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Influence of Deep Breathing on Heart Rate Variability in Patients with Ischemic Heart Disease

M. Tamošiūnaitė
Department of Informatics, Kaunas Magnus Universit,
Vileikos str.8, LT-3035 Kaunas, Lithuania, e-mail: minija_tamosiunaite@fc.vdu.lt
G. Urbonavičienė, A. Vainoras, G. Gargasas, S. Kaminskienė
Institute of Cardiology*, Kaunas University of Medicine,*
Sukileliu Av. 17, LT-3007 Kaunas, Lithuania
I. Blužaitė, H. Rickli
Division of Cardiology, Department of Internal Medicine, Kantonsspital St. Gallen,
CH-9007 St. Gallen, Switzerland, phone: +41 71 494 1111; fax: +41 71 494 6142 ; e-mail: ina.bluzaite@kssg.ch

Introduction

Heart rate variability (HRV) represents the sympathetic and vagal activity and is one of the most promising markers for cardiovascular mortality, including sudden cardiac death [1]. The predictive value of depressed HRV is independent of other factors established for post-infarction risk stratification, such as depressed left ventricular ejection fraction, increased ventricular ectopic activity, and presence of late potentials [2]. For prediction of all-cause mortality, the value of HRV is similar to that of left ventricular ejection fraction, and according to some studies HRV is superior to left ventricular ejection fraction in predicting arrhythmic events (sudden cardiac death and ventricular tachycardia) [3]. During deep breathing, changes in heart rate occur primarily because of alterations of vagal-cardiac activity [4, 5]. An impairment of this system can lead to depressed HRV [6].

The aim of this study was to evaluate HRV in deep breathing conditions for patients with ischemic heart disease, using regular measures, and to extend the method by investigating HRV changes in consecutive breathing cycles.

Methods and study population

The study consisted of two parts, one was carried out in the Department of Cardiology at Kaunas medical University and the other - Division of Cardiology, Department of Internal Medicine, Kantonsspital St. Gallen, Switzerland.

The first study population was composed of 121 patients admitted with myocardial infarction (MI), and stable or unstable angina to the Department of Cardiology, Kaunas medical Clinics, 74.6% male and 25.4% female. Coronary angiography was performed for all the patients. The patients were classified into three classes. The first class conssited of patients with MI. The patients without myocardial infarction were further classified based on the results of coronary angiography: the second class consisted of patients with stenosis of coronary artery lumen ≤30% and the third class - with stenosis of coronary artery lumen ≥50 %.

The deep breathing HRV test was performed on 3-7 days after admission. All patients had no signs of severe heart failure, were in sinus rhythm and did not interrupt standard therapy which included beta blockers. The test was performed in the morning in the patient's room after being in the supine position for 10 minutes. Before beginning the test, patients were taught to breathe at a rate of 6 respiration cycles per minute: 5 seconds for each inhalation and 5 seconds for each exhalation. All tests were performed by a single examiner who raised her hand as a signal to start each inhalation and lowered it to start each exhalation. High resolution ECGs (1 min. duration, 2 kHz, 12 bit, 12-lead) were recorded at rest. The heart rate variability interval (R-R intervals between adjacent QRS complexes resulting from sinus node depolarization) was measured automatically. R-R intervals surrounding premature ventricular contractions were excluded from the analysis. The change in heart rate was calculated as the difference between the shortest and the longest R-R interval: HRV = [60.000/Short R-R interval (msec)] - [60.000/Long R-R interval (msec)], measured in beats per minute.

The other study population consisted of 47 unselected patients, 72% male and 27% female, consecutively referred for coronary angiography due to chest pain, dyspnea or abnormal exercise test in Division of Cardiology, Department of Internal Medicine, Kantonsspital St. Gallen, Switzerland. Patients with other heart disease (valvular heart disease or cardiomyopathy), severe congestive heart failure (NYHA III-IV), unstable angina, atrial flutter, atrial fibrillation, multiple ventricular or atrial ectopy or conduction disturbances, that precluded measurement of heart variability were excluded from the study.

