, resulting in reduced LVEF [2]. This phenomenon described as post-ischaemic ventricular dysfunction was termed "myocardial stunning" by Braunwald and Kloner [3]. The occurrence of "stunning" in humans has been demonstrated after regional ischaemia (either exercise-induced or vasospastic) or global ischaemia (cardiac surgery or heart transplantation).

Our earlier observations revealed that in the majority of patients with CAD, the LVEF measured 1 hour after physical stress is significantly lower than 1 hour after rest injection [4].

Considering the "stunning" phenomenon to be responsible for the above observation, the authors performed the present study to examine whether the decrease of LVEF lasts as long as 3 hours after termination of exercise.

Material and methods

Forty-six patients (34 men and 12 women aged 25–74 years, mean 51.9 years), with angiographically confirmed coronary artery disease (CAD) were studied. Eighteen patients had a history

of myocardial infarction 3 months to 19 years (on average 4.1 ± ± 6.2 years) before the study. Control group (NMS) comprised 10 healthy subjects (6 women and 4 men) aged 41 ± 16 years.

Study protocol

All patients underwent myocardial perfusion SPECT at rest and during stress, using two-day protocol.

REST study. 740 MBq (20 mCi) ^{99m}Tc-Tetrofosmin (Myoview, Nycomed Amersham) was injected intravenously as a bolus, at rest, after overnight fasting. Myocardial SPECT was started 1 hour after injection and performed using a double head, large field of view gamma camera (Varicam, GE Medical Systems), connected to a dedicated computer (XPert, GE Medical Systems). The activity measurements were performed using gated technique, with the cardiac cycle divided into 8 sequences.

STRESS study. Bicycle stress testing was performed according to the Bruce protocol. The tracer was injected at the peak exercise. SPECT acquisitions, using the same acquisition protocol as described above, were performed twice, 1 hour and 3 hours after termination of stress.

From the data acquired at rest (R), 1h after stress (S1) and 3 hours after termination of exercise (S3) LVEF values were calculated by the method of Germano et al. using commercially available quantitative gated SPECT (QGS) software. Relative differences were calculated between LVEF values measured at R and S1 (ΔEF_{R-S1}), R and S3 (ΔEF_{R-S3}) as well as S1 and S3 (ΔEF_{S1-S3}), to assess LVEF changes.

For further analysis the LVEF value difference in each patient was considered significant when it exceeded 5% in relation to the earlier study.

Results

No significant differences of exercise parameters, such as workload, maximum heart rate obtained during stress, percentage of heart rate assumed in given patient to be maximum, as well as mean heart rate during acquisitions, were observed between normals (NMS) and CAD patients.

LVEF values measured at all time points were significantly lower in CAD patients that in control group (Table 1).

In normals mean LVEF values 1 h after rest injection were similar to those obtained 1 hour and 3 hours after stress injection (59.0 ± 4.1 v. 60.0 ± 5.9 v. 58.0 ± 4.6 respectively; $p > 0.05$) (Table 1, Fig. 1). Relative changes of LVEF values were as follows: $\Delta EF_{R-S1} = 1.7\% \pm 7.1\%$, $\Delta EF_{S1-S3} = -3.0\% \pm 6.2\%$ and $\Delta EF_{R-S3} = -1.7\% \pm 3.4\%$ (Fig. 2). One hour post exercise decrease of LVEF values greater than 5% was observed in 2 patients and 3 hours after injection also in 2 patients out of 10. However in one subject with decreased LVEF value after 1 h this parameter increased to rest value after 3 hours. In one patient decreased LVEF was observed only 3 hours after stress.

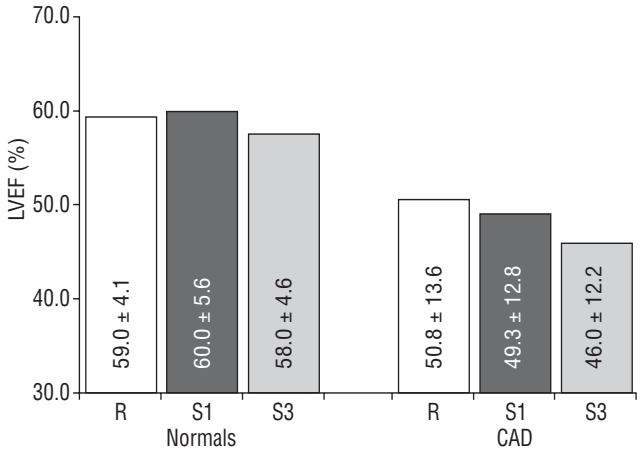

Figure 1. Comparison of LVEF mean values in patients with CAD and normals at three different acquisition time points: at rest (R), 1 hour after stress (S1) and 3 hours after stress (S3). In CAD LVEF values at stress were significantly lower than at rest and significantly deteriorated with time with the lowest values 3 hours after termination of exercise.

