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NON-LINEAR STRUCTURE ANALYSIS OF INTER-BEAT INTERVAL DATA AND THE RISK OF MORTALITY IN PATIENTS AFTER MYOCARDIAL INFARCTION

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A b s t r a c t

The scaling index method, a part of the theory of chaos, was applied to determine the risk of mortality in patients after myocardial infarction. The Holter 24-hour ECG recording was obtained from patients 7 to 14 days after the first signs of myocardial infarction. The scaling index alpha was determined in each patient. The fast method of index alpha calculation was used. The alpha index was determined for every beat, and an N(alpha) variation histogram was determined in each patient. For statistical analysis, log N(alpha=1.15) >3.0 was taken as a positive risk factor of cardiac death. A group of 14 patients, who died within a year of myocardial infarction, was compared with nine controls randomly selected from a group of 150 survivals. Sensitivity and specificity were calculated. The sensitivity and specificity of index alpha were compared with those of the standard risk factors: ventricular ectopic beats per hour (VPCs) >10; ejection fraction (EF) < 40%; positive late potentials (LP); baroreflex sensitivity (BRS) < 3ms/mmHg and SDNN index < 30ms. The values of sensitivity and specificity calculated for the respective parameters were: log N(alpha=1.15) > 3.0 (sensitivity 81%; specificity 58%); VPCs (44%; 29%); EF (75%; 55%); LP (63%; 40%); BRS (75%; 55%), SDNN index (56%, 36%). It is concluded that, in our group of patients, the scaling index alpha was a better indicator of the risk of mortality after myocardial infarction than the standard risk factors.

K e y w o r d s

Chaos, Heart rate variability, Arrhythmias, Myocardial infarction, Cardiac death, Risk stratification

INTRODUCTION

The increase in the body of information on the causes and mechanisms of sudden cardiac death has been one of the achievements in cardiovascular medicine during the forgoing decade. The development of better treatment strategies for individuals at risk of sudden cardiac death focuses attention on prediction of the risk. Patients who survive acute myocardial infarction can be considered a special group of risk patients. An increased risk of cardiac death in them is due to a number of factors, namely, presence of ventricular premature complexes per hour (VPCs/h) higher than 10 (*1*), presence of late potentials (LP) (*2*), ejection fraction (EF) below 40% (*3*), baroreflex sensitivity (BRS) below

3ms/mmHg (*4,5,6*) and decreased heart rate variability, e.g., SDNN index (mean of 5-minute standard deviations of RRs in 24 hours) below 30 ms (*7*). The papers cited provide only a few examples of the numerous prospective studies. The indices mentioned above show to have a prognostic value for the prediction of sudden cardiac death or total cardiac mortality, but it is unrealistic to consider that a single strategic approach will have a decisive impact on the prediction of risk. Therefore, besides the studies focused on special groups of patients at risk, i.e., those with coronary heart disease, cardiomyopathies, valvular disorders or functional abnormalities, studies on the potentiating effect of a combination of risk factors have been carried out (*6*).

Methods of non-linear dynamics have opened new and fundamentally different ways to the analysis of heart rate variability and cardiac arrhythmias (*8*). One of these new techniques is the „scaling index method" that can quantify the complexity of sinus rhythm and that of ectopic beats (*9*). This index covers autonomic tonic and reflex control of the heart as well as arrhytmic events.

The scaling index alpha may be calculated for every beat within 24 h, and a variation N(alpha) histogram may be determined (*9*). The disadvantage of this method is vast computer time consumption. We have suggested a fast method with lower requirements for both hardware and software and the aim of our previous study was to test its reliability (*10*). In the classical approach, the analysis was made for the whole signal of RR-intervals, which was 24 h long. The fast method was based on the analysis of 500 beats recorded at the beginning of each hour. This provided 24 N(alpha) histograms that were summed up to give one 24-hour N(alpha) histogram. The reliability of this fast method was tested by a comparison of each 24-hour histogram with three relevant 6-hour histograms (night, morning and afternoon). No difference was found in the determination of the scaling index alpha from 24-hour and 6-hour periods. The time of recording (morning, afternoon, night) did not play any role, either.

A comparison of the scaling index alpha with standard risk factors is decisive for the applicability of the scaling index method for risk prediction in patients in clinical practice. We have performed long-term studies on the prediction of cardiac death risks in patients after myocardial infarction (*5,6*). The aim of this study was to compare the sensitivity and specificity of the fast scaling index alpha with standard indicators of risk in the patients after myocardial infarction.

