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The Role of Exercise Test After Percutaneous Coronary Intervention

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1. Introduction

Cardiovascular diseases is the most common cause of death worldwide and coronary artery disease (CAD) still remains the leading cause of death in Latvia. The incidence of CAD in Europe is 20-40 thousands per one million people (Fox et al., 2006). According to the data of Health Statistics and Medical Technology Agency in Latvia 16 079 individuals died due to cardiovascular disease in 2009 (54% of total mortality rate). Mortality rate due to CAD is three times higher in Latvia than average in European Society in individuals group younger than 64 years. The loss of productive years of life has negative influence neither to private, nor public economical sector.

The common electrocardiographic finding on exercise stress test, which can be evident for CAD, is recurrent, load-induced ST-segment depression. It points to myocardial ischemia in patient with significantly narrowed coronary arteries in status of progressive oxygen demand, while at rest blood flow is not limited. The sensitivity of the stress test increases along with severity of disease. It is possible correctly to identify the patients with proximal several arteries disease or left main artery stenosis performing a standard exercise stress test, nevertheless it gives unsufficient prognostic information in patient with less severe obstructive disease.

Progression of coronary artery restenosis after percutaneous coronary intervention (PCI) is a clinical "final" result, which reflects complex pathophysiological process, including different combinations of residual coronary stenosis and neointimal proliferation. Unfortunately, the set of clinical symptoms is uncertain criteria for detection of coronary artery restenosis, patient's complaints could be similar to non-coronary pain post revascularization ('false-positive' symptoms), at the same time – "silent" ischemia may be present in many patients ('pseudo-negative' symptoms). Restenosis is observed in 25% of cases (data of balloon angioplasty) in asymptomatic patients with documented ischemic changes on exercise test (Bengston et al., 1990).

Discussions are still extended, whether early performed strategy of exercise test is with prognostic value for clinical events in patients after PCI. There are no conclusive results about association of complaints' limited exercise tests and long-term prognosis early after PCI.

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CAD patients with left main coronary artery (LM) stenosis is another one group of interest, and there is stable introduced invasive PCI treatment and stent implantation for this patients' group. It is important to evaluate the efficacy of new treatment, outcomes and following risk of cardiovascular events. Patients after LM PCI are at higher risk of thrombosis and restenosis, angiographic follow-up of these patients is expensive enough, with additional radiation dose and contrast amount for patients. Thus, high attention is focused on non-invasive investigation methods in patients with CAD.

The results of recent studies should be taken into account, that the higher risk of cardiovascular events is observed in patients with unstable atheromatous plaque, even in case if stenosis of coronary artery is not significant (in segment of this plaque location). Exercise test in this situation should be evaluated more precisely and seriously in order to improve the prognostic value of the method. The question is – whether exercise test (with electrocardiogramm (ECG)) can be used in evaluation of prognostic criteria for patient along with possibility to detect obstructive lesion of coronary arteries with a goal to decrease effectively the risk of sudden death and serious coronary events?

2. Objective of the study

The aim of the study was to evaluate effectiveness of medical and invasive treatment in patients with CAD after PCI by performing physical test and proving test prognostic value of cardiovascular events - clinical (myocardial infarction, recurrent hospitalization, cardiac death) and angiographic (restenosis and/or new stenosis of coronary arteries) events.

The main goals were defined:
1. to define specific criteria of exercise stress test for possible restenosis diagnostics;
2. to develop the algorhythm for the patients' functional status evaluation after PCI, as well as for evaluation the possibility of coronary artery stenosis correction (intervention);
3. to create the prognostic model, which can help to evaluate and reveal the patients with unfavorable long-term outcomes or unsatisfactory treatment results timely;
4. to integrate targeted follow-up patients' programme.

3. Materials and methods

The follow-up programme was developed in 1990 in the Latvian Centre of Cardiology and surveyed patients with CAD which underwent PCI treatment method.

The programme has been proceeded since the first patient was treated with the method of coronary angioplasty in Latvia.

The study was implemented from January, 2004 till January, 2009. The patients with established CAD (based on coronary angiography data) were included in the study. The patients underwent invasive treatment – PCI in the Latvian Centre of Cardiology. The number of performed PCIs during mentioned period of time – 16 109. All patients were informed about possibility to be included in the follow-up programme.

The data of 7 300 patients with CAD and complete 24-months follow-up after PCI were included in the study.

The patients were observed in defined follow-up periods of time after PCI by performing exercise stress test (veloergometry – bicycle ergometer exercise test):

- 1-3 months after invasive treatment – immediate risk evaluation and correction of medical treatment;
- 3-6 months after PCI – distant period – determination of possibility of restenosis and correction of medical treatment;
- 12-24 months after PCI – late period – determination of possibility of restenosis and correction of medical treatment.

Control coronary angiography was performed based on indications, which included following patients groups:

- patients with new-onset angina proved by ischemic changes on ECG during exercise stress test;
- patients without typical coronary complaints, but with registered ischemic changes on exercise test ECG;
- patients with non-sufficient information on exercise test in order to evaluate indications for coronary angiography, therefore exercise test with additional visualization method was performed – myocardial perfusion scintigraphy.
- Patients without indications for control coronary angiography underwent the correction of medical treatment (if it was needed) and were included in the next scheduled exercise test control.

Large patients group was revealed during the follow-up process – patients without typical coronary chest pain but with registered ischemic changes on ECG during exercise test. These patients were defined like „silent" ischemia patients group which has the higher risk of cardiovascular events and worse prognosis.

All the patients of this group underwent control coronary angiography and were divided into different groups according to angiographic finding:

- patients with restenosis of coronary artery (in previously repaired segment);
- patients with new stenosis of coronary artery;
- patients without restenosis or new stenosis on angiographic finding.

Patients with restenosis or new stenosis underwent PCI and were included in consequent follow-up plan and medical treatment correction. Patients without restenosis or new stenosis continued previously defined follow-up plan.

The analysis of used medications groups was performed because of medical treatment correction during follow-up process. It was dependent on obtained data during exercise test (e.g., arterial blood pressure and/or heart rate, compliance of these parameters changes to physical load, etc.). Medications after performed PCI (recommended on discharge) and in one year follow-up period were compared.

Very high risk patients were included into the separate group analysis (400 patients) with LM stenotic lesion. All patients were informed about possibility to be included in the 24 months follow-up plan. 133 patients have accomplished complete follow-up programme (1, 3, 6, 12 and 24 months after PCI). In order to define precise indications for control coronary angiography, myocardial perfusion scintigraphy with physical or pharmacological test was performed in this patients group (94 examinations). This examination was performed in 12-24 months period after PCI in patients without indications for control angiography.

Phone follow-up survey was also performed in this patients group in order to clarify possible coronary events – hospitalization, myocardial infarction or death. Patients groups with and without performed follow-up programme were compared.

SPSS 12.0.1. version was used for statistical analyses. Baseline characteristics were summarized as frequencies and percentages for categorical variables and as means and SDs for continuous variables. Analyses were performed using χ^2/Fisher exact test for categorical variables and Student t test/ *ANOVA* method for continuous variables. The correction with *Tukey* test was performed in *post hoc* analysis for multiple comparisons correction. Differences were considered statistically significant at $p<0.05$.

3.1 Exercise test – veloergometry

Exercise stress test – veloergometry was performed in sitting or reclining position in patients of the study, depending on used bicycle ergometer (in sitting position – veloergometer „Ergometrs 900" and since April, 2008 – veloergometer „e-bike" for test performing in reclining position). Modified Bruce protocol was used during exercise test – standardized load grading programme according to the protocol accepted by Latvian Cardiology Society:

• first degree – three minutes with 50 Watt (W) load;
• second degree – three minutes with 100 W load;
• third degree – three minutes with 150 W load;
• fourth degree – three minutes with 200 W load;
• fifth degree – three minutes with 250 W load.

Maximal allowed load was defined as 250 W. In specific cases (if it was necessary) or according to patient condition (patients with chronic heart failure) the protocol was accommodated individually – the load was increased for 25 W every three minutes with the beginning of second degree of the test protocol.

ECG was monitored continuously during the test time, increasing the load till the goal heart rate was achieved – 85 % of maximal heart rate according (appropriate) to concrete age or the load was limited by symptoms of ischemia.