The deep breathing HRV-test was conducted with the patient in a supine position connected to the standard electrocardiogram (ECG) leads. The test was performed after the patient had been in the supine position for 5

minutes. Before beginning the test, patients were taught to breathe at a rate 3 respiration cycles per 30 seconds: 5 seconds for each inhalation and 5 seconds for each exhalation. The ECG was recorded at a speed of 25 mm/sec. for 30 seconds while the patient breathed as instructed. The R-R intervals between adjacent QRS complexes were measured manually. The change in heart rate was calculated as the difference between the shortest and the longest R-R interval. Coronary angiography was performed by Judkins technique with multiple projections. Coronary stenoses were quantified visually and with the help of callipers. A luminal narrowing $\geq$ 50% of the cross-section was considered to represent as a hemodynamically significant coronary artery lesion.

Results

According to the results of the first study, HRV of the entire group was 16.1 ± 0.89 beats/min. HRV was less than 10 beats/min in 27% of the patients, between 10 to 20 beats/min in 46%, and more than 20 beats/min in 27%. HRV less than 10 beats/min was in 35% of patients after myocardial infarction, 27.6% in patients with coronary artery stenosis and 18.4% in patients without coronary artery stenosis (p=0.43, significantly different between patients with and without coronary artery stenosis). For the patients with myocardial infarction percentage of HRV less than 10 beats/min was higher in males: 45%. For the patients without myocardial infarction HRV less than 10 beats/min was 20% in males: 25% with coronary artery stenosis and 14.3% without coronary artery stenosis. HRV less than 10 beats/min in entire female group was 21.4%: 28.6% with coronary artery stenosis and 20% without coronary artery stenosis.

Comparing HRV parameters we have found significant differences only between the 2nd and the 3rd patients classes (table 1).

Table 1. Heart rate variability (HRV) parameters for all the patients expressed as mean±SE

Parameter	Class 1 n=38	Class 2 n=46	Class 3 n=37
maxRR	1024±32	1038±23	1029±28
minRR	820±24	832±16	781±22
sdnn	35.2±4.2	44.4±3.5	47.2±5.1
meanRR	909±26	922±18	908±21
meanhr	67±2	65.7±1.3	67±1.6
HRV, beats/min	14.9±1.3	14.2±1.0*	19.6±2.1*

*p<0.05

Time sequences of RR interval variability in five consecutive deep breathing inhalation-exhalation cycles were analyzed. To better observe existing patterns we were not using variability measures in beats per minute, which employ inverse proportionality and thus nonlinearly transform data, but were exploring differences in milliseconds between minimal interval in the inhalation phase, and maximum interval in the exhalation phase. Though individual realizations were quite disperse (Table 2), a clear pattern was observable when analyzing the averages inside classes (Fig. 1). Another view of Fig. 1 where difference between variability in consecutive cycles is plotted against cycle length (first of the two compared) is provided in Fig. 2.

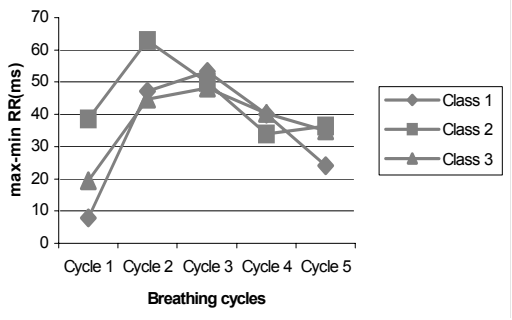

Fig. 1. Change of difference in ms between minimum RR in inhalation and maximum RR in exhalation vs. the number of deep breathing cycle

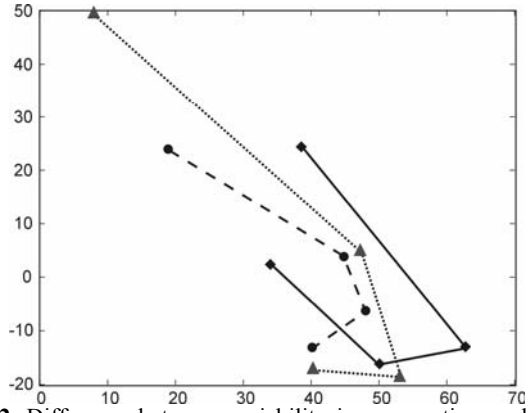

Fig. 2. Difference between variability in consecutive cycles vs. variability of the first of the two cycles being compared: dotted line – Class 1, solid line – Class 2, dashed line – Class 3

For all three classes the pattern was as follows: heart rate was less variable in the first cycle, more variable in the second or second and third, and variability again was falling in the fourth and fifth cycle. Although reliable difference between the analyzed classes was not observed for either individual cycle (Table 3), the obvious time pattern might be of interest when analyzing and interpreting results of deep breathing test: e.g. due to the fact that the biggest variability is obtained in the second and third cycle it might be theorized that 30 second and 1 minute deep breathing test results might be comparable. Yet one should be careful with this sort of conclusions due to substantial variability between realizations, as demonstrated by standard deviations in Table 2. It should be, however, noted, that though variability of RR exhalation-inhalation max-min differences inside a classes was big, in each class the decisive proportion of individual cases demonstrated either rising-rising-falling-falling, or rising-falling-falling-falling pattern for the analyzed parameter in the five respiration cycles.

