Myocardial perfusion and left ventricular function in long-term follow-up and prognosis of electrostimulation cardiomyoplasty

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Abstract

BACKGROUND: Twenty two patients with congestive cardiac failure treated surgically by the dynamic cardiomyoplasty (CMP) with m. latissimus dorsi were examined. Myocardial perfusion was assessed with $^{199}TlCl$ scintigraphy combined with dipyridamole stress-test. In order to obtain direct evidence of myocardial perfusion from muscular flap we have also injected a bolus of ^{99m}Tc into a. thoracodorsalis, with simultaneous blood sampling from coronary sinus. Haemodynamic parameters were assessed using radionuclide angiography.

METHODS: In a year of follow-up all the patients were assigned to one of two groups: eleven patients demonstrated improvement in clinical status (first group) and in another group comprising eleven persons no positive effect or deterioration were obvious (second group). The patients of the first group before operation revealed two times less persistent defect size than patients of the second group. Analysis of integral index of persistent defect revealed more expressive differences between groups. Before the surgical treatment the patients with improvement in clinical status after cardiomyoplasty demonstrated greater size of reversible defect in comparison with patients of the second group. In second group coronary fraction of thallium accumulation was in 1.4 times higher in comparison to first group, as result of myocardial hypertrophy in patients with bad prognosis. It was not considerable differences between two groups in II/m level before cardiomyoplasty. Before the surgical treatment the patients with improvement in clinical status after cardiomyoplasty demonstrated greater ejection fraction in comparison with patients of the second group.

RESULTS: Cardiomyoplasty led to decrease in the mean size of reversible defects due to indirect revascularization. For this hypothesis testified the fact that in patients after cardiomyoplasty nuclide appeared in coronary sinus at the 10–12th seconds after injection into artery thoracodorsalis through anastomoses between the latissimus dorsi muscle and the myocardium. The time of appearance of the second wave of rise gamma-counting in blood samples from coronary sinus reflects the repeated entry of radiopharmaceutical in myocardium after recirculation.

Key words: cardiomyoplasty, prognoses, thallium-199 myocardial perfusion imaging, radionuclide angiocardiography

Introduction

Disturbances of pump function of left ventricle and the haemodynamic insufficiency resulting from extensive myocardial ischemic catastrophes are factors shortening life expectance and badly deteriorating physical work capacities in ischemic cardiomyopathy due to restricted efficiency of medical treatment in such conditions and immanent problem of donorship in programs of heart transplantation (1). Last years gave evidencies for electrostimulating cardiomyoplasty with latissimus dorsi muscle as effective tool for treatment of patients with severe myocardial pump failure (2, 3).

Improvement of central haemodynamic was demonstrated in the course of follow-up of patients underwent cardiomyoplasty, possibly as a result of improvement in left ventricular pump function and also due to decrease in left ventricular dilatation (4, 5). At the same time, high mortality of these patients as bad as severe cardiac insufficiency and high rate of surgical complications remain to be the main problem of this surgical technique (6).

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Recently we reported about prognostic value of gated equilibrium radionuclide ventriculography and ^{199}TlCl myocardial perfusion scintigraphy for prediction of clinical condition during the early period after cardiomyoplasty (7). As regard to long-term prognosis of cardiomyoplasty, the usefulness of scintigraphy has not been studied.

The aim of the study was to assess prognostic value of myocardial perfusion and left ventricular function for evaluation of long term results of cardiomyoplasty in heart failure patients.

Material and method

Patients' population

Twenty two men with chronic coronary artery disease (CAD) aged 32–59 (mean age 47.5 + 1.7) were studied. The diagnosis was verified in everybody in the course of clinical study at admittance, comprising ECG-controlled bicycle stress-test, echo cardiac studies in B, M, and doppler modes, selective coronary angiography and ^{199}TlCl exercise myocardial perfusion scintigraphy (8). Everybody of these patients did had one or more acute transmural myocardial infarctions (AMI) in their history, resulting in aneurysm of left ventricle (LV), in particular, in ten a single myocardial infarction was documented, eight patients — underwent two and four did three episodes of AMI. All the patients demonstrated severe depression of left ventricular pump function with ejection fraction < 40%) and developing cardiac insufficiency (III–IV NYHA).