Following indications were defined for the test discontinuation:

a. typical increasing chest pain and/or ST-segment changes on ECG (ST-segment depression > 2 mm – as a relative indication for the test interruption, ST-segment depression > 3 mm – as a absolute indication for the test interruption);
b. ST-segment elevation > 1 mm (if pathologic Q-wave is not present on ECG at rest);
c. arrhythmias (supraventricular tachycardia, multiple politope and pair premature beats (extrasystoles));
d. systolic blood pressure decrease (> 10 mmHg compared with onset blood pressure level), despite of the load increase;
e. hypertension (> 250 mmHg systolic and > 115 mmHg diastolic blood pressure);
f. central nervous system symptoms (ataxy, weakness, syncope);
g. signs of decreased perfusion (cyanosis);
h. fatigue, dyspnoe, leg cramps, claudication;
i. complete left His bundle branch block;
j. achieved submaximal heart rate;
k. patient's request to terminate the test;
l. technical problems.

Exercise test was defined as positive, if there were registered changes on ECG associated with myocardial ischemia:

• horizontal or downslopping ST-segment depression or elevation, greater than or equal with 1 mm 60 msec after QRS complex;

- especially, if these changes were associated with chest pain, appeared at lower load (< 75 W) and lasting for more than 3 minutes after load was finished.

Following parameters were analized:

a. Electrocardiographic parameters:
   - maximal ST-segment depression;
   - maximal ST-segment elevation;
   - configuration (shape) of ST-segment depression (horizontal, downslopping, upslopping);
   - the number of leads ST-segment changes registered in;
   - duration of ST-segment changes at the test phase of rest (after load discontinued);
   - ST/pulse index;
   - ventricular arrhythmias induced by exercise;
   - the time to ST-segment changes appeared at.

b. Hemodynamic parameters:
   - maximal heart rate;
   - maximal systolic blood pressure;
   - maximal double rate-pressure product (Robinson index) (maximal heart rate multiply by maximal systolic arterial pressure, divided by 100)
   - total exercise (load) time;
   - hypotension (arterial pressure decrease under the blood pressure level before load was started);
   - chronotropic incompetence.

c. Symptomatic parameters:
   - angina provoked by load;
   - load-limiting symptoms;
   - time to the onset of angina.

Following information was included in the protocol of veloergometry (accordingly the methodological guidelines):

- maximal load;
- total time of the load;
- heart rate at the beginning;
- initial systolic and diastolic blood pressure;
- maximal heart rate;
- maximal systolic and diastolic blood pressure;
- double rate-pressure product;
- the intensity and quantity of ECG changes;
- recovering period after load;
- patient's complaints;
- test termination reasons;
- tolerance of the exercise (load) (high, satisfactory, lowered, low);
- load-limiting factors.

The data mentioned above (collected from veloergometry test protocols) were included into the total database of the study.

There were no any complications registered during exercise test perfoming – myocardial infarction, life-threating arrhythmias or death.

Myocardial perfusion scintigraphy was perfomed in patients at the case of embarrassing interpretation of ECG, and in order to evaluate the indications for control coronary angiography.

Myocardial perfusion scintigraphy was also performed in patients after LM PCI.

3.2 Coronary angiography and PCI

The information about atherosclerotic lesions degree of coronary arteries was collected and included into the total database of the study (based on coronary angiography finding). Follow-up period results were included – data of coronary angiography finding (restenosis and/or new stenosis of coronary artery(-ies)), acute coronary events (recurrent hospitalization, myocardial infarction, coronary artery bypass grafting, recurrent coronary angiography and/ or PCI).

The result of revascularization was defined, basing on the data of coronary angiography finding:

- successful PCI defined as a dilatation of coronary artery stenosis with complete revascularization, if residual stenosis of coronary artery(-ies) does not exceed 50 % (Wenaweser et al., 2008);
- incomplete revascularization defined as a residual stenosis (narrowing of the lumen of artery after performed PCI) greater than or equal with 50 % in any coronary artery (Chalela et al., 2006).

Restenosis of coronary artery at the follow-up period was defined as a narrowing of coronary artery(-ies) lumen greater than or equal with 50 % and progression of coronary artery disease, if new stenosis of coronary artery was diagnosed (Chalela et al., 2006).

4. Results

4.1 Data registry of the patients with coronary artery disease treated with PCI

In total 7300 patients with established CAD and performed treatment with PCI, with complete follow-up programme – 1, 3, 6 and 12 months follow-up visits, were included into the study. The patients underwent physical stress test, correction of used medications plan and doses of drugs, if it was necessary, and the control of risk factors. Control coronary angiography was performed in 2583 patients accordingly the indications.

Indications for performance of control coronary angiography were determined basing on exercise test (13% of cases), restenosis on angiography was detected in 6.4% of the total patients' group.

In the patients' group with left main artery stenosis (LM group) 400 patients were observed, 133 of them worked out complete follow-up program and underwent control coronary angiography. Myocardial perfusion scintigraphy was performed in 98 LM-patients in order to evaluate more precisely the indications for coronary angiography.

In total patients' group 1226 patients (17%) showed coronary complaints, and ST-segment changes on ECG, which could be associated with myocardial ischemia, were observed in 975 patients (13% of total number of patients). According to the indications these patients underwent coronary angiography. In general, angiographically confirmed coronary artery restenosis was diagnosed in 470 patients (6.4%) of all controlled patients' group (7300) (Figure 1.).
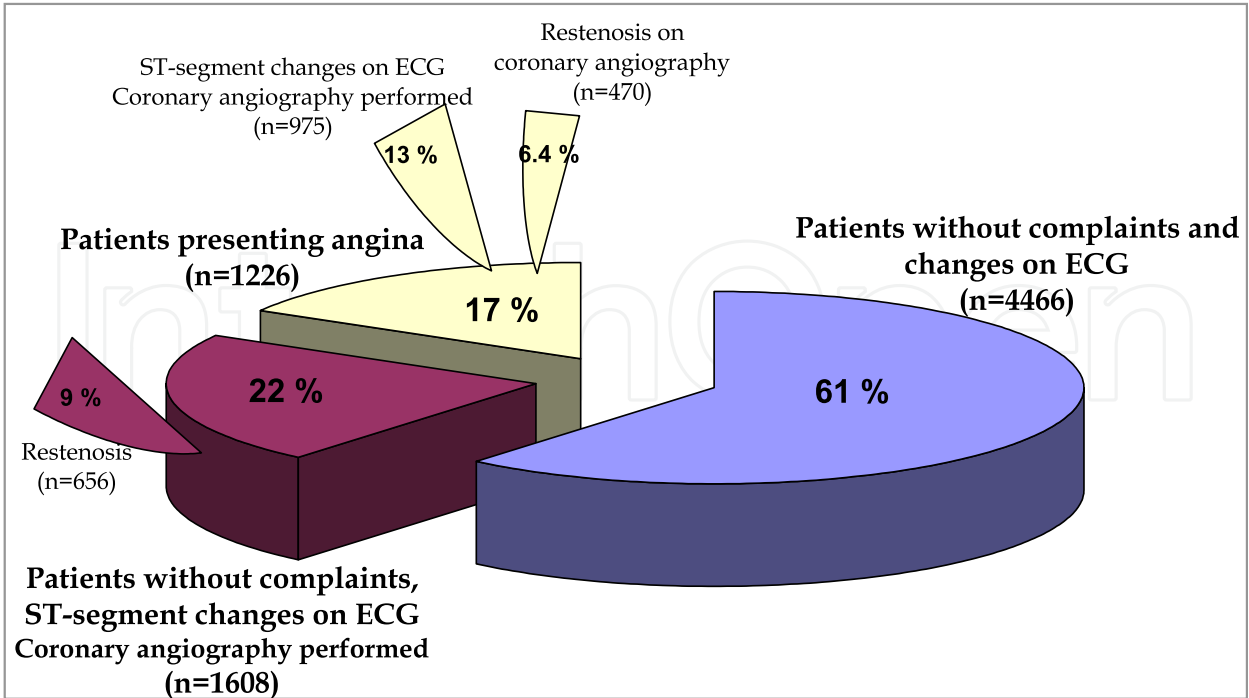
Fig. 1. Results of the follow-up programme (the total number of the patients – 7300).

