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The value of Holter monitoring with heart rate variability assessment in predicting restenosis after successful percutaneous transluminal coronary angioplasty of isolated stenosis of left anterior descending artery

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Abstract

Background: *The aim of our study was to examine the value of Holter monitoring and changes of heart rate variability (HRV) parameters in patients undergoing percutaneous transluminal coronary angioplasty (PTCA) and to assess their value for detection of restenosis after the elective PTCA of single-vessel coronary artery disease.*

Methods: *56 consecutive patients were studied — 41 men and 15 women (mean age: 56.2 ± 8.3 years) with left anterior descending artery stenosis who underwent successful PTCA. All patients underwent 24 hour Holter monitoring with HRV assessment within 1 week after PTCA and then again before repeated follow-up angiography.*

Results: *Repeated coronary angiography revealed restenosis in 15 patients and no signs of significant stenosis in the remaining 41 patients. The sensitivity of standard ST-segment depression criteria for the prediction of restenosis was low (ranging from 7% to 27%), with quite high specificity (80–93%) and very low diagnostic accuracy (17–36%). However, the presence of ventricular extrasystoles (≥ 50 during 24 h registration) was statistically significantly associated with quite a high likelihood of the presence of restenosis — sensitivity (53% and 47%), specificity (76% and 85%) and diagnostic accuracy (44% and 54%), respectively. In baseline recordings the significantly higher values of rMSSD ($p < 0.05$) and pNN_{50} ($p = 0.61$) had been found among patients who later developed restenosis, compared to those*

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that did not. The sensitivity of rMSSD ≥ 30 ms for the prediction of restenosis was 60%, specificity 76%, diagnostic accuracy 47%. Also the sensitivity of pNN_{50} ≥ 8% for prediction of restenosis was high and equalled 60%, specificity 78% and diagnostic accuracy 50%.

Conclusions: *The value of a 24 hour Holter ST-segment monitoring in the prediction of restenosis seems to be limited. The possible correlation between frequent ventricular extrasystoles and the presence of restenosis needs further studies. The value of heart rate variability in the prediction of restenosis remains to be defined.* (Folia Cardiol. 2006; 13: 404–413)

Key words: percutaneous transluminal coronary angioplasty, restenosis, Holter monitoring, heart rate variability

Introduction

Despite the significant progress that has been made in recent years in the percutaneous revascularization of the heart muscle — mainly attributable to the fact of empowering the balloon angioplasty technique (PTCA) with the implantation of coronary stents (especially drug-eluting ones) and to the use of varied pharmacotherapy — the phenomenon of restenosis still remains the main problem for an invasive cardiologist to be faced with. As it has been shown in previous studies, restenosis occurs in 15–50% of patients following the procedure of coronary angioplasty and the implantation of a coronary stent seems to decrease the risk of restenosis — depending on the type of lesion — only up to a dozen or so percent.

There is a considerable difference between the percentage of clinically symptomatic restenosis and the angiographically proven significant stenosis within the dilated vessel, which may suggest the need to perform a check-up angiography in all patients undergoing angioplasty procedures. Nevertheless, such approach has been introduced to some clinics of cardiology in the world. It is very expensive, carries a certain risk of adverse effects of invasive procedures, and — as it seems — lacks sufficient evidence to prove its advisability. Alternative strategy includes an attempt to determine, with the use of noninvasive examination, the group of patients treated with angioplasty procedures that are suspected to have developed restenosis and to perform check-up angiography only in those selected patients. The true value of noninvasive examination techniques (that is their sensitivity and specificity) used to determine the group of patients with restenosis, still remains an open question.

Standard electrocardiographic exercise test on a treadmill is a noninvasive method that is most often used to evaluate patients after coronary angioplasty procedures. But owing to its relatively low sensitivity and specificity in identifying patients with restenosis, other methods to evaluate those patients are continuously searched for.