Surgical treatment

Left-side cardiomyoplasty was performed in all the patients. It comprises the formation of natural biomechanical assistor of left ventricle by mobilisation of latissimus dorsi muscle stimulated by bioregulated pacemaker setup in the mode «1 stimulus per 4 contractions of LV» (6).

Protocol of the study

In all patients 2–4 weeks before and within early (2–4 weeks) and late period (1–10 years) after the operations we carried out planar ^{199}TlCl myocardial perfusion imaging combined with dipyridamole test and also radionuclide angiography.

Thallium-199 imaging

^{199}Tl chloride (produced by Nuclear Physics Institute of the Tomsk Politechnical University) in a dose of 185 MBq was injected at peak heart rate controlled by ECG in the course of dypiridamole stress-test. The imaging study began 10–15 minutes later after the injection of ^{199}Tl. High energy parallel collimator was used for the thallium-199 scans. Scans were obtained in three projections — anterior, 45-degree left anterior oblique and left lateral, each for a fixed time of 6 minutes, using Omega 500 Gamma camera (by Technicare Co., Ohio), acquired into 128 x 128 matrix with 20% wide window centered at 72.5 KeV. Redistribution scans were obtained in 4 hours after exercise imaging. Redistribution images were compensated for decay automatically (8).

Radionuclide Angiography

Radionuclide angiography was performed in patients at rest in supine position. In vivo red blood cell labelling was carried out by anterocubital intravenous injection of stannous pyrophosphate kit (TCK-7 by CIS, or Pyrphotech, by Diamed) followed by 720 MBq of Technetium-99m as fresh eluate obtained from commercial Mo-99 generator (Izotop Inc., Moscow) 10 minutes later.

Five minutes after injection of the radionuclide, the camera was positioned in a 40–45° left anterior oblique projection with 10–15° of caudal tilting so as to separate the right and left ventricles. Acquisition matrix was 64 x 64, and each cardiac cycle was proportionally divided into 16 frames triggered by a R-wave of the electrocardiogram. Data were collected with acquisition of over 2 000 000 counts. Each study acquired in this way was processed in order to determine the left ventricular ejection fraction (EF) and to analyse the regional kinetic abnormalities using a functional imaging technique.

Radiometry of blood samples from coronary sinus

In 6 patients 6–18 months later after CMP the study of coronary flow was performed using Angioscop 33D (Siemens Medical, Erlangen). 370 mCi of 99m-Technetium-labelled human serum albumin (TCK-2 by CIS) were injected into selective catheter placed into left thoracodorsalis artery in a volume as small as 2 ml using automatic high-pressure injector. Synchroneously we took out 2 ml blood samples every 2 sec from catheter placed into coronary sinus of the patient, in the course of 40 sec after selective intraarterial injection. Blood samples taken from coronary sinus were counted using a well-counter system (Tracor Analytic) and time-activity curve was plotted. The same protocol was also performed in four non-operated volunteers with verified diagnosis of coronary artery disease.

Image processing and data analysis

Analysis was performed by two experienced observers, unaware of the identity of the patient. When analysing the perfusion scintigraphy we have employed the following indices: size of reversible perfusion defect (RDS, as a quota of total area of myocardium) size of persistent perfusion defect (PDS, also as a quota of total area of myocardium); ^{199}Tl uptake count in reversible (RDU) and persistent perfusion defects (PDU) were quantified. Integral indices of severity of reversible (RDII) and of persistent perfusion defects (PDII), were calculated employing uniform formula (9):

$$DII = \frac{NU - DU}{NU} DS$$

Here
DII — integral index of perfusion defect,
DU — ^{199}Tl uptake in perfusion defect, either PDU or RDU,
NU — the minimal level of ^{199}Tl uptake in normal myocardium,
DS — size of the perfusion defect.

