SCRIPTA MEDICA (BRNO) – 73 (1): 31–34, *January 2000*

SYMPATHETIC OVERACTIVITY AND MORTALITY IN PATIENTS AFTER MYOCARDIAL INFARCTION

HONZÍKOVÁ N.[1], FIŠER B.[1], SEMRÁD B.[2]

[1] Department of Physiology, Faculty of Medicine, Masaryk University, Brno
[2] First Department of Internal Medicine, Faculty of Medicine, Masaryk University, Brno

A b s t r a c t

The aim of the present study was to evaluate the impact of autonomic dysfunction (AD) on mortality in patients after myocardial infarction. One hundred sixty two patients were investigated 7 to 21 days after the first signs of myocardial infarction; 20 patients died during next two years. Heart rate variability was determined as the SDNN index (mean of the standard deviations of all normal-to-normal intervals for all 5-minute segments of a 24-hour recording) and baroreflex sensitivity (BRS) was estimated by means of spectral analysis. The BRS<3 ms/mmHg and/or SDNN index<30 ms (mean of the standard deviations of all normal-to-normal intervals for all 5-minute segments of a 24-hour recording) were taken as markers of AD. A stratification of patients was performed according to the number of risk factors (ejection fraction<40%, presence of late potentials, more than 10 ventricular extrasystoles per hour on a 24-hour ECG). In a subgroup with one or two risk factors there were 64 patients, 32 of them with AD and 32 without AD. The mortality was 6.25% in patients without AD and 31.25% in patients with AD (P<0.025). It is concluded that, in the patients after myocardial infarction, AD increased the 2-year mortality five-times.

K e y w o r d s

heart rate variability, baroreflex sensitivity, myocardial infarction, risk of sudden cardiac death

INTRODUCTION

Patients surviving acute myocardial infarction (MI) are at risk of sudden cardiac death. Extensive research has focused on the association of sudden cardiac death after MI with various clinical tests of heart function.

Sympathetic overactivity associated with low parasympathetic activity is an autonomic dysfunction (AD) which increases cardiac mortality.

The aim of the present study was to evaluate the impact of AD on the mortality of patients after myocardial infarction.

MATERIALS AND METHODS

One hundred sixty two patients were investigated 7 to 21 days after the first signs of myocardial infarction; 20 patients died during the following two-year period

Blood pressure measurements and Holter recordings were taken before discharge, i.e., 7 to 21 days after the first signs of MI. The 24-hour ECG was recorded on a two-channel Oxford Excell electrocardiograph (Abington, UK).

Heart rate variability (HRV) was determined as the SDNN index (mean of the standard deviations of all normal-to-normal intervals for all 5-minute segments of a 24-hour recording). Baroreflex sensitivity (BRS) was estimated by means of spectral analysis of spontaneous fluctuations of systolic blood pressure and cardiac intervals (Finapres, 5-minute recording, metronome-controlled breathing, 20 breaths per minute).

Beat-to-beat values of systolic blood pressure and pulse intervals were measured and their mean values and SDs were calculated. For spectral analysis, the data were linearly interpolated and equidistantly sampled at 2 Hz. The linear trend was removed. Autocorrelation and cross-correlation functions, autospectra and cross-spectra, coherence and a modulus between spectra were calculated. The modulus of transfer function between variations in systolic pressure and pulse intervals was used for estimation of BRS. The modulus (H) was calculated in the frequency range (f) by the following equation:

$$H(f) = Gxy(f) / Gx(f)$$

where Gxy(f) corresponds to the cross-spectral density between systolic pressure and pulse intervals and Gx(f) corresponds to the power spectral density of systolic pressure. The value of modulus at a frequency of 0.1 Hz was taken as a measure of BRS (in ms/mmHg) because fluctuations at this frequency originate primarily in blood pressure and are transformed to changes in pulse intervals by baroreflex. The 0.1 Hz rhythm is often shifted to lower frequencies in patients after MI. Therefore, the value of modulus was assessed in the frequency range of 0.07 to 0.12 Hz at the highest coherence (*1*).

The BRS<3 ms/mmHg and/or SDNN index<30 ms were taken as markers of AD. A stratification of patients was performed according to the number of risk factors (0-1) in a patient.

The following risk factors were evaluated: decreased contractility (echocardiographic ejection fraction<40%, risk factor I), arrhythmogenic substrate (presence of late potentials on averaged ECG, risk factor II) and presence of a trigger factor (more than 10 ventricular extrasystoles per hour on a 24-hour ECG, risk factor III). Mortality in the post-MI patients was followed up for 2 years.