One of the methods to be used in search of restenosis in patients after angioplasty procedures is Holter ECG monitoring. The evaluation of the ST-segment in Holter ECG monitoring as a marker of cardiac ischemia has a diagnostic and prognostic power. Episodes of significant ST-segment alterations are considered to reflect ischemia in patients with a history of coronary artery disease and are often attributed with a prognostic power.

Relatively few trials explore the importance of ECG Holter monitoring in patients after coronary angioplasty procedures, though the advantages of ambulatory monitoring of ST-segment seem to be undeniable, especially in the evaluation of spontaneous anginal episodes that occur during specific types of exercise, which cannot be reproduced in clinical conditions, or during a specific time of a day.

ECG Holter monitoring allows to observe silent ischemia episodes or ischemia-induced arrhythmias that are frequently the first manifestation of restenosis after angioplasty procedures.

Another method that may be used to estimate restenosis in patents after angioplasty procedures is the assessment of heart rate variability (HRV). This name is used to address momentary fluctuations of the duration of consecutive RR intervals of the sinus rhythm, that are registered by means of Holter ECG monitoring. Sinus rhythm variability is controlled by the autonomous nervous system, its sympathetic and parasympathetic part. The activity of both parts is subject to continuous changes. The activity of the sympathetic system (vagus nerve) prevails at rest and under these circumstances it contributes mostly to heart rate variability — the influence of activation is fast and it lasts for a relatively short period of time. Adrenergic stimulation, on the other hand, rises slowly and it is limited by the activity of the vagus nerve, simultaneously modulating its activity [1, 2].

As it has been shown in many reports, reduced sinus rhythm variability is an independent risk factor in patients suffering from acute myocardial infarction. The most proven indicator in this case is the SDNN parameter, the value of which lower than 50 ms is an indicator of the unfavorable prognosis [2–4].

Despite few reports concerning the use of Holter ECG monitoring with heart rate variability assessment in patients after angioplasty procedures that are suspected to develop restenosis, patophysiologic and pathogenetic factors seem to support its use for that purpose, and therefore the attempt to use it to assess the incidence of restenosis seems to be justified.

The aim of the study was to estimate the ability of ECG Holter monitoring with heart rate variability assessment to identify patients with restenosis after the successful coronary angioplasty procedure.

Methods

The study included patients with symptomatic coronary artery disease, in which the presence of significant, isolated stenosis (> 50% of lumen diameter of the artery) of the left anterior descending artery (*de novo* lesion), eligible for balloon angioplasty, was found during angiographic examination.

Exclusion criteria of the study included:

— presence of hemodynamically significant lesions (stenosis of >50% of lumen diameter) in other coronary arteries, except for diagonal branches;
— complete occlusion of the left anterior descending artery (LAD);
— past myocardial infarction with impaired left ventricular ejection fraction (below 40%);
— chronic atrial fibrillation;
— use of digitalis preparations or medications that prolong the QT interval;
— lack of patient's consent to be included in the study and to undergo control coronarography.

During the enrollment period of the study (15 October 2000 – 31 July 2001), 814 angioplasty procedures, including 390 procedures within the left anterior descending artery, were performed at Hemodynamic Laboratory of the Chair and 1st Department of Cardiology, Poznań University of Medical Sciences. Most of them (n = 315) were procedures performed in patients with atherosclerotic lesions also present in other arteries. During that period there were 75 angioplasty procedures performed in patients with isolated lesion within LAD. The study group consisted of 56 consecutive patients, fulfilling the inclusion criteria of the study — those patients were included in the successive analysis. The remaining 19 patients were not included in the study for the following reasons: lack of consent to participate in the study (7 patients), lack of consent to undergo control coronarography (3 patients), past myocardial infarction with significant impairment of left ventricular ejection fraction (5 patients), chronic atrial fibrillation (2 patients), treatment with digitalis preparations or other medications that prolong the QT interval (4 patients — including 2 with atrial fibrillation).

In the study group of 56 patients there were 41 men and 15 women, mean age 56.2 ± 8.3 years (min. 38, max. 73 years). The time period from the onset of symptoms to the angioplasty procedure was considerably diversified, from 1 up to 120 months and its mean length equaled 16.5 ± 26.2 months.