Exercise test is useful in detection of patients with „silent" ischemia (22%), which have the indications for control angiography; restenosis is found in 9% of this patients group.
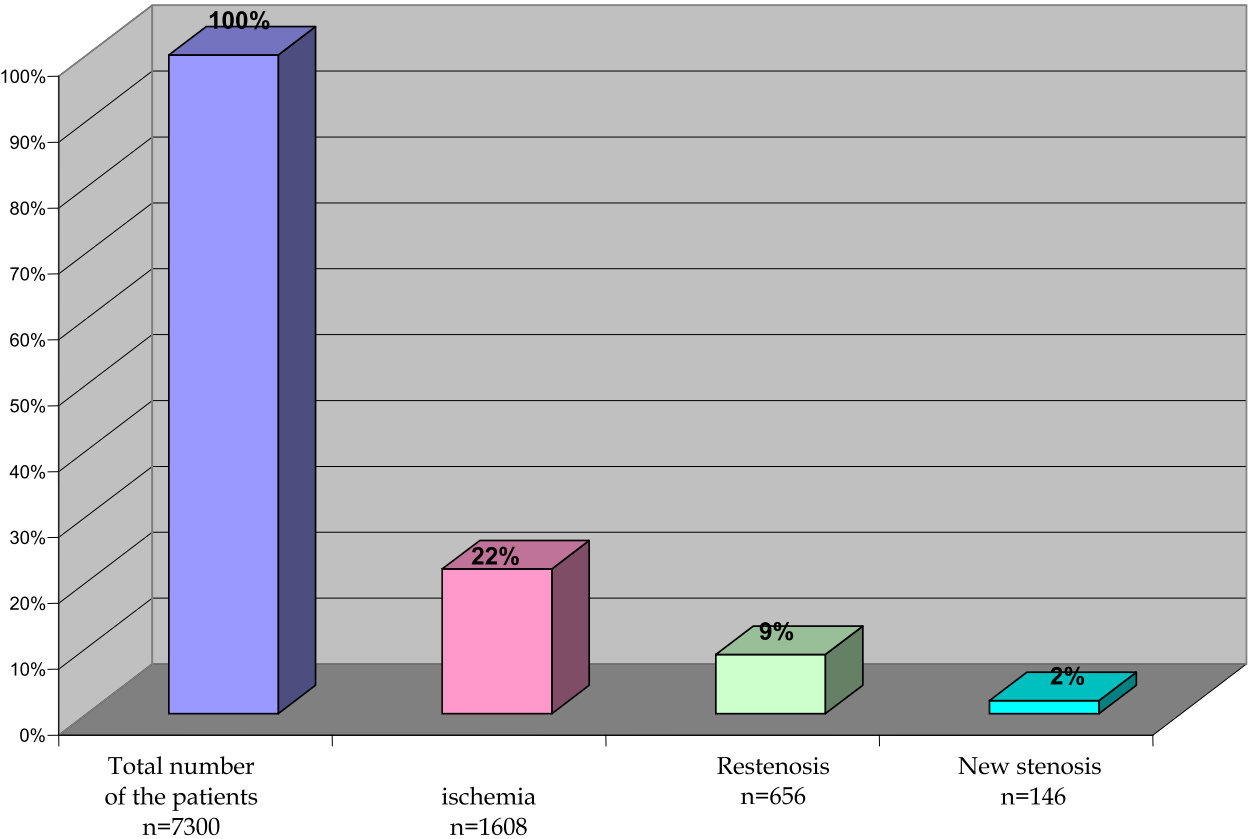

Fig. 2. Patients with „silent" ischemia.

It was observed during patients follow-up, that a separate group of the patients is forming, which is characterized by no complaints of chest pain, but significant ST-segment changes on exercise test ECG (so-called, silent ischemia, poor prognostic factor). These are 22% of the patients (1608 patients), all of them underwent coronary angiography. Restenosis of coronary artery was detected in 656 patients (9% of the total number of patients) and new hemodinamically significant stenosis in coronary artery (> 50% of artery lumen) – in 146 patients (2%) of this patients group (Figure 2.).

4.2 New specific criteria in restenosis diagnostics

Several new specific criteria were found in restenosis diagnostics field additionally to ST-segment ischemic changes on ECG during exercise stress test – reduced load tolerance, decreased maximal heart rate and maximal systolic blood pressure, maximal rate-pressure product (double product) – Robinson index, also increased ST/pulse index (ST/p index).

Differences in parameters derived from exercise tests in patients with restenosis, new stenosis and in patients without restenosis/new stenosis on coronary angiography are shown in Figure 3.
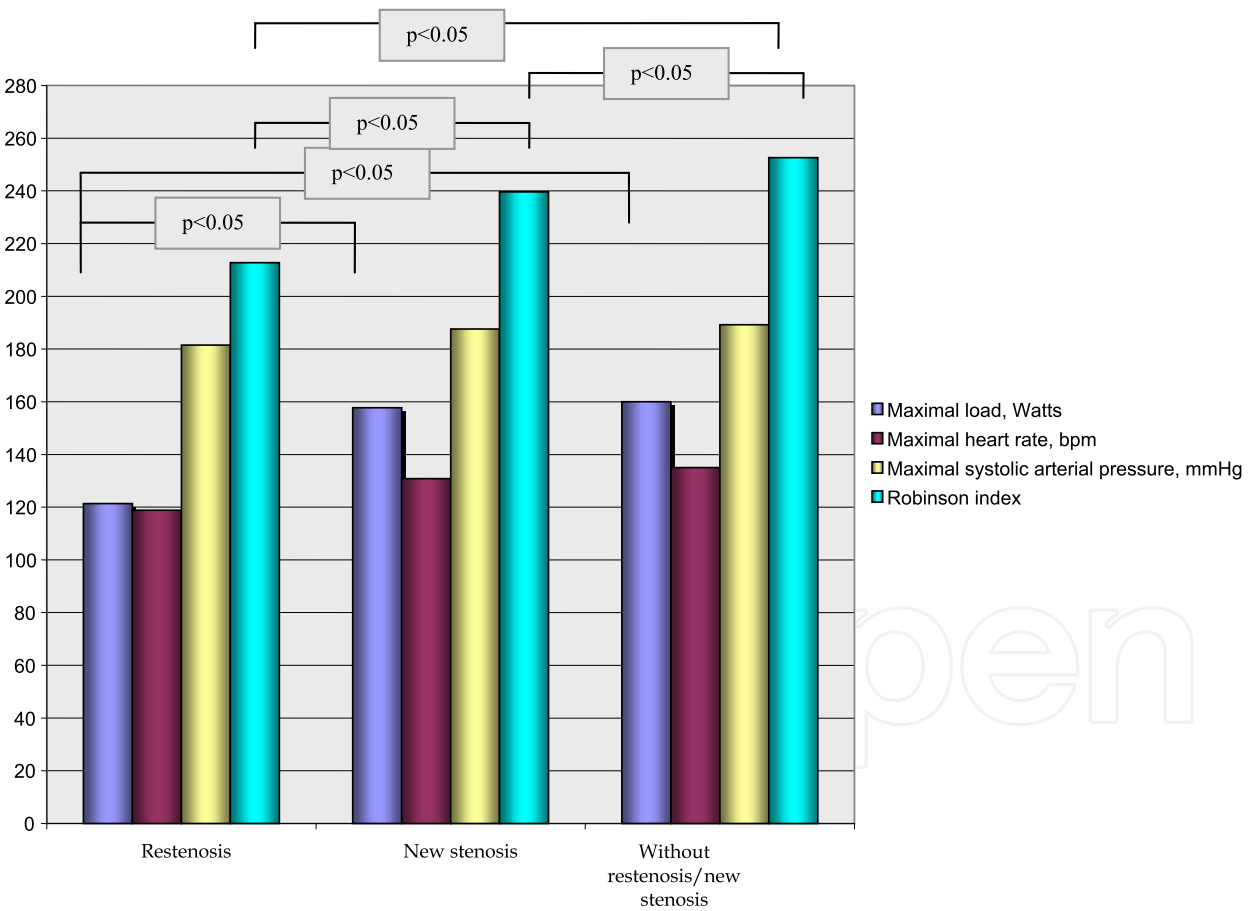

Fig. 3. Results of exercise test in „silent" ischemia patients' group.