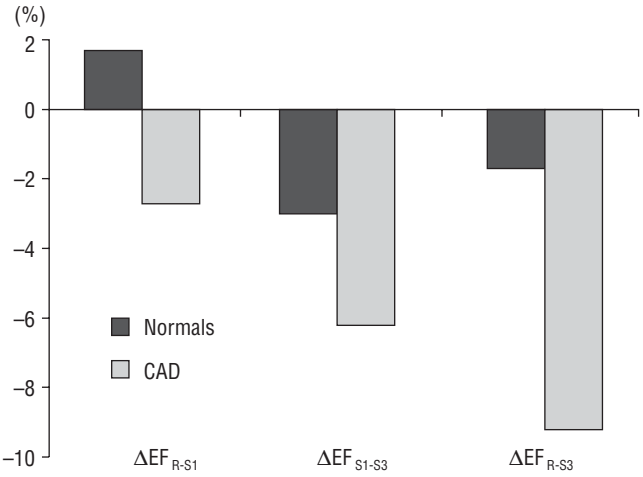

Figure 2. Comparison of relative LVEF changes between different acquisition time points in control group (dark shaded bars) and CAD (light shaded bars). In patients with CAD relative decrease of LVEF between rest and 3 hours after stress was significantly more negative than in control group ($p < 0.01$).

Table 1. LVEF at rest and after stress in patients with CAD and in control group (NMS)

Group	n	LVEF			p**		
		R × (±SD)	S1 × (±SD)	S3 × (±SD)	R v. S1	R v. S3	S1 v. S3
NMS	11	59.0 (4.1)	60.0 (5.9)	58.0 (4.6)	NS	NS	NS
CAD	46	50.8 (13.6)	49.3 (12.8)	46.0 (12.2)	< 0.05	< 0.001	< 0.001
p*		< 0.05	< 0.01	< 0.01			

*t-test for unpaired data, **t-test for paired data

CAD subjects showed slightly but significantly lower LVEF values determined 1h after stress than after rest injection (50.8 ± ± 13.6 v. 49.3 ± 12.8; $p < 0.05$). More expressed reduction of LVEF values with high statistical significance was observed 3 hours after stress injection as compared to both R and S1 study (50.8 ± ± 13.6 v. 46.0 ± 12.2; $p < 0.001$ and 49.3 ± 12.8 v. 46.0 ± 12.2; $p < 0.001$ respectively) (Table 1, Fig. 1). Relative changes of LVEF values between all time points were negative ($\Delta EF_{R-S1} = -2.7\% \pm \pm 9.2\%$; $\Delta EF_{S1-S3} = -6.2\% \pm 7.8\%$; $\Delta EF_{R-S3} = -9.2\% \pm 6.7\%$) and those between R and S3 were significantly greater than in control group ($p < 0.01$) (Fig. 2). One hour post exercise decrease of LVEF values greater than 5% in relation to rest values was observed in 18 patients and 3 hours after injection in 36 patients out of 46, which difference in frequencies was significant ($p < 0.02$) (Table 2, Fig. 3). In 31 patients relative decrease of LVEF 3 hours after stress was greater than 5% compared to stress value after 1 hour. Only in 3 patients was LVEF measured at S3 higher than at S1 with a relative increase greater than 5%. In the remaining subjects the LVEF changes between S1 and S3 did not exceed 5% (Fig. 4)

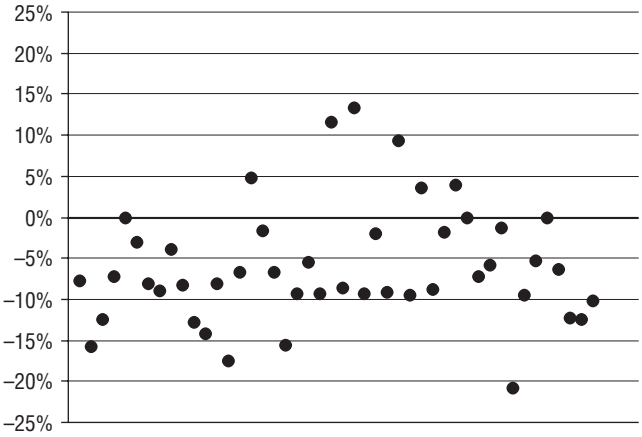

Figure 4. Relative changes of LVEF between 1st and 3rd hour after termination of physical exercise.