Among the patients of the study group, 29 patients (52%) had previously undergone myocardial infarction — in most cases (n = 18) it was a non-Q infarction of the anterior wall of the heart. During medical history data collection 29 patients (52%) reported arterial hypertension, 8 patients (14%) — type 2 diabetes (treated with oral medications in 5 patients, with insulin in 3 patients).

The study described above is a part of a broader programme, in which the importance of various noninvasive examinations, used to evaluate the incidence of restenosis in patients after angioplasty procedures, was assessed. Those examinations included a standard electrocardiographic exercise test on a treadmill (Bruce's method), ECG with the evaluation of the QT-dispersion at rest and during exercise, 24-hour ECG Holter monitoring with the assessment of heart rate variability and signal averaged electrocardiogram with the registration of late ventricular potentials. The part of the programme concerning the importance of ECG Holter monitoring with the assessment of heart rate variability is presented in the current paper.

Following the procedure of coronary angiography and coronary angioplasty of an isolated lesion within the left anterior descending artery, inclusion criteria into the programme were taken into consideration, as well as possible exclusion criteria. The patient was then informed in detail about the aim, advantages and possible risk related to the participation in the study. The patient had an opportunity to receive the exhaustive explanation of possible questions or doubts and gave their consent to participate in the study in writing, having got acquainted with an "Information for the patient" about the principles regarding the participation in the programme.

During in-hospital stay related to coronary angiography and concurrent angioplasty procedure, the angiographic assessment of the localization of the lesion being subject to angioplasty was performed before and after the procedure, adverse effects of the procedure were estimated, and echocardiographic examination was performed, including the evaluation of left ventricular ejection fraction.

In addition to that, during the in-hospital stay related to the procedure (or within 7 days from the procedure) each patient underwent among other examinations a 24-h Holter ECG monitoring with assessment of heart rate variability (according to the methodology described below).

During in-hospital stay after 6 months form the angioplasty procedure:

— each patient underwent 24 h Holter ECG registration with the assessment of HRV;
— control coronary angiography was performed in each patient with possible concurrent angioplasty in case of angiographically confirmed restenosis (stenosis of > 50% of the diameter of the artery within the previously dilated segment).

The study protocol described above was accepted by the Local Committee for Ethics in Scientific Studies at the Medical University of Poznan.

Coronary angiography and angioplasty were performed according to generally accepted rules, based on the Guidelines of ACC/AHA and Polish Cardiac Society (PCS). During angioplasty procedure a stent was successfully implanted in each patient. The lesion found was estimated before and after PTCA procedure with the use of QCA system: the reference diameter of the artery (RD), the minimal lumen diameter of the artery (MLD), the percentage of stenosis of lumen diameter and the length of stenotic lesion were evaluated. Primary and restenotic lesions were regarded as significant if the stenosis observed was greater than 50% of lumen diameter.

24 hour Holter ECG monitoring with the assessment of HRV — Holter monitoring was performed in all patients following the angioplasty procedure and after 6 months, before control coronary angiography, according to the guidelines of PCS [1]. ECG recording was performed for a minimum of 18 hours with the use of three-channel tape recorder DRG RT300 with 7 electrodes. Data reading was performed with the use of a Personal Computer set and each result was then verified by a cardiology specialist. The occurrence of silent ischemia, arrhythmic profile and HRV were assessed. Ischemia was defined as the presence of an episode of significant ST-segment lowering of 1 mm (at 60 ms distance from the J-point), of inclined or horizontal course, maintaining for at least 1 minute.

For the assessment of arrhythmic profile the total daily number of ventricular extrasystoles, number of pairs and number of extrasystoles per 1000 sinus evolutions were taken into account.