Patients with restenosis on coronary angiography (first group) showed definitely ischemic changes on exercise ECG at lower physical load 121.4±33.2 W compared with those patients' group with neither restenosis, nor new stenosis on coronary angiography (third group) – 160.0±25.8 W (p<0.05). Achieved maximal heart rate and systolic blood pressure during

physical load also showed lower parameters in the first group, which is characterized by double rate-pressure product compared in both groups – 212.8±42.9 and 252.62±36.9, accordingly, in the first and third patients' group (p<0.05) (Figure 4.).
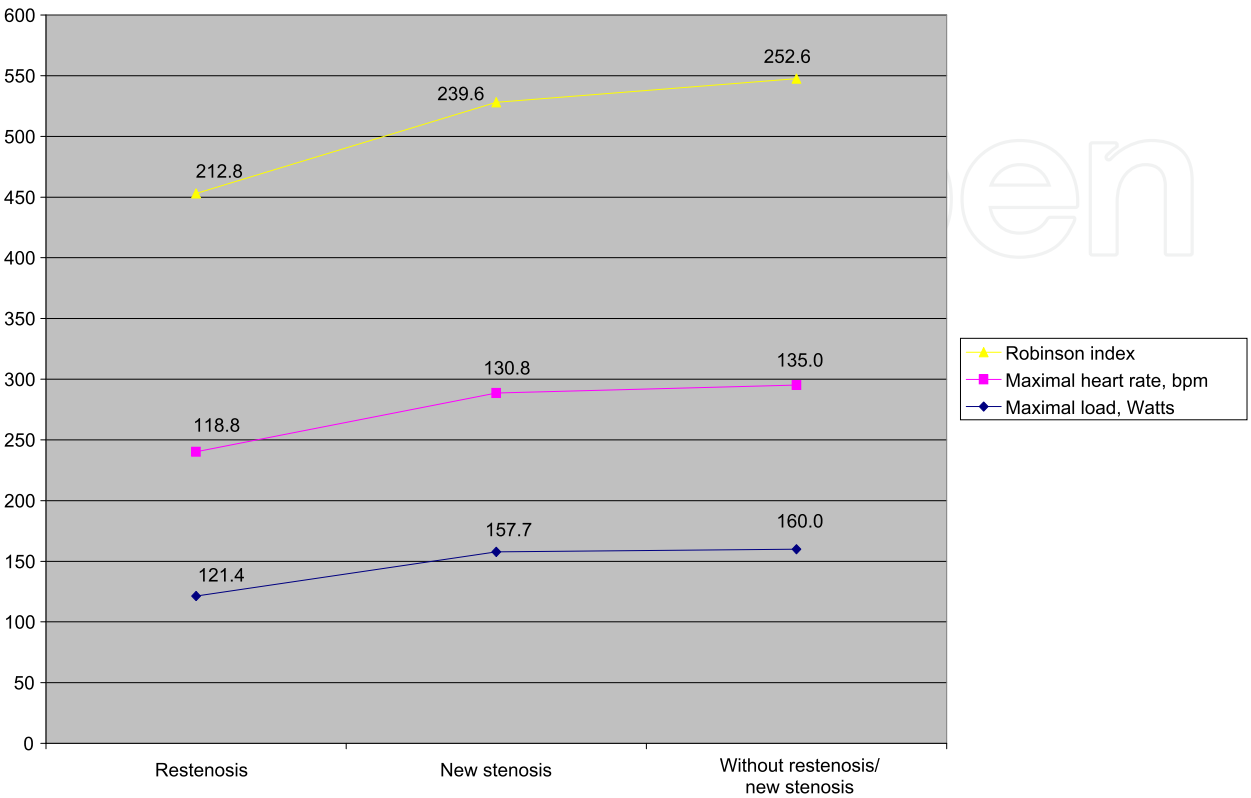

Fig. 4. Analysis of average parameters of veloergometry data (maximal heart rate, maximal systolic arterial pressure, maximal rate-pressure product – Robinson index).

Patients' groups/ Parameter on veloergometry	Maximal physical load, W	Maximal heart rate (when ECG changes appear)	Maximal systolic blood pressure	Robinson index (rate-pressure product)	ST/pulse index
1. Restenosis (n=656)	121.4±33.2	118.8±14.6	181.5±28.3	212.8±42.9	1.3±0.5
2. New stenosis (n=146)	157.7±38.5	130.8±14.9	187.6±30.7	239.6±46.9	1.0±0.3
3. Without restenosis/ new stenosis (n=806)	160.0±25.8	135.0±40.1	189.2±23.3	252.62±36.9	0.9±0.2

Table 1. Analysis of average parameters of veloergometry data (achieved physical load, maximal heart rate, maximal systolic blood pressure, Robinson index, ST/pulse index).

Parameters of neither maximal heart rate, nor maximal systolic arterial blood pressure, and so Robinson index, accordingly, are significantly lower in patients' group witht coronary artery restenosis. The most important parameter, which can reflect patient's risk of restenosis more precisely is ST/pulse index. In restenosis group this parameter is the highest one (1.3±0.5) (Table 1. and 2.).

p value (between patients' groups)	Load, Watts	Maximal heart rate	Maximal systolic blood pressure	Robinson index	ST/pulse index
First and second group	< 0.05	< 0.05	0.012	< 0.05	< 0.05
Second and third group	0.396	0.118	0.48	< 0.05	0.004
First and third group	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05

Table 2. Statistical analysis in comparison of different patients' groups.

4.3 Patients with left main coronary artery (LM) stenosis

The database of the patients with LM stenosis was created.

The group of the patients (n=400) with LM stenosis and performed PCI with drug-eluting stents (DES) was analyzed. In a period of years 2005-2010, 133 patients accomplished complete follow-up programme. Veloergometry was regularly performed in 3, 6, 12 and 24 months after PCI, also control coronarography was performed in 6-12 months after PCI.

Clinical characteristics of the patients:

LM patients group – 80% of the patients are males, with mean age 61.3 ± 9.8 years. The most part of the patients is characterized with most important risk factors of coronary artery disease: in 96% of cases – dyslipidemia, in 77% of cases – arterial hypertension, smoking habits – active smokers (18%) or ex-smokers (30.8%). Previous myocardial infarction – in 45.1% of patients, positive family history (first-line relatives at young age with CAD) in 36.1% of cases (Table 3.).

All the patients underwent LM PCI: 47 patients (38%) underwent solely LM PCI and 86 patients (65%) – also PCI additionally in other artery (Table 4.).

The changes of the parameters registered on exercise test (maximal heart rate, maximal systolic blood pressure and Robinson index) in every follow-up period (independently of the follow-up data on coronary angiography) are showed in Table 5.

4.3.1 Association of veloergometry results with clinical events

Recurrent hospitalization was ascertained for 14 patients (8.3%) in analysis of clinical events in follow-up period. The reasons for recurrent admission to the hospital: in two cases – myocardial infarction, in four cases – chest pain (angina) (three of these patients underwent recurrent coronary angiography), in two cases – next step PCI, in two cases – heart rhythm disorders (in one case – implantation of permanent pacemaker), in one case – stroke, in one case – elevated arterial blood pressure, in two cases – non-coronary reasons for hospitalization.

Characteristics	Prevalence
Gender (males), n (%)	107 (80.5)
Age, mea(±SD)	61.3 (± 9.8)
Dyslipidemia, n (%)	96 (72.2)
Arterial hypertension, n (%)	77 (57.9)
Diabete mellitus, n (%)	11 (8.3)
Smoking status:	
Active smoker, n (%)	24 (18.0)
Ex-smoker, n (%)	41 (30.8)
Non-smoker, n (%)	51 (38.3)
Positive family history, n (%)	48 (36.1)
Prior myocardial infarction, n (%)	60 (45.1)
Prior PCI, n (%)	26 (19.5)
Prior coronary artery bypass grafting, n (%)	7 (5.3)

Table 3. Clinical characteristics of the patients (demographic parameters and risk factors of coronary artery disease) (n=133).

Characteristics	Prevalence
Coronary artery disease:	
One-vessel disease, n (%)	51 (38.3)
Two- vessel disease, n (%)	54 (40.6)
Three- vessel disease, n (%)	28 (21.1)
Complete/incomplete revascularization, %	40/27
PCI LM only, n (%)	47 (38.0)
PCI LM and other artery:	47 (35.3)
PCI LAD, n (%)	
PCI LCx, n (%)	26 (19.5)
PCI RCA, n (%)	14 (10.5)
PCI RIM, n (%)	4 (3.0)
PCI D_1, n (%)	3 (2.3)
PCI M_1, RPL, RPD, n (%)	1 (0.8)

LM–left main coronary artery; *LAD*–left anterior descending artery; *LCx*–left circumflex artery; *RCA*–right coronary artery; *RIM*–ramus intermedius; *D_1*–first diagonal branch; *M_1*–first marginal branch; *RPL*–right posterolateral branch; *RPD*-right posterodiaphragmal branch.