RESULTS

In a subgroup of 94 patients without risk factors there were not differences in mortality between patients with AD (4%) and without AD (4.5%). In 6 patients with three risk factors, mortality was 66.6%; five of them had AD. In a subgroup with one or two risk factors, there were 64 patients; 32 of them with AD and 32 without AD. Mortality was 6.25% in patients without AD and 31.25% in patients with AD (P<0.025). It is concluded that autonomic dysfunction increased the 2-year mortality five-times in patients after myocardial infarction.

DISCUSSION

The most important factor deciding about the destiny of the post-myocardial infarction patients is the activity of the autonomic nervous system. An ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) study performed in 23 centres evaluated the independent prognostic value of two markers of autonomic activity, BRS and heart rate variability, in 1284 patients after myocardial infarction. During a mean follow-up of 21 months there were 49 cardiac deaths. BRS was determined by the phenylephrine method and was significantly lower in the deceased patients (4.6±3.0 versus 7.6±5.0 ms/mmHg, P<0.0001). Survival analysis employed the traditional cut-off values of 3.0 ms/mmHg for BRS. An approximately five-fold increase of mortality in patients with low BRS was observed (*2*).

We confirmed the importance of BRS and heart rate variability as prognostic indexes, using the non-invasive method of determination of BRS by spectral analysis (*3*,*4*).

A correlation between the ejection fraction and the myocardial norepinephrine concentration indicates that sympathetic overactivity is related to the degree of cardiac contractility deterioration (*5*). For this reason the question of whether sympathetic overactivity measurement brings additional information could not be answered. The present study revealed that the noninvasive determination of autonomic dysfunction was useful.

The stratification of post-myocardial infarction patients in relation to risk factors for cardiac death is now more important than it was in the past because at present there is a possibility to treat patients at risk with implantable, cardioverter-defibrillator devices.

Honzíková N., Fišer B., Semrád B.

ZVÝŠENÁ SYMPATICKÁ AKTIVITA A MORTALITA U NEMOCNÝCH PO INFARKTU MYOKARDU

S o u h r n

Cílem této studie bylo zhodnocení vlivu autonomní dysfunkce (AD) na mortalitu nemocných po infarktu myokardu. 162 nemocných bylo vyšetřeno 7-21 dní po prvních příznacích infarktu myokardu, 20 nemocných zemřelo během dvou let. Variabilita srdeční frekvence byla určena jako SDNN index, baroreflexní sensitivita (BRS) byla zjištěna pomocí spektrální analýzy. BRS<3 ms/mmHg a/nebo SDNN index<30 ms byly považovány za ukazatele AD. Stratifikace nemocných byla provedena podle počtu rizikových faktorů (ejekční frakce<40 %, přítomnost pozdních potenciálů, více než 10 komorových extrasystol za hodinu na 24-hodinovém EKG). V podskupině s jedním nebo dvěma rizikovými faktory bylo 64 nemocných, 32 mělo a 32 nemělo AD. Mortalita byla 6,25 % u nemocných bez AD a 31,25 % u nemocných s AD (p<0,025). Uzavíráme, že AD zvětšila pětkrát dvouletou mortalitu u nemocných po infarktu myokardu.

Acknowledgements

This study was supported in part by a grant 4731-3 from the Grant Agency of the Czech Ministry of Health and a grant CEZ: J07/98: 141100004 from the Czech Ministry of Education.

REFERENCES

1. *Honzíková N, Fišer B, Honzík J.* Non-invasive determination of baroreflex sensitivity in man by means of spectral analysis. Physiol Res 1992;29:31-37.
2. *La Rovere MT, Bigger JT, Marcus FI et al.* Prognostic value of depressed baroreflex sensitivity. The ATRAMI study. Circulation 1995; 92(Suppl I):76.
3. *Honzíková N, Semrád B, Fišer B, Labrová R.* Heart rate variability and baroreflex sensitivity in healthy subjects and in postinfarction patients treated by thrombolysis. Exp and Clin Cardiology 1997;2:69-72.
4. *Honzíková N, Semrád B, Fišer B, Labrová R.* Risk stratification after myocardial infarction. Scripta Medica 1997;70:153-158.
5. *Schofer J, Mathey D.* Herzinsuffizienz. Fortschritte in der Therapie. Stuttgart, New York: Georg Thieme Verlag, 1991:112.