MATERIALS AND METHODS

Subjects

We studied patients discharged from the coronary care unit during a two-year follow-up period. The diagnosis of acute myocardial infarction was based on conventional clinical, electrographic and enzymatic criteria. The aim of our study was to evaluate the feasibility of a fast scaling index alpha and of other non-invasive indices of the risk of sudden cardiac death, as a standard clinical regimen. Therefore, the patients were examined under an appropriate treatment procedure. A group of

14 patients who died within a year of myocardial infarction was compared with nine controls randomly selected from a group of 150 survivals.

The Ethics Committee of Masaryk University approved of this study and all the patients gave their informed consent.

Protocol

The majority of Holter monitorings, BRS determinations, echocardiogaphic investigations and signal- averaged ECG recordings were carried out between day 7 and 14 before the patients were discharged from hospital. When the disease required longer hospitalisation, the investigation lasted up to 21 days, which occurred only in a few cases.

Holter Monitoring

A two-channel, 24-hour ECG recording (Oxford Excel) was performed. The recordings were manually edited, with artefacts being removed, as follows:

a) Arrhythmias were evaluated and classified (ventricular ectopic beats: simple, bigeminal, multiform, repetitive or R on T) and the count of ventricular ectopic beats was determined.

b) Heart rate variability was expressed as the SDNN index, i.e., the mean of standard deviations of normal-to-normal RR intervals determined in 5-minute periods during a 24-hour ECG recording.

c) The fast scaling index alpha was determined in each patient (*10*). The alpha index was determined for every 500 beats recorded at the beginning of each hour. This provided 24 N(alpha) histograms that were summed up to give one 24-hour N(alpha) histogram, and an N(alpha) variation histogram was determined in each patient. For statistical analysis, log N(alpha=1.15) > 3.0 was taken as a positive risk factor of cardiac death.

Baroreflex Sensitivity Assessment, Spectral Analysis

Indirect continuous blood pressure recordings, lasting for 3 min (Finapres, Ohmeda) were performed on finger arteries in sitting, resting patients between 9 a.m. and noon. Recordings were taken during spontaneous and synchronised breathing. During the latter, only the rhythm of breathing was controlled at a frequency of 20 breaths per min by metronome (0.33 Hz); the subjects were allowed to adjust the tidal volume according to their own comfort.

Beat-to-beat values of systolic pressure and of pulse intervals were measured for further analysis. Power spectra, coherence and modulus between pulse intervals and systolic pressure spectra were calculated (*11*). The value of modulus at a frequency of approximately 0.1Hz was taken as the measure of baroreflex sensitivity (BRS).

Ejection Fraction

A two-dimensional echocardiogram was obtained using an Acuson 128 XP/10 unit. An evaluation of the left ventricular ejection fraction was performed.

Late Potentials

Late potentials were evaluated using the HIPEC-analyser ECG Averaging System. Filtering at 40 Hz was used and 200 beats were averaged to achieve a final noise less than 0.3 microvolts. The presence of late potentials was defined as positive if two of the three criteria were met: a filtered QRS complex longer than 120 ms, a root mean square voltage of the last 40 msec of the filtered QRS complex less than 25 microvolts, and the duration of low-amplitude signals (less than 40 microvolts in the terminal portion of the QRS complex) longer than 40 msec. A prolonged QRS was not considered a positive criterion if the QRS duration, derived from a standard ECG, was greater than 120 msec.

The sensitivity and specificity of all risk indices were compared.

RESULTS

Table 1 shows comparisons of the sensitivity and specificity of the fast scaling index alpha-log N(alpha=1.15) >3.0, of an occurrence of ventricular premature complexes higher than 10/h, of the SDNN index lower than 30 ms, of an ejection fraction lower than 40%, of baroreflex sensitivity less than 3 ms/mmHg and of positive late potential that were determined in 14 patients who died within a year of examination and in nine survivors. The sensitivity and specificity of the scaling index alpha, a measure of heart rate variability and arrhythmias which has an advantage of structural complexity, appeared to have the highest predictive value.