Table 4. Caracteristics of angiographic and PCI data of the patients (n=133).

Data of exercise test/ follow-up period	1-3 months	3-6 months	6-12 months	12-24 months	>24 months
Maximal heart rate (bpm ± SD)	118 ± 16	122 ± 17	121 ± 16	119 ± 15	119 ± 15
Maximal systolic blood pressure (mmHg ± SD)	180 ± 31	181 ± 29	182 ± 29	183 ± 31	184 ± 32
Robinson index(max heart rate x max systolic blood pressure/100) ± SD	213.27±51.02	220.93±52.55	221.55±45.9	217.84±47.68	219.32±48.46

Table 5. Mean values of parameters analyzed on exercise test follow-up (maximal heart rate, maximal systolic blood pressure, Robinson index).

Indications for control angiography were defined according to ST-segment ischemic changes on ECG and/or typical patients' complaints during exercise test.

Control angiography in follow-up period was performed in 33.8% of cases – 3-6 months after PCI, in 36.8% and in 10.5% of cases – 6-12 months and 12-24 months after PCI, respectively.

4.3.2 Analysis of the results of control exercise tests (1-3 and 3-6 months after PCI) and coronary angiography

There was no significant difference between patients group with LM restenosis and/or other coronary artery restenosis on control coronary angiography and patients group without diagnosed restenosis, analyzing maximal achieved physical load in early follow-up period (control exercise test performed 1-3 and 3-6 months after PCI).

Statistically significant difference (in maximal achieved physical load analysis) was observed comparing with the patients group with new coronary artery stenosis on control coronary angiography: these patients achieved lower maximal load on 1-3 months control exercise test – 90 ± 17 W vs. 129 ± 26 W, accordingly (p=0.027).

There was no significant difference observed between patients with and without LM restenosis (or other artery restenosis) in analysis of achieved maximal heart rate during exercise test 1-3 and 3-6 months after PCI, also between patients groups with and without diagnosed new artery stenosis on coronary angiography (Table 6.).

	Maximal heart rate (mean ± SD)				
Exercise test control (months after PCI)	'Restenosis' group	Number of the patients	'Non-restenosis' group	Number of the patients	p (between groups)
1-3 months	114.70 ± 8.87	10	118.49 ± 19.96	49	0.49
3-6 months	120.93 ± 17.43	15	122.07 ± 16.92	58	0.82
6-12 months	119.06 ± 14.63	16	120.69 ± 15.39	55	0.71
12-24 months	112.79 ± 10.03	14	120.58 ± 15.71	38	0.09
> 24 months	112.4 6± 13.48	13	120.74 ± 15.90	38	0.10

Table 6. Maximal heart rate analysis in different exercise test control periods.

In maximal systolic blood pressure analysis, almost statistically significant difference was observed (trend) between 'restenosis' group and 'non-restenosis' patients group on exercise test 1-3 months and 3-6 months follow-ups (Table 7.).

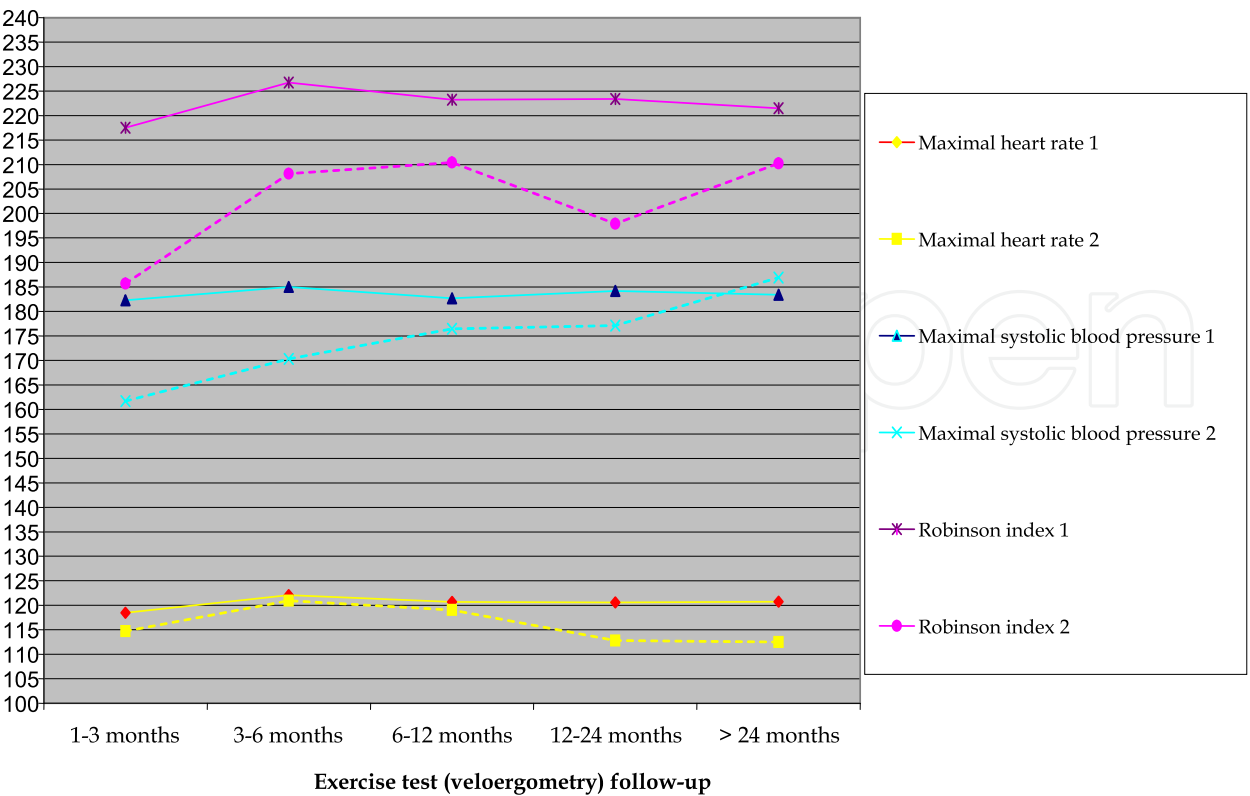| Maximal systolic blood pressure (mean ± SD)					
Exercise test control (months after PCI)	'Restenosis' group	Number of the patients	'Non-restenosis' group	Number of the patients	p (between groups)
1-3 months	161.70 ± 23.64	10	182.27 ± 32.32	49	0.06
3-6 months	170.33 ± 27.55	15	185.00 ± 28.91	58	0.08
6-12 months	176.44 ± 37.51	16	182.67 ± 26.22	54	0.45
12-24 months	177.14 ± 30.76	14	184.16 ± 30.60	38	0.47
> 24 months	186.92 ± 32.27	13	183.39 ± 32.90	38	0.74

Table 7. Maximal systolic blood pressure in different exercise test control periods.

The difference in analysis of double product (maximal rate-pressure product) or Robinson index was expected, on basis of previously obtained results. The following trend was observed – patients with coronary artery restenosis at control coronary angiography 1-3 months after performed PCI showed lower parameters of Robinson index. In turn, independently of stenosis location – LM or other coronary artery, or patients with new detected coronary artery stenosis – statistically significant difference and association with Robinson index changes between patients groups was not ascertained.
Variability of Robinson index changes on exercise test could become possible additional parameter to ST-segment changes in restenosis diagnostics (Table 8., Figure 5.).

Robinson index (mean ± SD)			
Exercise test control (months after PCI)	'Restenosis' group	'Non-restenosis' group	p (between groups)
1-3 months	185.70 ± 32.96	217.51 ± 54.09	0.08
3-6 months	208.12 ± 56.00	226.73 ± 53.81	0.24
6-12 months	210.41 ± 51.57	223.22 ± 45.16	0.34
12-24 months	197.89 ± 27.17	223.41 ± 50.73	0.08
> 24 months	210.23 ± 46.75	221.48 ± 50.63	0.49

Table 8. Robinson index analysis in different exercise test control periods.