Coronary fraction (CF) of ^{199}Tl accumulation was calculated as fraction of the injected dose absorbed by myocardium, i.e. as ratio of myocardial count to injected dose of ^{199}TlCl. The index „lung/myocardium" (L/M) was calculated as the ratio of mean count per pixel over the region of left lung to the of mean count per pixel over the whole region of myocardium in the anterior projection.

Statistics

Results were expressed as means with standard deviation shown. Comparisons of data were carried out using one-way analysis of variance and the paired and unpaired t test as appropriate.

Results

Clinical parameters

After a year of follow-up all patients were divided into two groups. The first group included 11 patients with improvement in clinical status, which was observed during 1.5–2 months after surgery: improvement cardiac insufficiency (up to I–II degree), increase in tolerance exercise mean on 30–40 Watt (in 5 patients on 100 Watt), decrease in attack of angina pectoris and sublingual nitroglycerine dose.

The second group included 11 patients with no or negative clinical effect. All of them demonstrated deterioration of cardiac insufficiency, decrease in physical work capacity. Two patients of second group died within 3–6 months after cardiomyoplasty, and four did during two-year period after cardiomyoplasty. The cause of death in two cases was myocardial infarction, sudden cardiac death in three cases and in one it was ischemic stroke.

Dipyridamole myocardial perfusion imaging

Before cardiomyoplasty all patients had great persistent perfusion defects as result of scar or aneurysm. Patients of the first group before operation revealed two times smaller PDS than patients of the second group (Table 1). Mean values of PDS after cardiomyoplasty remained unchanged in both groups. Analysis of PDII revealed more prominent differences between groups: before the cardiomyoplasty PDII in the first group was 2,4 times more than in second one.

Before the cardiomyoplasty we found reversible defect in 10 (91%) patients of the first group and in 5 (45.5%) patients of the second group. Before the surgical treatment the patients who later demonstrated improvement in clinical status after cardiomyoplasty did have greater size of reversible defect in comparison with patients of the second group. We observed significant decrease in size of the reversible defect in the first group of patients already during early post-operative period (in 2 patients defects disappeared entirely). In patients with no or negative clinical effect mean values of reversible defect's size were not changed at early post-operative period and they insignificantly decrease in remote period after cardiomyoplasty. Same differences between groups were observed in IIRD: before surgery IIRD in the first group was two times more than in second group. But only IIRD of first group of patients considerable decrease after cardiomyoplasty.

In second group CF was 1.4 times higher in comparison to first group, as result of myocardial hypertrophy in patients with bad prognosis. No considerable change in the coronary fraction of thallium-199 was demonstrated at early or later periods after the surgery in both groups of patients. In a year after cardiomyoplasty considerable increase in CF was observed in second group of patients.

There were no considerable differences between two groups in Il/m level before and in one month after cardiomyoplasty. In patients of the group with good clinical effect in one month and a year after cardiomyoplasty considerable reduction in thallium lung