For the assessment of sinus rhythm variability, according to guidelines of PCS, ESC and NASPE [1], the following sinus rhythm variability indexes were calculated:

— SDNN — standard deviation of all RR intervals of sinus rhythm;
— SDNNI — index of standard deviation of all RR intervals of sinus rhythm;
— SDANN — standard deviation of the average of consecutive 5-minute series of RR intervals of the whole recording;
— rMSSD — square root of mean sum of squared differences between consecutive RR intervals;
— pNN_{50} — percentage of differences between consecutive intervals exceeding 50 ms.

Statistical analysis

An initial phase of statistical analysis — explorative data analysis — included the inspection of data completeness, reasonableness, the fulfillment of logical criteria for certain ranges, as well as basic properties of empirical distributions of attributes with the identification of atypical results (outliers). The assessment of conformity of the distributions of investigated attributes with normal distribution was performed with the use of Shapiro-Wilk test. In cases of discordance of investigated attributes with normal distribution, median value and mean deviation as a measure of dispersion were used. Mann-Whitney test was used for the analysis of the significance of differences between median values.

The remaining attributes, having a distribution significantly different compared to normal distribution, for which in most cases no positive values were recorded, were treated as categorial attributes and for their analysis a precise Fisher test (2×2 table) or chi-square test according to Pearson's method and maximum likelihood method (tables 2×3 and larger) were used.

The attributes, the distribution of which did not significantly differ from normal distribution, were demonstrated by means of arithmetic average ± ± standard deviation (SD) and the intergroup comparison was performed with the use of a t-Student test for non-linked attributes.

The indexes of diagnostic efficacy (sensitivity, specificity, the predictive value of positive and

negative result, odds ratio with 95% confidence interval) were calculated with the use of standard equations for contingency table 2 × 2.

Results

Evaluation of the incidence of restenosis

Control coronary angiography after 6 months from the angioplasty procedure was performed in all patients. Significant (> 50%) restenosis in LAD was found in 15 patients (26.8%). All of those patients had previously undergone angioplasty of LAD with stent implantation. In-stent restenosis was diagnosed in 11 patients (20%) and restenosis proximal to the stent implantation site in 4 patients (6.8%). Among 11 patients with in-stent restenosis implantation site: in 3 patients (5.5%) total occlusion of the artery was observed, in next 3 patients (5.5%) — diffuse restenosis within the stent and spreading beyond its limits, and in the remaining 5 patients (9.0%) — focal restenosis that did not spread beyond the limits of the stent.

Excluding the patients with total occlusion of the artery, the percentage of stenosis of the artery lumen diameter, calculated with use of QCA in the remaining 12 patients equaled 67±7% on average. In 4 patients restenotic lesion was described as significant (50–70% of lumen diameter of the artery — minimal 58%) and in the remaining 8 as critical (> 70% of lumen diameter of the artery).

In 7 patients after QCA calculations, the lesion within LAD was regarded as borderline (stenosis of 40–50% of lumen diameter of the artery). Borderline characteristics of the lesion was independently confirmed by three experienced cardiologists — in case of discrepancy of their opinion, the patient was qualified to undergo another coronary angiography with functional assessment of lesion significance with the use of the fractional flow reserve evaluation method (FFR). Dubiety concerning the type of lesion arouse in case of 4 patients that had undergone FFR evaluation within LAD confirming hemodynamically insignificant characteristics of the lesion (FFR values > 0.75 in each patient; min. 0.78, max. 0.91). All of those 7 patients were finally included into the group without restenosis.

The remaining 34 patients (60.7%), in which coronary angiography with QCA calculation had not demonstrated restenosis of the artery greater than 40%, were included into the group without restenosis.

For the successive consideration it was assumed that in the study group restenosis occurred in 15 patients (26.8%) and no restenosis was demonstrated in 41 patients (73.2%).

The group with restenosis was not different compared to the group without restenosis as regards sex, age, period of angina occurrence before the angioplasty procedure, the incidence of angina at rest, CCS class, past myocardial infarction, arterial hypertension, diabetes or nicotinism. Also the end-diastolic diameter and left ventricular ejection fraction were comparable in both groups. Detailed clinical characteristics of both study groups is shown in Table 1.