Patients with angiographically detected coronary artery stenosis have achieved lower physical load (in Watts), not achieving submaximal pulse, because of termination the veloergometry, if ischemic changes or typical chest pain is appearing. This explains the curve difference of Robinson index in patients with and without coronary artery restenosis, also, statistically significant difference between mentioned groups is not present in analysis of maximal achieved heart rate and maximal systolic blood pressure. However, oscillations of Robinson index parameters are obviously seen in patiens of 'restenosis' group in relative

Exercise test (veloergometry) follow-up

1 – without restenosis on control coronary angiography
2 – with restenosis on control coronary angiography

Fig. 5. Analysis of different exercise test parameters (Robinson index, maximal heart rate and maximal systolic blood pressure) during follow-ups in patients with and without coronary artery restsenosis (on control angiography).

risk period – 6-12 months follow-up. These curves repeatedly are establishing the role of targeted follow-up programme after performed PCI for more precise evaluation of risk of restenosis, taking into account not only patient's complaints and ischemic changes on ECG, but also the changes of Robinson index parameters in dynamics.

It is supposed, that the number of analyzed patients was not sufficient for statistical significance between groups in ST/p index analysis, in order to definitely conclude the role of this parameter in restenosis diagnostics (Table 9.)

ST/pulse index (mean ± SD)					
Exercise test control	**'Restenosis' group**	**Number of the patients**	**'Non-restenosis' group**	**Number of the patients**	**p (between groups)**
1-3 months after PCI	0.76 ± 0.55	10	0.59 ± 0.44	49	0.28
3-6 months after PCI	0.72 ± 0.35	15	0.61 ± 0.45	58	0.36
6-12 months after PCI	0.76 ± 0.47	16	0.59 ± 0.41	55	0.16

ST/pulse index (mean ± SD)					
Exercise test control	'New stenosis' group	Number of the patients	'Without new stenosis' group	Number of the patients	p (between groups)
1-3 months after PCI	1.07 ± 0.98	6	0.57 ± 0.34	53	0.01
3-6 months after PCI	0.80 ± 0.67	7	0.61 ± 0.40	66	0.27
6-12 months after PCI	0.76 ± 0.54	11	0.61 ± 0.40	60	0.28

Table 9. ST/pulse (ST/p) index in LM patients' group according to angiographic finding (restenosis, new stenosis of coronary artery or without detected restenosis or new stenosis of coronary artery).

In LM patients' group analysis – 50% of cases of coronary artery restenosis are detected in early period (3-6 months after PCI), left 43% and 7% – 6-12 and 12-24 months after PCI, respectively. Angiographic results in early coronary angiography follow-up period (3-6 months after performed PCI) correlate with ECG changes on 1-3 months control of physical test: there is statistically significant difference between patients groups – ST-segment depression on exercise ECG is obvious in all patients with restenosis established at control coronary angiography (Table 10.).

	3-6 months	6-12 months	12-24 months
Restenosis	50%	43%	7%
ST-segment changes	ST-segment depression	ST-segment depression	ST-segment depression

Table 10. Restenosis and ST-segment changes on exercise ECG prior the control coronary angiography.

The sensitivity of veloergometry test in 1-3 months – 29%, specificity – 100 %. Lower parameters of Robinson index also were registered in this patients' group.
Correlation of ST-segment changes with restenosis development is obvious also in later control of veloergometry (3-6 months after PCI). The sensitivity of veloergometry test – 50%, specificity – 86 %. All the patients with diagnosed new coronary artery stenosis (in other coronary artery) at control coronary angiography (3-6 months after PCI) showed ST-segment depression on exercise ECG in early stress test control (1-3 months), but in patients group without restenosis ECG without any dynamical changes is observed in 92.9% of cases. The sensitivity of the test – 33%, specificity – 93 %.

4.4 Algorithms
Basing on the previously obtained data and on the significance of exercise test in patients' follow-up after performed PCI, several algorithms were developed for evaluation of patients' functional status after PCI, also for evaluation of possible treatment strategy of coronary artery stenosis.
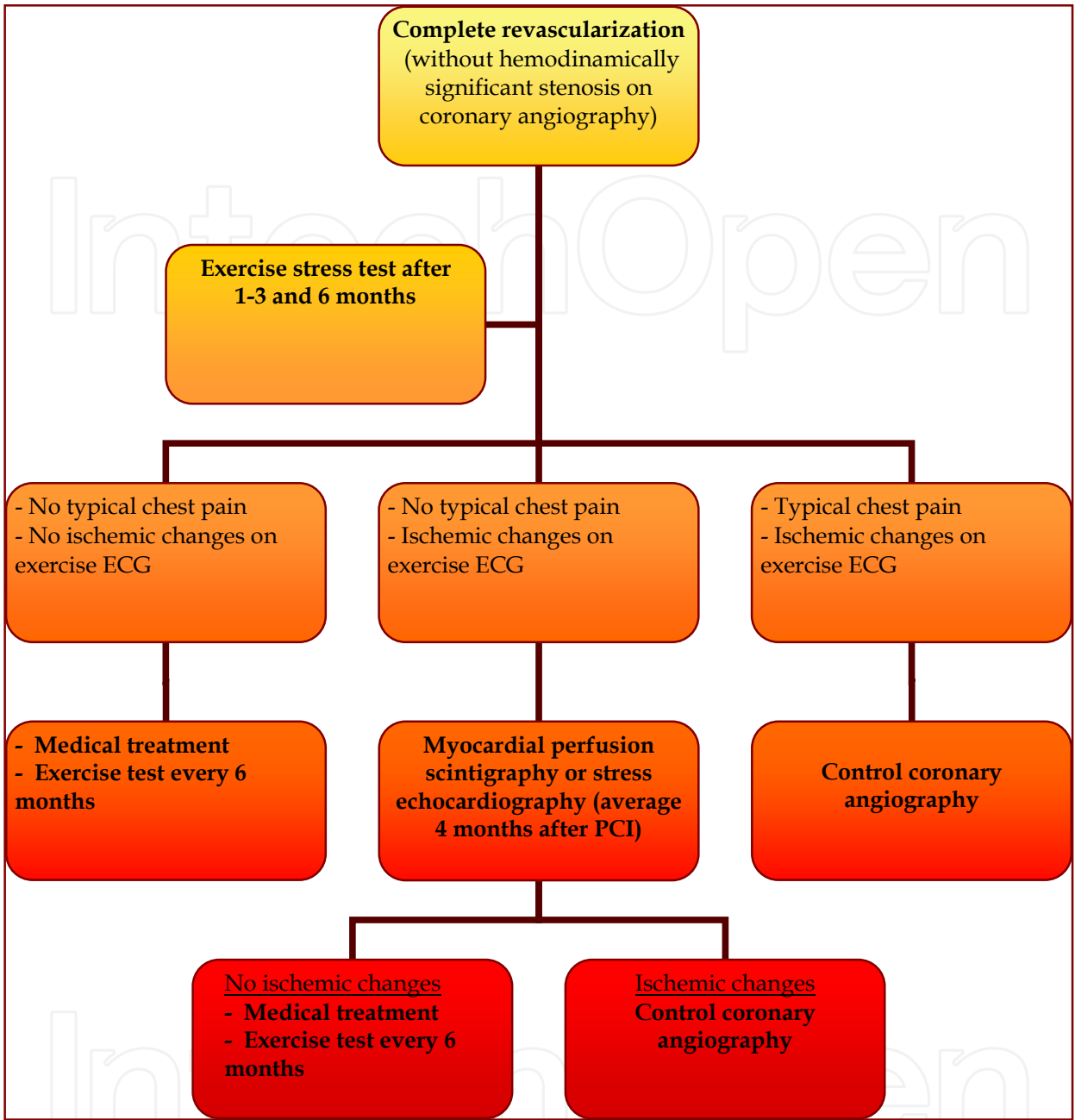
Fig. 6. Exercise test algorithm in patients after PCI (complete revascularization).