Table 1. Radionuclide parameters before and after cardiomyoplasty

Radionuclide parameters	Groups of patients	Before CMP	4 weeks after CMP	1 year after CMP
PDS	Group 1 n = 11	20.9 + 3.6	20.3 + 4.3	20.6 + 4.4
(%)	Group 2 n = 11	40.9 + 3.1**	35.9 + 2.7*	41.7 + 2.7*
PDU	Group 1 n = 11	31.9 + 4.1	31.6 + 4.4	33.0 + 4.0
(%)	Group 2 n = 11	27.6 + 2.5	29.7 + 3.2	29.3 + 2.5
IIPD	Group 1 n = 11	9.8 + 2.2	9.1 + 2.1	8.6 + 2.3
(%)	Group 2 n = 11	23.0 + 3.0**	19.0 + 3.0*	22.0 + 3.1*
RDS	Group 1 n = 10	16.1 + 2.9	8.3 + 1.9#	8.9 + 1.7#
(%)	Group 2 n = 5	7.0 + 3.4*	7.0 + 2.1	3.5 + 1.7*
RDU	Group 1 n = 10	33.1 + 3.6	36.5 + 6.3	37.0 + 5.0
(%)	Group 2 n = 5	17.1 + 6.0*	24.6 + 6.0	27.8 + 10.1
IIRD	Group 1 n = 10	6.4 + 1.3	2.0 + 0.6#	3.2 + 1.0#
(%)	Group 2 n = 5	3.0 + 1.6*	2.6 + 0.9	1.5 + 1.0
Il/m	Group 1 n = 11	0.65 + 0.04	0.60 + 0.02	0.59 + 0.02
	Group 2 n = 11	0.71 + 0.04	0.64 + 0.04	0.73 + 0.03*
CF	Group 1 n = 11	2.38 + 0.18	2.27 + 0.12	2.27 + 0.11
%	Group 2 n = 11	3.22 + 0.11*	3.09 + 0.10*	4.00 + 0.32*#
EF	Group 1 n = 11	33.1 + 2.3	32.6 + 3.0	34.8 + 2.8
%	Group 2 n = 11	19.9 + 1.8**	22.1 + 2.0*	19.8 + 2.0**

Group1 — patients with improvement in clinical status; Group 2 — patients with bad clinical effect; CMP — dynamic cardiomyoplasty; Il/m — index „lung/myocardium"; PDS — persistent perfusion defect size; PDU — ^{199}Tl uptake in persistent perfusion defects; PDII — integral index of persistent perfusion defects; RDS — reversible perfusion defect size; RDU ^{199}Tl uptake in reversible perfusion defects; RDII — integral index of reversible perfusion defects; CF — coronary fraction of ^{199}Tl accumulation; Il/m — index „lung/myocardium"; n — number of cases; EF — left ventricular ejection fraction; * — $p < 0.05$; ** — $p < 0.01$: Group 2 compared with Group 1; # — $p < 0.05$: before cardiomyoplasty compared with after.

accumulation was found only in 3 patients with significant increase in thallium-199 lung uptake before operation (Figure 1). But in a year after cardiomyoplasty differences in Il/m between groups were shown significant.

Catheterisation of a. thoracodorsalis and coronary sinus blood sampling

Radioactivity of blood samples taken from coronary sinus after 99mTc-HSA injection show the increase in the rate of scintillation count in blood samples by 37–48% over background values at the 10–12th sec after injection of radioactivity into a.thoracodorsalis. Repeated rise up to 83% was exhibited at the 18th sec of the study (Figure 2a). Control patients revealed the increase in count of blood samples beginning only from the 18th sec (Figure 2b).

Radionuclide angiocardiography

Before the surgical treatment the patients with improvement in clinical status after cardiomyoplasty demonstrated greater ejection fraction in comparison with patients of the second group ($p < 0.01$). From 9 patients with preoperative EF less then 25% only two had improvement in clinical status after surgery. Other 7 patients had cardiac events, including five deaths.

In the first group of patients only two of them had considerable increase in ejection fraction in one year after cardiomyoplasty. In the second group of patients ejection fraction remained not changed in postoperative period.

Discussion

During the last years there were the some issues about opportunities of surgical treatment of patients with severe cardiac insufficiency by a cardiomyoplasty method using the latissimus dorsi muscle (3, 4, 7). It was shown the positive clinical and haemodynamic effects of operation, which were explained by improvement of left ventricular contractility and reduction of a degree it dilatation (4, 5).