Differences between consecutive breathing cycles proved to be more significant than differences inside a cycle between classes. Results of paired t-tests between first and second, second and third, third and fort, forth and fifth breathing cycles for each class are provided in Table 4. It may be noted that differences are significant only for Class 1, which is the class with most significant both haemodynamical and structural heart changes, while

Table 2. Max-Min RR difference in ms for five individual breathing cycles; mean values (standard deviations) are provided for every class

	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
Class 1	7.9 (65.5)	47.2 (68.8)	53.3 (69.9)	40.0 (45.4)	24.1 (56.2)
Class 2	38.5 (94.2)	62.9 (83.0)	49.8 (65.6)	33.8 (37.1)	36.4 (41.3)
Class 3	19.3 (80.3)	44.7 (57.6)	48.1 (63.6)	40.2 (46.8)	34.9 (52.5)

Table 3. Difference between means in Max-Min RR difference for three classes, difference (significance level) are provided

	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
Class 1 vs Class 2	-30.7 (0.10)	-15.7 (0.36)	3.5 (0.81)	6.3 (0.50)	-12.3 (0.25)
Class 1 vs Class 3	-11.7 (0.50)	2.6 (0.87)	5.3 (0.74)	-0.2 (0.99)	-10.9 (0.40)
Class 2 vs Class 3	19.0 (0.34)	18.3 (0.27)	1.8 (0.90)	-6.5 (0.49)	1.5 (0.88)

Table 4. Paired sample t-test for changes in variability on the transition between consecutive breathing cycles. Mean difference between Max-Min RR for three classes, in the notation difference (significance level) are provided

	Cycle 1 vs. Cycle 2	Cycle 2 vs. Cycle 3	Cycle 3 vs. Cycle 4	Cycle 4 vs. Cycle 5
Class 1	49.4 (0.03)	4.8 (0.71)	-18.7 (0.09)	-17.1 (0.05)
Class 2	24.4 (0.18)	-13.2 (0.31)	-16.1 (0.12)	2.7 (0.60)
Class 3	23.6 (0.25)	3.8 (0.77)	-6.7 (0.51)	-13.1 (0.52)

changes with the breathing cycles are less significant in other two classes. The result prompts a hypothesis that maybe not variability in deep breathing by itself, but rather lability of that variability with breathing cycles might come out as a diagnostic parameter.

According to the second study results, HRV of the entire group was 7.7 ± 0.7 beats/min. HRV less than 10 beats/min was 75% in patients with coronary artery stenosis and 46.6% in patients without coronary artery stenosis (p=0.26). HRV less than 10 beats/min was 67.6% in male group: 73% with coronary artery stenosis and 50% without coronary artery stenosis. HRV less than 10 beats/min was 61.5% in female group: 83.3% with coronary artery stenosis and 42.8% without coronary artery stenosis.

Discussion

The changes in heart rate associated with respiratory activity are mediated primarily by a combination of changing levels of efferent cardiac vagal and sympathetic activity and mechanically induced sinus node stretch with each respiration [7]. The degree of the contribution from each of these components is related to the frequency and amplitude of the respiratory signal, the mean level of vagal and sympathetic activity, and the mechanical state of the airways. Our previous works have not shown relation between heart rate variability parameters and coronary artery stenosis: comparing HR variability parameters, that were evaluated from 5 min. ECG at rest, between the first (coronary artery stenosis ≤30%) and second patient group (coronary artery stenosis ≥50%) significant differences were not found. Concurrently, deep breathing test gave significantly different proportions of cases with less than 10 beats/min between patients with and without coronary artery narrowing in the first study. Though the study population was small and the result should not be interpreted as a conclusive one, the result is concordant with the hypothesis that HRV measures obtained during deep breathing are more informative than the ones in regular conditions.