Patients with complete revascularization (Figure 6):

- Exercise test should be performed in 1-3 months after PCI in patients with complete revscularization (performed with PCI method);
- Patients should continue medical treatment and exercise test control every 6 months, if angina or ischemic changes on exercise ECG are not present;
- Patients should undergo myocardial perfusion scintigraphy investigation or stress echocardiography in case of no angina, but with presentation of ischemic changes on exercise ECG. If ischemic changes are not present on additional examination tests, medical treatment shoul be continued and control of exercise test every 6 months;
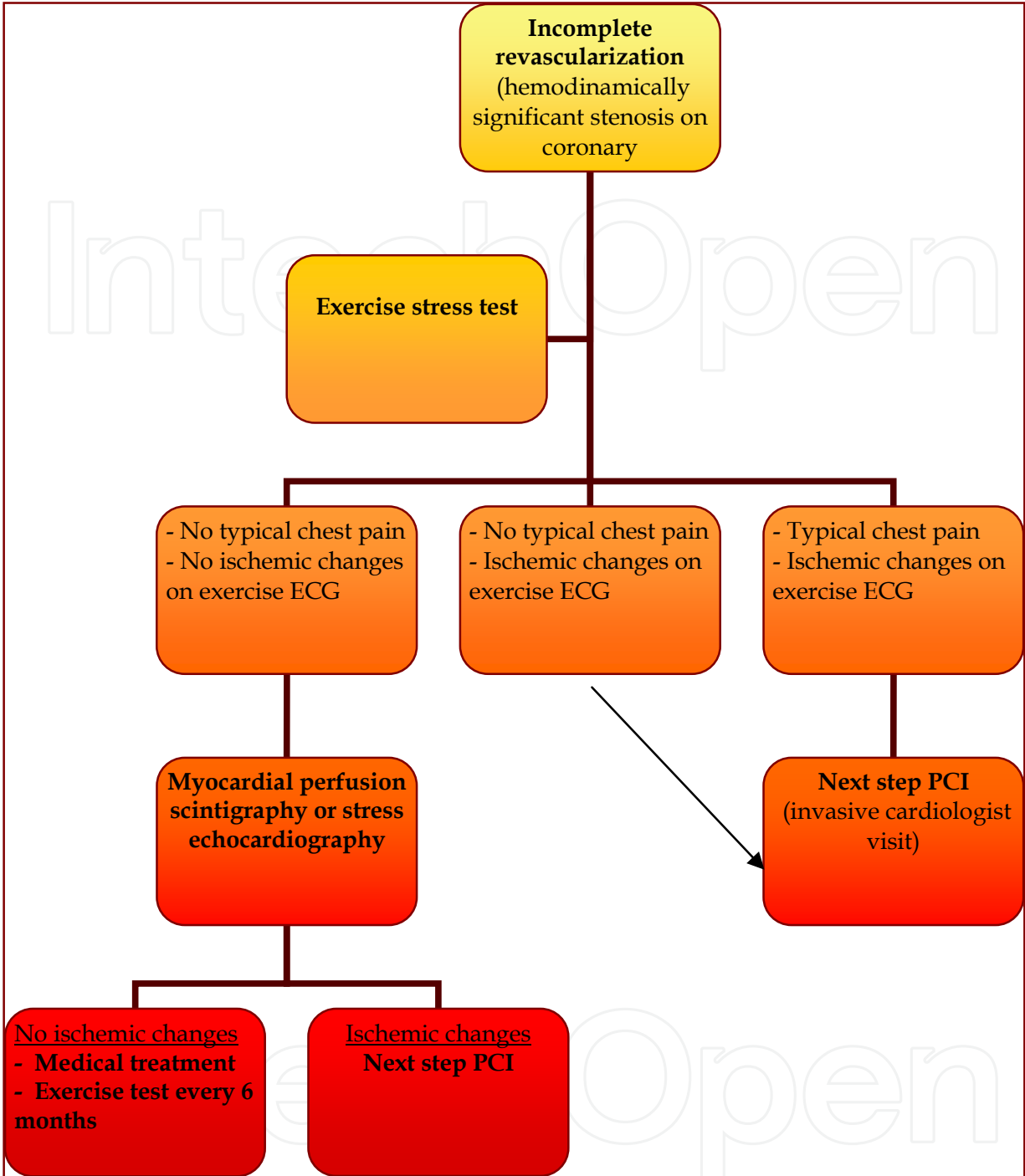
Fig. 7. Exercise test algorithm in patients after PCI (incomplete revascularization).

- In case of angina and ischemic changes on exercise ECG patients should undergo control coronary angiography.

Patients with incomplete revascularization (Figure 7.):

- Exercise test should be performed in 1-3 months after PCI in patients with incomplete revascularization (and hemodinamically sigfnificant stenosis, left on angiography);
- Myocardial perfusion scintigraphy investigation or stress echocardiography should be performed in case of no angina and no ischemic changes on exercise ECG. If ischemic

changes are present (in additional investigations), next step PCI should be performed. If ischemic changes are not present, patients should continue medical treatment and perform exercise test every 6 months;

- In case of ischemic changes on exercise ECG, independently of patient's complaints, next step PCI should be performed.
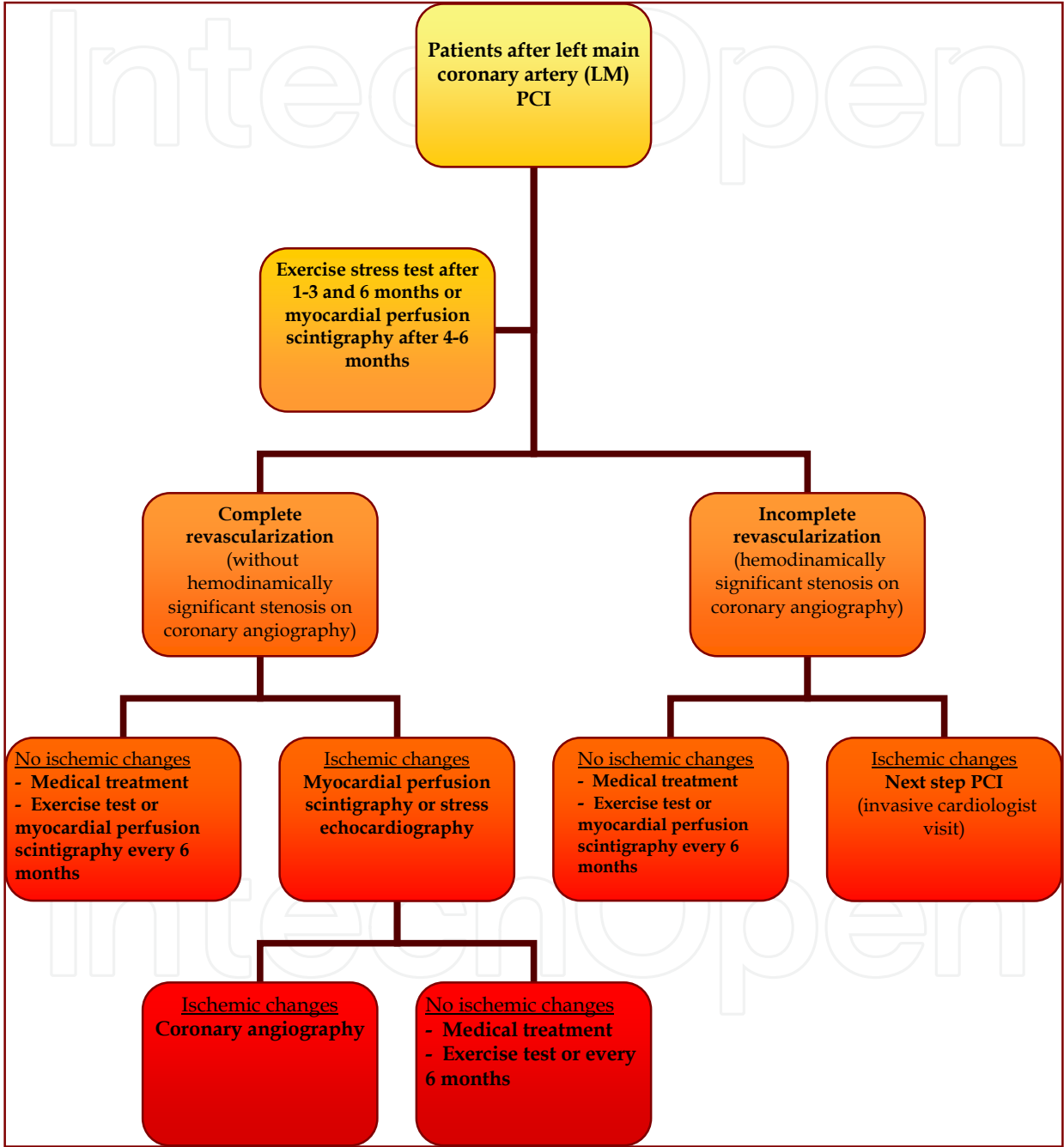

Fig. 8. Exercise test algorithm in patients after LM PCI.