However, only the effect of muscular heart assistance cannot give full explanation of the expressed improvement in a clinical condition and positive changes of haemodynamical parameters

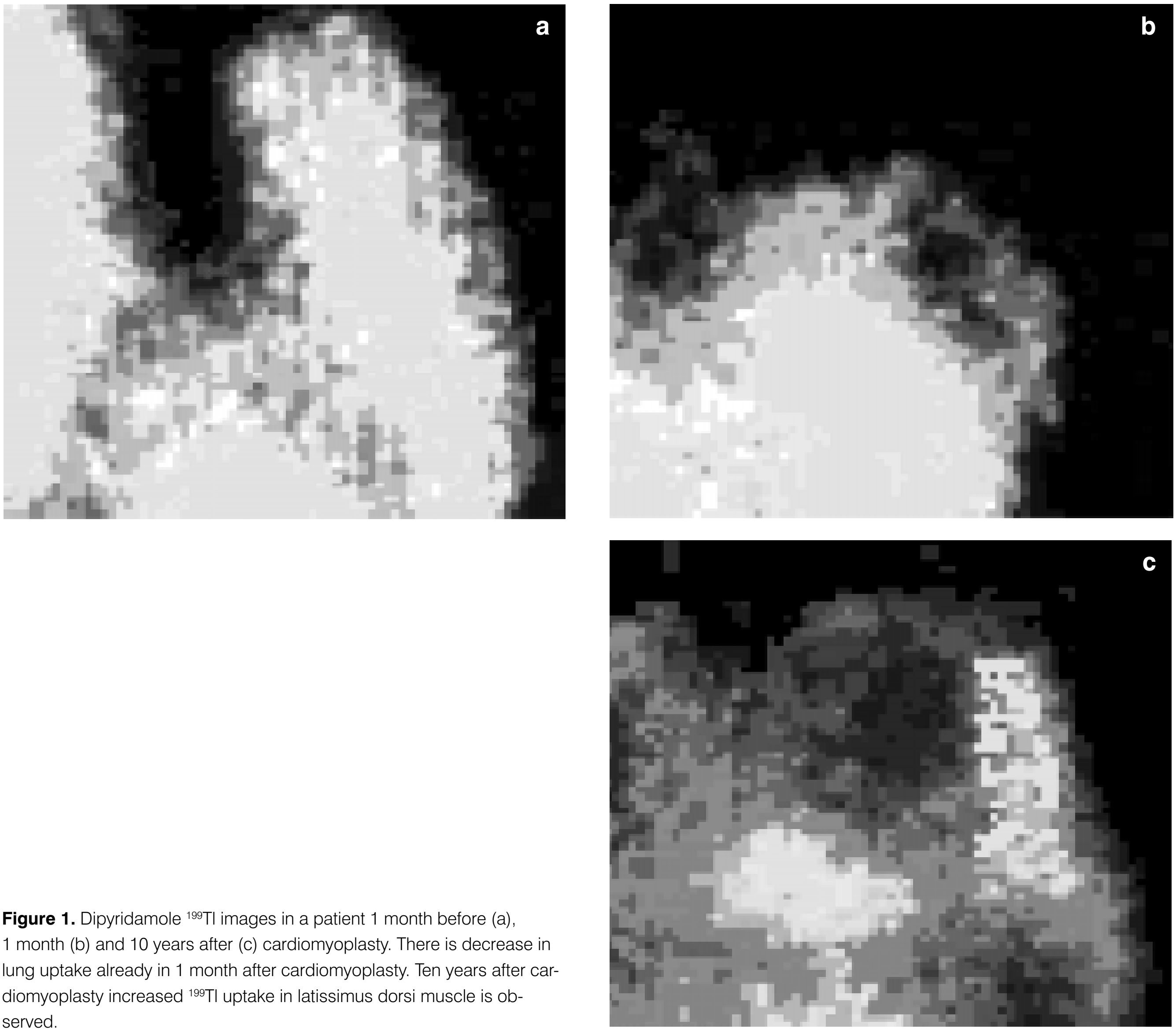

Figure 1. Dipyridamole ^{199}Tl images in a patient 1 month before (a), 1 month (b) and 10 years after (c) cardiomyoplasty. There is decrease in lung uptake already in 1 month after cardiomyoplasty. Ten years after cardiomyoplasty increased ^{199}Tl uptake in latissimus dorsi muscle is observed.