Table 1

Sensitivity and specificity of the fast scaling index alpha and five standard indices of the risk of cardiac death determined in our group of 14 deceased patients and nine survivors of myocardial infarction

RISK FACTOR	SENSITIVITY [%]	SPECIFICITY [%]
N(alpha=1.15) > 3.0	81	58
Ventricular premature complexes >10/hour	44	29
SDNN index < 30 ms	56	36
Ejection fraction < 40%	75	55
Baroreflex sensitivity < 3 ms/mmHg	75	55
Late potentials – positive	63	40

DISCUSSION

The high rate of sudden cardiac death is a serious public health problem (*12*). The development of new treatment strategies, e.g., implantation of a defibrillator, has gained practical importance for the prediction of sudden cardiac death risk. Ischaemic injury to the myocardium is frequently complicated by ventricular arrhythmias, the obvious cause of sudden cardiac death. An increased sympathetic and/or a decreased parasympathetic nervous activity enhance the risk of cardiac death. Parasympathetic activity, which exerts a protective effect against the appearance of ventricular tachyarrhythmias, is often altered in patients after myocardial infarction. It is, therefore, of particular interest to assess an approach to the quantification of increased arrhythmogenity and

impaired autonomic control of the heart, which will have a meaningful impact on risk predicting. An assessment of the complexity of factors influencing the sequence of pulse intervals might increase the predictive value of heart rate variability and arrhythmias because these are expressed in the form of one complex index.

In recent years, the chaos theory has been applied to the analysis of heart rate and blood pressure control *(13,14)*. It is probable that the complexity of arrhythmias is linked to the underlying electrophysiological mechanism. According to this view, low-complexity arrhythmias relate to a stable electrophysiological substrate (probably a re-entry within a stable myocardial scar), whereas high-complexity arrhythmias indicate an unstable substrate (e.g., transient ischaemia, early and late after-depolarisation). The advantage of the alpha index for determination of the complexity of arrhythmias lies in the use of one value only. This seems to offer the best approach to the qualitative evaluation of physiological and pathological conditions (*15,16*)

Our study presents a modified approach to the application of an alpha index technique. We used a set of non-invasive tests for assessment of the risk of sudden cardiac death together with a fast scaling index alpha. The main aim of our study was to test whether the examination of the fast scaling index alpha (*10*) in post-infarction patients could improve the stratification procedure. It was clearly shown that the complexity analysis technique of the distribution of pulse intervals is a promising tool for determination of the risk of cardiac death.

Honzíková N., Semrád B., Fišer B.

NELINEÁRNÍ STRUKTURNÍ ANALÝZA TEPOVÝCH INTERVALŮ A RIZIKO SMRTI U PACIENTŮ PO INFARKTU MYOKARDU

S o u h r n

Porovnali jsme predikční hodnotu normalizovaného indexu alfa (teorie chaosu) a standardních neinvazivních indexů rizika srdeční smrti u pacientů po infarktu myokardu (IM). Normalizovaný index alfa (index lokální fraktální struktury distribuce stavů tepových intervalů ve fázovém prostoru) jsme určili z 24-hod záznamů EKG u pacientů 7–14 dnů po infarktu myokardu. Stanovili jsme rychlou metodou alfa index každého tepového intervalu a distribuční histogram N(alfa) u 14 pacientů, kteří zemřeli v průběhu jednoho roku po IM a u 9 kontrol náhodně vybraných ze 150 žijících pacientů. Jako kritickou hodnotu rizika pacienta pro statistickou analýzu jsme vzali hodnotu logN(alfa=1.15)>3. Porovnali jsme sensitivitu a specificitu normalizovaného indexu alfa a standardních indexů srdeční funkce – ejekční frakce (EF)<40%; počtu extrasystol za 1 hod., (VPCs)>10; pozitivních pozdních potenciálů (LP); citlivosti baroreflexu (BRS)<3ms/mmHg a SDNN indexu<30ms. Sensitivita a specificita jednotlivých parametrů: log N(alfa=1.15)>3.0 (sensitivita 81%; specificita 58%); VPCs (44%; 29%); EF (75%; 55%); LP (63%; 40%); BRS (75%; 55%), SDNN index (56%, 36%). Ukazuje se, že přesnost určení rizika srdeční smrti na základě neinvazivně získaných indexů srdeční funkce může být zvýšena při použití nelineární strukturní analýzy tepových intervalů.

A c k n o w l e d g e m e n t s

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