Assessment of Holter ECG monitoring for identification of patients with restenosis

Holter ECG registration was performed in all patients after angioplasty procedure and after 6 months, before control coronary angiography. The incidence of silent ischemia, arrhythmic profile and HRV were assessed.

In the first examination the two groups of patients — with and without restenosis — were not

Table 1. Clinical and echocardiographic characteristics of patients in the group with and without restenosis.

	Restenosis (n = 15)	No restenosis (n = 41)	p
Men/women	12/3	29/12	NS
Age (years)	58.9 ± 9.3	55.2 ± 7.8	NS
Period of anginal symptoms before PTCA (median; months)	8	5	NS
Anginal symptoms at rest	8 (53%)	23 (56%)	NS
CCS class (mean)	2.8 ± 0.7	2.8 ± 0.7	NS
Past myocardial infarction	7 (47%)	22 (54%)	NS
Arterial hypertension	7 (47%)	22 (54%)	NS
Diabetes	0 (0%)	8 (20%)	NS
Nicotinism	7 (47%)	17 (41%)	NS
Diastolic diameter of left ventricular [mm]	48.3 ± 4.4	49.7 ± 6.4	NS
Left ventricular ejection fraction	54.5 ± 7.9	56.2 ± 7.1	NS

PTCA — percutaneous transluminal coronary angioplasty

Table 2. Indexes of diagnostic efficacy of ischemic episodes and ventricular extrasystoles (VES) registered in Holter ECG monitoring after angioplasty procedure to identify patients with restenosis.

Parameter	Sensitivity	Specificity	PPV	NPV	OR	95% CI	p
ST 1.0–2.0 mm	27	83	36	76	1.776	0.434–7.19	NS
ST > 2.0 mm	7	93	25	73	0.905	0.087–9.44	NS
VES > 50/24 h	53	76	44	82	3.543	1.025–12.224	0.055
VES ≥ 1:1000	20	85	33	74	1.458	0.315–6.759	NS

PPV — positive predictive value, NPV — negative predictive value, OR — odds ratio, CI — confidence interval

different from each other as regards mean, minimum and maximum heart rate.

Arrhythmic profile in the two examinations was also assessed. The total number of ventricular extrasystoles a day and the number of extrasystoles per 1000 of sinus rhythm evolutions were taken into account.

In the first examination, ventricular extrasystoles (VES) were present in 39 patients (min. 1; max. 10.025 extrasystoles) and no VES were found in 17 patients. In 9 patients the burden of VES was greater than 1:1000 (min. 1:1000, max. 120:1000). It has been observed that VES in number greater than 50 a day were present more often in the group of patients with restenosis. Among 18 patients with such number of VES, restenosis occurred in 8 (44%), while among 38 patients with total number of VES a day lower than 50, restenosis occurred only in 7 patients (18%) — the difference observed was statistically significant ($p < 0.05$).

In the first ECG recording, the episodes of ischemia were observed cumulatively in 13 patients (20%). In 9 patients the episodes consisted of ST-segment lowering of 1.0–2.0 mm, in 2 patients > 2.0 mm and in the remaining 2 — both 1.0–2.0 and > 2.0 mm. It was determined if the ischemic episodes found in Holter monitoring immediately after the procedure allow to predict the occurrence of restenosis. Results of the analysis described above are shown in Table 2.

In the second Holter ECG recording, performed before control coronary angiography, ventricular extrasystoles were present in 37 patients (min. 1; max. 14,114) and no VES were observed in 18 patients (in one patient [MS; no. 23] Holter ECG registration could not be assessed for technical reasons). It has been observed that the number of VES greater than 50/24 h was recorded more often in the group of patients that developed restenosis. Among 13 patients with such number of VES, restenosis occurred in 7 patients (54%), while among 42 patients with daily number of VES lower than 50 restenosis developed only in 8 patients (19%) — the difference observed was statistically significant ($p < 0.05$). In 8 patients VES burden was greater than 1:1000 (min. 1:1000, max. 153:1000) — in that group restenosis was diagnosed in 5 patients and no restenosis was found in 3 patients — the difference observed was statistically significant ($p < 0.05$).