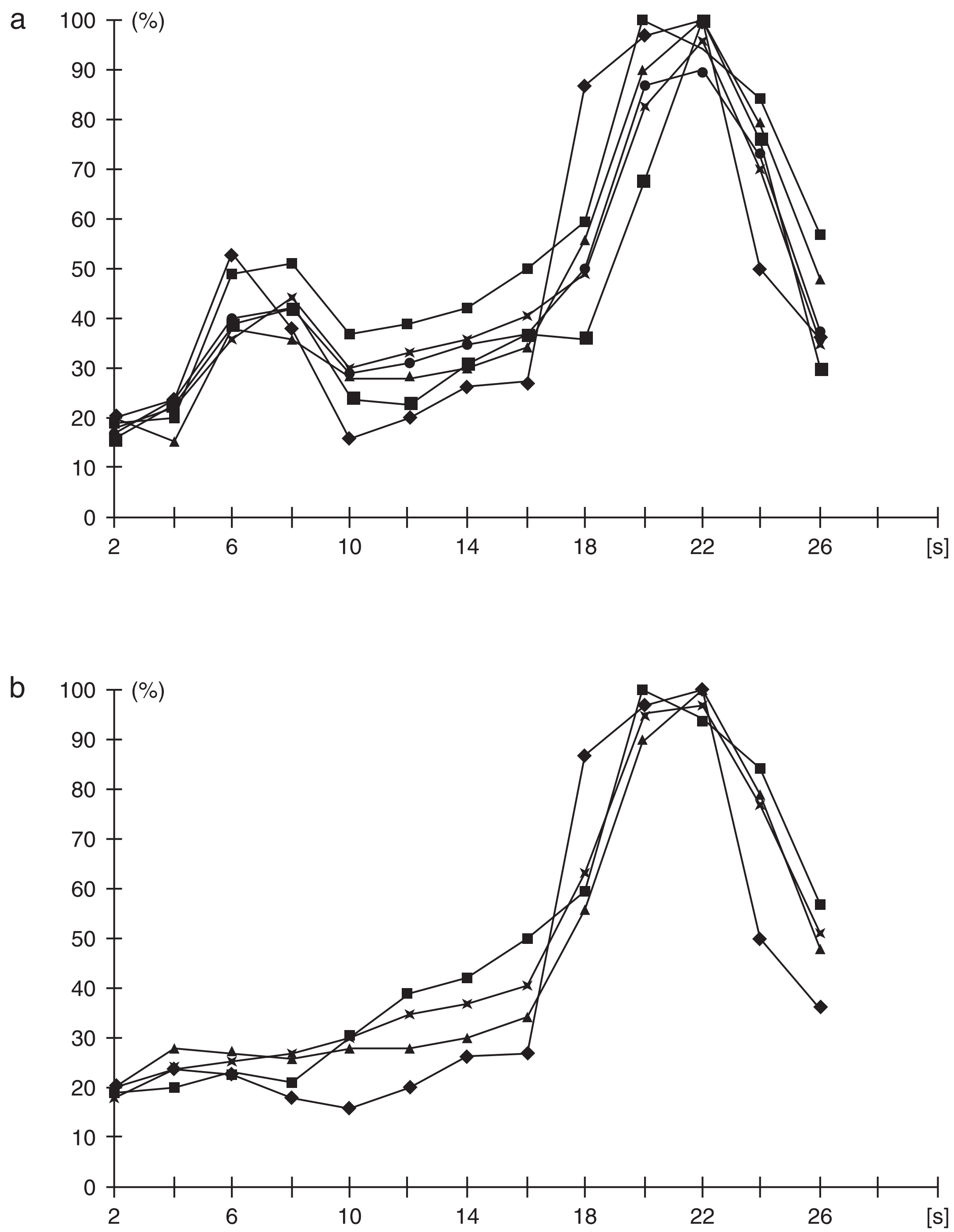

Figure 2. Time-activity curves of dynamics of ^{99m}Tc input into coronary sinus after its injection in a. thoracodorsalis in patients after cardiomyoplasty (a) and non-operated volunteers (b).