Discussion

Gated myocardial SPECT is performed to assess LV perfusion and function in the majority of nuclear medicine departments. The gating may be done during the acquisition of either the rest or the stress study. Several observations have shown that LV function measured post stress may not represent true LV function at rest in patients with exercise-induced ischaemia because of post-ischaemic myocardial stunning [2, 5–7].

PET flow tracer studies demonstrated that 5-20 min after cessation of exercise, regional flow in the ischaemic regions of myocardium returns to baseline condition [8]. Taking into account this observation, it might be presumed that the time limit of 1 hour after exercise is long enough for perfusion to return to baseline condition.

Johnson et al. reported deterioration of post-exercise LVEF (measured 15–30 min after termination of stress) in 36% of patients with reversible myocardial ischaemia [6]. Our study showed similar results in all patients 1 hour after exercise (39%, 18/46).

However, comparing LVEF determined at rest and 3 hours after termination of stress, our study showed deterioration of LVEF in 78% (36/46) of the total group of patients with CAD. In the healthy subjects this phenomenon was not observed even if the stress parameters exceeded those applied in CAD.

The mechanisms responsible for deterioration of LVEF observed in patients with CAD after stress is not clear enough. There are several hypotheses trying to explain that phenomenon. One of these hypotheses is myocardial stunning resulting from exercise.

However, the pathogenesis of myocardial "stunning" is not clear. Animal studies showed that vessel occlusion maintained for 10–20 minutes did not always lead to tissue necrosis (9). Release of vessel occlusion followed by the increased blood flow (hyperaemic phase) was associated with only partial recovery of wall motion abnormalities. At least two hypotheses have been proposed: "oxyradical" — the influence of generated oxygen-derived free radicals and "calcium hypothesis" — transient calcium overload on reperfusion [7]. Mitochondrial calcium overload leads to decrease of ATP production while the sarcoplasmatic calcium overload may activate intracellular proteases which destroy the filaments [10]. The final result appears to be decreased responsiveness of contractile filaments resulting from the above processes. The delay in functional recovery of miocyte after ischaemia may be dependent on time required for damaged filaments' reparation.

Our results showed in the majority of patients with CAD decreased contractility of LV present 3 hours after termination of stress even if that phenomenon was not observed 1 hour after cessation of exercise. This finding may suggest that changes in stunned myocardium metabolism persist much longer than was presumed and in several patients become more pronounced with time. Taking into account that suggestion, the time needed for LV

Table 2. LVEF changes in 46 patients with CAD after stress in comparison with results obtained at rest

Change	S1	S3	p
Decrease	18	36	< 0.02
No change	18	9	NS
Increase	10	1	< 0.02
Total	46	46	

*p — Mann-Whitney U-test

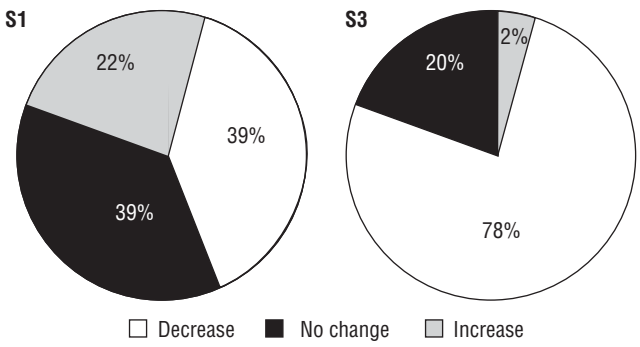

Figure 3. Frequency of LVEF changes in post stress acquisitions in relation to rest values. Decrease of LVEF was observed in the majority of patients with CAD 3 hours after stress injection.

functional recovery after physical stress seems to be much longer than a patient's usual stay in the diagnostic department.

One should consider another possible influence on LVEF values after exercise — the accuracy of gated SPECT automatic analysis. In patients with reduced endocardial tracer uptake the automatic edge detection of the QGS program may fail to identify myocardial surfaces. That may underestimate the post-stress LVEF values. However, in our study this phenomenon seems to have a limited influence. Only in a few patients were the above border lines in the stress study not similar to those at rest.

Conclusions

The impairment of the left ventricular function caused by physical stress is observed in patients with CAD 1 hour after exercise, but it increases markedly in frequency and grows stronger during the next 2 hours.

Patients with CAD who underwent cardiac examination connected with physical stress should remain under observation for several hours after termination of exercise.

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