In the second Holter ECG recording, episodes of ischemia were observed in 13 patients (20%). In 7 patients there were episodes of ST-segment lowering of 1.0–2.0 mm, in 1 patient > 2.0 mm and in the remaining 5 patients both 1.0–2.0 mm and > 2.0 mm. It has been assessed if the episodes of ischemia observed in Holter ECG recording before control coronary angiography allow to predict the occurrence of restenosis. Results of the analysis described above are shown in Table 3.

Assessment of heart rate variability examination for identification of patients with restenosis

Heart rate variability analysis was also performed during 24 h Holter ECG monitoring, that was

Table 3. Indexes of diagnostic efficacy of ischemic episodes and ventricular extrasystoles (VES) registered in Holter ECG monitoring before control coronary angiography to identify patients with restenosis.

Parameter	Sensitivity	Specificity	PPV	NPV	OR	95% CI	p
ST 1.0–2.0 mm	27	80	33	74	1.455	0.365–5.79	NS
ST > 2.0 mm	7	88	17	71	0.500	0.053–4.674	NS
VES > 50/24 h	47	85	54	81	5.104	1.344–19.379	< 0.05
VES ≥ 1:1000	33	95	63	81	6.17	1.254–30.334	< 0.05

PPV — positive predictive value, NPV — negative predictive value, OR — odds ratio, CI — confidence interval

performed in all patients after the angioplasty procedure and after 6 months — before control coronary angiography.

One patient (MS; no. 23) was excluded from that analysis, because it was impossible to assess his second Holter ECG recording for technical reasons.

In the evaluation of heart rate variability the following indexes of sinus rhythm variability were calculated according to standard procedure: SDNN, SDNNI, SDANN, rMSSD and pNN_{50}.

Significant differences were observed in initial recording between the group of patients with restenosis and the group without restenosis, concerning two of the calculated parameters: rMSSD and pNN_{50}, that were lower in the group of patients without restenosis compared to patients with restenosis. Detailed results of that analysis are shown in Table 4.

In the second recording that was performed before control coronary angiography no significant differences between the group of patients with restenosis and patients without restenosis were observed concerning any calculated heart rate variability parameter. Detailed results of that analysis are shown in Table 5.

Prognostic value of selected heart rate variability parameters for the determination of the probability of restenosis was also assessed. The analysis included two parameters: rMSSD and pNN_{50} that were significantly different in patients with restenosis and patients without restenosis in the initial recording. Assuming rMSSD value ≥ 30 ms as the cut-off point it was found that such value allows to determine the probability of the occurrence of restenosis with sensitivity of 60% and specificity of 76%. Moreover, the value of $pNN_{50} \geq 8\%$ in initial recording allows to predict the occurrence of restenosis with sensitivity of 60% and specificity of 78%. Detailed results of that analysis are shown in Table 6.

Table 4. Results of heart rate variability assessment in patients with restenosis and patients without restenosis — initial recording after percutaneous transluminal coronary angioplasty.

	Restenosis (n = 15)	No restenosis (n = 40)	P
SDNN	119.6 ± 30.3	118.8 ± 30.7	NS
SDANN	106.7 ± 30.7	109.3 ± 30.7	NS
SDNNI	50.1 ± 14.9	44.8 ± 11.9	NS
rMSSD	34.0 ± 14.6	24 ± 8.8	< 0.05
pNN_{50}	9.1 ± 6.8	5.2 ± 5.2	0.61

Table 5. Results of heart rate variability assessment in patients with restenosis and patients without restenosis — second recording before control coronary angiography.

	Restenosis (n = 15)	No restenosis (n = 40)	P
SDNN	129.1 ± 35.4	121.8 ± 30.5	NS
SDANN	114.2 ± 36.8	107.1 ± 29.8	NS
SDNNI	53.4 ± 18.5	52.9 ± 13.0	NS
rMSSD	31.1 ± 15.8	29.8 ± 9.9	NS
pNN_{50}	9.0 ± 11.3	8.4 ± 7.4	NS

Discussion

Assessment of the incidence of restenosis in Holter ECG monitoring

In the first and second recording there were no differences between the group of patients with and without restenosis, as regards mean, minimum and maximum heart rate.