in patients after cardiomyoplasty (10). Such improvement can be connected with increase in myocardial blood flow as the result of nondirect «microvascular» revascularization. Methods of indirect revascularization have begun to develop earlier in 1930–1940 years of this century. Most popular of variants of such approach was the model of aseptic pericarditis for stimulation of angiogenesis (11).

Cardiomyoplasty is always concomitant with the development of aseptic inflammation in the area of mechanical contact of latissimus dorsi muscle with myocardium (12). It is the assumptions has confirmed weak diffuse 99mTc-pyrophosphate uptake in the myocardium in all patients in early period after cardiomyoplasty.

Besides in 1993 Mannion J.D. et al (13) have published experimental data, according to which acute and chronic stimulation of m.latissimus dorsi after cardiomyoplasty increase in myocardial blood flow, accordingly, on 35% and 27%. Simultaneously authors have shown that blood flow in chronically ischemic myocardium increase as result of collateral flow of a skeletal muscle. Thus according to the data Brown M. et al (14), electrical stimulation of a skeletal muscle increase in density of a capillary in the muscle.

As electrostimulated cardiomyoplasty represents a combination of mechanical influence on myocardium by m.latissimus dorsi and effect it electrostimulation, it is probable, that both these influences improve in myocardial blood flow.

Such improvement especially was expressed in reversible defects, which reflect areas of viable myocardium.

The improvement in myocardial perfusion in patients after cardiomyoplasty, first, may be results of reduction of left ventricular end-diastolic volume as result of assistance effect of latissimus dorsi muscle (15) and decrease in compression of subendocardial coronary vessels.

Second, decrease or disappearance in perfusion defect size may be results of indirect revascularization of myocardium because of formation of anastomoses between the latissimus dorsi muscle and the myocardium. Anatomical and angiological studies indicated well developed nervous-vascular supply of m. latissimus dorsi (16). For this hypothesis testified the fact that in patients after cardiomyoplasty nuclide appeared in coronary sinus at the 10–12th seconds after injection into artery thoracodorsalis appears in coronary sinus through anastomoses between the latissimus dorsi muscle and the myocardium. The time of appearance of the second wave of rise gamma-counting in blood samples from coronary sinus reflects the repeated entry of radiopharmaceutical in myocardium after recirculation.

The extent of irreversible myocardial damage (persistent defect size) and the left ventricular ejection fraction are the major determinants of prognosis in patients after myocardial infarction (17,18,19). These dates are confirmed in our investigation: in patients with improvement in clinical status after CMP persistent defect size was two times less and the left ventricular ejection fraction was two times high then in patients with bad clinical effect.

The ll/m is one of the most sensitive parameters of LV dysfunction development (20, 21). The increase in thallium uptake in the lungs is the result of high pulmonary capillary pressure because of LV insufficiency (22). The decrease in the ll/m in the patients after cardiomyoplasty indicates to the decrease in pulmonary congestion and is indirect sign of the improvement in pump function of the heart.

There are some reports on the direct dependence between thallium accumulation in myocardium and the degree of its hypertrophy (23). So the decrease in CF value is found to be a favourable sign.

So radionuclide methods provide useful information for prognostic evaluation of cardiomyoplasty long-term results. The predictors of heart failure aggravation or death after cardiomyoplasty are severe reduction of LV function, large myocardial scar and high-level of CF as result of myocardial hypertrophy.

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