Patients after left main coronary artery (LM) revascularization (Figure 8.):

- Exercise test should be performed in 1-3 months after LM PCI. Myocardial perfusion scintigraphy could be performed in 4-6 months in case of inconclusive ECG;

- Patients should continue medical treatment and should perform exercise test every 6 months in case of no hemodinamically significant stenosis on coronary angiography;
- Myocardial perfusion scintigraphy investigation or stress echocardiography should be performed in case of ischemic changes on exercise ECG. If If ischemic changes are present (in additional investigations), coronary angiography should be performed. If ischemic changes are not present, patients should continue medical treatment and perform exercise test every 6 months;
- Patients with incomplete revascularization and angiographycally with hemodynamically significant stenosis are left, exercise test should be performed in 1-3 months after PCI. If ischemic changes are not present, patients continue medical treatment and perform exercise test every 6 months. In case of ischemic changes on exercise test, patient should visit invasive cardiologist in order to make decision of next step PCI.

5. Discussion

In this study we raised the question whether physical exercise test alone beside accurate diagnosis of obstructive lesions provides an opportunity to prognose cardiovascular risk. We claim that this is possible, which is demonstrated in our study by a significant number of patients with silent ischemia. The potential gain from reducing the risk of reverse cardiac events is actually greatest in those with silent ischemia at the time of follow-up presentation, because those patients are at especially high risk (Pepine and Deedwania, 1994). Nowadays it is clear that chest pain in history does not correlate tightly with ischemic ST-segment deviation following physical loading and with haemodynamically significant stenosis on angiography either.

Published data as well as national and international guidelines state that physical exercise test following PCI is a useful method in diagnosis of restenosis in high risk or symptomatic patients and should be conducted six months after intervention (Gibbons et al., 2002). Our results showed that the exercise test should be done not later than three to six months after intervention. The highest rate of restenosis was observed in patients after interventional treatment of LM disease in 1-3 months after procedure. The importance of the physical test does not decrease later; more than third part of all documented restenosis was registered at six months after intervention (including the patients with newly diagnosed stenosis on coronary angiography). One year after PCI the specific weight of restenosis was 16.7% of all diagnosed restenosis.

The clinical value of exercise electrocardiograms following interventional therapy in the early period is high in evaluation of early post-interventional results (Roffi et al., 2003). This is supported with our results, which demonstrated high specificity of exercise test performed in the first six months after PCI. Exercise electrocardiograms 1–3 months after PCI did not show a shift of the ST-segment for all patients without restenosis. However, angiography depression of the ST-segment was registered on exercise electrocardiogram only for patients with restenosis. This demonstrates a clear correlation between ST-segment depression and restenosis.

Adequate implementation of drug therapies depending on patient clinical and functional status allow to reach goals set by national and international guidelines. Based on epidemiological studies, even small decreases in low density lipoprotein cholesterol and blood pressure levels translate into significant reductions in cardiovascular morbidity and mortality (LaRosa et al., 2005). Moreover, especially important is the patient compliance, which can be achieved through frequently scheduled visits.

The clinical course and prognosis of patients with coronary artery disease can be modified favourably by successful translation of recommendations for secondary coronary prevention into effective clinical care. Crucial to the outcome of any preventive strategy is patient attitude to lifestyle modification and compliance with drug therapies over the long term. We tend to claim that an aggressive follow-up programme could help us to reach the goals in secondary prevention of coronary artery disease set by European Societies and Latvian Society of Cardiology.

The physical exercise test is a safe method with high specificity, but is limited by poor test sensitivity for the evaluation of efficacy of interventional and medical treatment for patients with coronary artery disease. A focussed exercise test performed on a regular basis indirectly influences clinical results and prognosis. Timely set diagnosis of restenosis provides necessary treatment measures, therefore, alienating adverse cardiac events such as unstable angina and myocardial infarction. Moreover, an exercise test performed on a regular basis provides essential corrections in drug therapy. After comparison of drug therapies recommended three months and one year after PCI, we can conclude that regular follow-ups provide the opportunity to sustain acceptable patient compliance and use of medications even twelve months after an intervention.

A focussed follow-up programme with an exercise test allows to evaluate clinical status of patients as well as to determine timely possible risk of restenosis, to adapt medication doses, to reduce risk factors and to influence positively patient compliance. The exercise test provides accurate estimation of possible restenosis in patients with complete revascularization. In patients with incomplete revascularization the exercise test specificity is reduced. Taking into account the results of the current study, we are sure, that focussed physical exercise test should be advised for all patients after interventional treatment. It is of high importance to achieve submaximal heart rate during the exercise test. In all cases when this is not possible for any reason, myocardial perfusion scintigraphy is indicated.

Advantages of the study (benefits)

The results of this study can be used with a goal to determine possible risk of restenosis in a time, to prescribe medications according to patient's functional status, to correct possible risk factors, which can have negative influence on development of disease.

Regular patients' follow-ups increase the compliance of the patients and 'participation' in treatment process, thus increasing accuracy of data and foundation of the results.

Possible disadvantages (limits) of the study

Irregular patients' follow-ups, thus exclusion from statistycal analysis.

Insufficient information about patient recurrent hospitalization at district hospital. Also the variability in medical treatment (general practitioner like „middle stage" between patient and cardiologist).

The lack of patients compliance in medication use, the lack of motivation in modification of their possible risk factors.

Low availability of myocardial perfusion scintigraphy, thus, not possibility to perform necessary investigation in position of diagnosis making and more detailed evaluation of clinical situation.

6. Conclusions

1. Exercise test (veloergometry) is established as a safe method with high specificity, but lower sensitivity in evaluation of invasive and medical treatment efficiacy in patients

with CAD, evolving different invasive treatment methods (with drug-eluting stents, balloon angioplasty, etc.)

2. The database of the patients with left main coronary artery stenosis was analyzed, evaluating the efficacy of invasive treatment of left main stenosis, analyzing possible progression of restenosis and evaluating following treatment steps.
3. New specific criteria were extracted for risk evaluation and detection with exercise stress test.
4. Algorithms were developed for CAD patients' clinical status evaluation after percutaneous coronary intervention.
5. Follow-up programme with targeted exercise test allows to personalize exact treatment strategy and risk factor correction for each patient individually.

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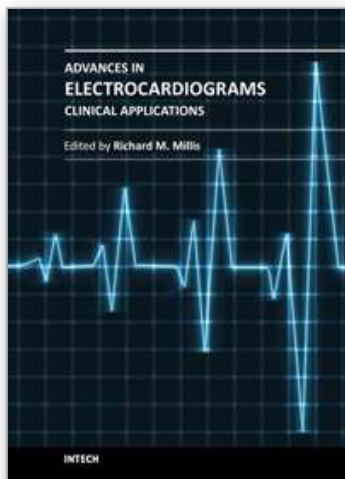
Advances in Electrocardiograms - Clinical Applications

Edited by PhD. Richard Millis

Electrocardiograms have become one of the most important, and widely used medical tools for diagnosing diseases such as cardiac arrhythmias, conduction disorders, electrolyte imbalances, hypertension, coronary artery disease and myocardial infarction. This book reviews recent advancements in electrocardiography. The four sections of this volume, Cardiac Arrhythmias, Myocardial Infarction, Autonomic Dysregulation and Cardiotoxicology, provide comprehensive reviews of advancements in the clinical applications of electrocardiograms. This book is replete with diagrams, recordings, flow diagrams and algorithms which demonstrate the possible future direction for applying electrocardiography to evaluating the development and progression of cardiac diseases. The chapters in this book describe a number of unique features of electrocardiograms in adult and pediatric patient populations with predilections for cardiac arrhythmias and other electrical abnormalities associated with hypertension, coronary artery disease, myocardial infarction, sleep apnea syndromes, pericarditides, cardiomyopathies and cardiotoxicities, as well as innovative interpretations of electrocardiograms during exercise testing and electrical pacing.

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