In the first Holter ECG recording, similarly to the second recording, episodes of ischemia were observed in 13 patients. The analysis of Table 2 and 3 shows that their diagnostic efficacy to identify patients with restenosis was poor (sensitivity of 7––27%, specificity of 80–98%).

In the first Holter ECG recording, ventricular extrasystoles occurred in 39 patients and in 9 patients their burden was greater than 1:1000. It has been observed that extrasystoles in number greater than 50/day occurred more often in the group of patients that developed restenosis and the difference observed was statistically significant. Similar observations also concern the second Holter ECG

Table 6. Indexes of diagnostic efficacy of selected heart rate variability parameters for the identification of patients with restenosis.

Parameter	Sensitivity	Specificity	PPV	NPV	OR	95% CI	p
rMSSD ≥ 30 ms (0 mm)	60	76	47	84	4.650	1.325–16.32	< 0.05
$pNN_{50} \geq 8\%$ (0 mm)	60	78	50	84	5.333	1.497–19.01	< 0.05

PPV — positive predictive value, NPV — negative predictive value, OR — odds ratio, CI — confidence interval

recording that was performed before control coronary angiography, in which ventricular extrasystoles occurred in 37 patients and in 8 patients their burden was greater than 1:1000. Also in that recording it has been observed that extrasystoles in number greater than 50/day occurred more often in the group of patients that developed restenosis and the difference observed was statistically significant. Though the sensitivity of that parameter for identification of patients with restenosis — as it results from Table 2 and 3 — is not too large (approximately 50%), it is still undoubtedly larger than the sensitivity of ST-segment lowering recorded in Holter ECG registration (it reaches the maximum value of 27%), being similarly specific. Hence the positive and negative prognostic values of arrhythmia as a marker of restenosis are definitely larger than those of the ischemic episodes observed.

Relatively few studies concern the significance of Holter ECG monitoring in patients after coronary angioplasty procedures. A successful coronary angioplasty procedure causes a decrease in a number and duration of ischemic episodes that are recorded in Holter monitoring, which has been demonstrated in several studies [5–7]. Angioplasty leads to nearly total resolution of symptomatic ischemic episodes, nevertheless episodes of silent ischemia may be still present in some patients; moreover, they occur also in some patients in whom they were not observed before the procedure [5, 7]. The occurrence of ischemic episodes after PTCA may also be the result of incomplete revascularization [5, 8].

The sensitivity of Holter monitoring to identify myocardial ischemia reported in literature varies from 58% to 81% and the specificity from 61% to 95%. It depends however on the probability of coronary artery disease occurrence in the investigated population [1]. Then why in our study the sensitivity of recorded ischemic episodes to identify patients with restenosis was so small and it varied from 7% to 27%? It results primarily from the characteristics of the study group (patients with one-vessel disease) and the large number of patients with asymptomatic restenosis. Some explanation may also be found in the results published by Campbell et al. [9] who demonstrated that ischemic changes in Holter recording occur only in those patients with angina pectoris, in whom they appear at small workload during exercise test (before the end of 6th minute of the test according to Bruce's protocol at heart rate lower than 150/min) or maintain more than 5 minutes after the termination of exercise — in our study group such patients were few.

We made one interesting observation that untill now has not been reported by other authors, concerning higher sensitivity of ventricular extrasystoles recorded in ECG monitoring (criterion: > 50/day) compared to ischemic changes — with similar specificity of those parameters — for identification of patients with restenosis. Higher incidence of ventricular extrasystoles recorded after 6 months in patients with restenosis may be explained by the influence of ischemia, but such explanation of the origin of arrhythmia immediately after the procedure of complete revascularization of the heart seems to be unfounded.

Reference to the results of studies already published is also difficult, since in available literature (MEDLINE) that matter has been discussed by authors of only one study over a small group of 41 patients [10], and they demonstrated, similarly to our results, that ischemic changes that appear after the procedure of angioplasty do not allow to predict the presence of restenosis.

Assessment of the incidence of restenosis with heart rate variability examination

Heart rate variability analysis was also performed during 24 h Holter ECG monitoring, that was performed in all patients after the angioplasty procedure and after 6 months — before control coronary angiography. In evaluation of heart rate variability, the following indexes of sinus rhythm variability were calculated according to standard procedure: SDNN, SDNNI, SDANN, rMSSD and pNN_{50}.

In the initial evaluation, higher values of rMSSD and pNN_{50} were observed in patients with restenosis than in patients without restenosis, and the difference was statistically significant. There were no differences between those two groups in other parameters. In the second recording, performed before control coronarography, no significant differences of values of any HRV parameter were observed between the groups of patients with and without restenosis.

The interpretation of those observations is fairly difficult. The differences of rMSSD and pNN_{50} observed in the first recording between patients with and without restenosis may favor the decision that the patients in whom those parameters have higher values are more at risk of developing restenosis than other patients. For the two parameters an attempt was made to determine cut-off values to differentiate the group of patients with and without restenosis. It was established that rMSSD values ≥ 30 ms as well as pNN_{50} values ≥ 8% in the initial recording allow to determine the probability

of the occurrence of restenosis with a fairly high sensitivity and specificity. Lack of differences in the calculated HRV parameters after 6 months after PTCA suggests that the HRV assessment at that stage is rather insignificant for the identification of patients with restenosis.

Few authors assessed the influence of angioplasty procedures on changes of heart rate variability parameters. Wennerblom et al. [11] observed a decrease of rMSSD and pNN50 in patients with angina after a successful PTCA procedure compared to a healthy, age-matched control group, while SDNN and SDANN values were not different in those two groups of patients. After 1 and 6 months from the angioplasty procedure those differences faded away, hence the conclusion that after a successful angioplasty procedure reduced parasympathetic activity normalizes gradually, while the sympathetic activity (related to the increased mortality after myocardial infarction), represented by SDNN and SDANN, does not change. Similarly to Wennerblom, Osterhues et al. [12] observed a statistically insignificant decrease of rMSSD, pNN_{50} and SDNNI, while the values of SDNN and SDANN had increased.

Research on heart rate variability parameters in patients with acute myocardial infarction undergoing primary angioplasty [13] or postponed angioplasty [14] also indicate biphasic reaction of the autonomous nervous system, characterized by an initial decrease and successive increase of vagus nerve activation with a gradual decrease of sympathetic activation.

Those observations are partially coherent with ours. In our study group in patients without restenosis an initially reduced parasympathetic activity was observed (represented by rMSSD and pNN_{50}) which then gradually normalized in such a way that after 6 months there was no difference between the group of patients with and without restenosis. According to Osterhues et al. [12] it may prove that the restitution of normal autonomic activity is delayed after successful revascularization, however it remains undetermined why the parasympathetic activity after angioplasty procedure is reduced in patients in whom restenosis is not found in the successive observation.

It is virtually impossible to relate to studies that have already been published on the influence of restenosis after angioplasty on HRV parameters. In the available literature (MEDLINE) the authors of only one study of a small group of 25 patients have focused on that issue [15] and discovered a decrease of SDNN index in patients with restenosis, while SDANN and rMSSD remained unchanged. Those observations are different from ours, hence the conclusion that the actual role of heart rate variability assessment in patients after PTCA needs some further studies.

Conclusions

1. The role of ST-segment analysis in 24-hour Holter ECG recording for the evaluation of the occurrence of restenosis after an angioplasty procedure of an isolated lesion within coronary arteries seems to be limited.
2. The observed correlation of a more frequent incidence of restenosis with abundant ventricular arrhythmia in 24-hour Holter ECG monitoring needs further studies.
3. The assessment of the actual role of heart rate variability in patients after PTCA procedure needs further evaluation.

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