The results are also concordant with the findings of other studies of the deep brathing test. HRV during deep breathing test has shown that vagal-cardiac activity is diminished in patients with coronary artery disease. Using this method, Bennet et al. [8] and Mackay et al [9] demonstrated that HRV during deep breathing proved to be a sensitive diagnostic test of autonomic nervous control of the heart in patients with diabetes mellitus. This test was also useful for patients after myocardial infarction. Patients with HRV >=10 beats/min were found to be at minimal risk for cardiac death [5].

Analysis of the change of variability during deep breathing period gave a clear pattern of first growing than falling variability. Though at this point we do not have a physiological interpretation why this sort of dynamics happens, but the results shows that deep breathing test may provide more information than currently used overall variability in 30 seconds or one minute. As it may be seen from Fig. 1 and Fig. 2 behaviour of variability is more similar in Class 1 (MI), and Class 3 (coronary artery narrowing) which both include patients with haemodynamical changes, but differs to some extent for Class 2 which includes patients without significant haemodynamical changes. And furthermore, change of variability in MI class which is expected to have greatest heart lesions is the highest.

Results of the second study were not concordant with those of the first study. Absence of significant differences between classes in the second study could be explained by the fact that the patients in this contingent without significant coronary artery stenosis were regarded as having luminal narrowing < 50% of the crosssection. This way, there were a number of patients, which had borderline hemodynamically significant coronary artery lesions in the group of the patients considered as having no significant coronary narrowing. In the first study population the non significant coronary lesions were regarded as coronary luminal narrowing < 30% of the crosssection. Yet the most important difference was observed in the general proportion of patients with less than 10 beats/min. To some extent the difference could be attributed to difference between 30 second, and one minute test. Additionally, breathing standards were slightly different, and patients of the first study were hospitalized at the moment of performing the test, while those of the second study were

not. In general this shows that deep breathing test could be quite sensitive to a number of conditions, and better standartization needs be developed during further work on this test.

Conclusions

The value of HRV during deep breathing test was found to be lower in patients with coronary artery stenosis ≥ 50 % comparing to the patients with coronary artery stenosis ≤30% (p=0.02), that has shown diminished vagal-cardiac activity is in patients with coronary artery disease. Analyzing variability in five consecutive breathing cycles a rising-falling pattern was observed which was quantitatively more similar between MI and coronary artery narrowing classes. The lability of variability during deep breathing was expressed most in the myocardial infarction patients among the three analyzed classes.

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M. Tamošiūnaitė, G. Urbonavičienė, A. Vainoras, L. Gargasas, S. Kaminskienė, I. Blužaitė, H. Rickli. Dozuoto kvėpavimo mėginio įtaka ligoniams sergantiems išemine širdies liga // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2005. – Nr. 3(59). – P. 33–36.

ŠRV buvo įvertintas 121 ligoniui 3-7 stacionarizavimo dieną. Ligoniai buvo paprašyti gyliai pakvėpuoti 6 kartus per minutę, o ŠR buvo registruotas ir apkaičiuotas automatiniu būdu. Testo rezultatas buvo nustatytas kaip skirtumas tarp trumpiausio ir ilgiausio širdies ritmo intervalo: ŠRV = [60.000/trumpiausias R-R intervalas (ms)] - [60.000/ilgiausias R-R intervalas (ms)], matuojamas dūžiais/min. ŠRV mažiau 10 dūžių/min buvo 27 proc. ligonių, tarp 10 ir 20 dūžių/min - 46 proc. ligonių ir daugiau 20 dūžių/min - 27 proc. ištirtų ligonių. Mažiau 10 dūžių/min nustatyta 35 proc. ligonių, persirgusių miokardo infarktu, 27,6 proc, ligonių, kuriems nustatytos hemodinamiškai reikšmingos vainikinių arterijų stenozės ir 18,4 proc. ligonių, kuriems buvo nustatytos hemodinamiškai nereikšmingos vainikinių arterijų stenozės. ŠRV reikšmė gylaus kvėpavimo testo metu buvo patikimai mažesnė ligoniams, kuriems nustatytos hemodinamiškai reikšmingos vainikinių arterijų stenozės, lyginant su ligoniais kuriems nustatytos hemodinamiškai nereiksmingos stenozės (atitinkamai 14.2±1.0ir 19.6±2.1; p=0.02). Il. 2, bibl. 9 (anglų kalba, santraukos lietuvių, anglų ir rusų k.).

M. Tamošiūnaitė, G. Urbonavičienė, A. Vainoras, L. Gargasas, S. Kaminskienė, I. Blužaitė, H. Rickli. Influence of Deep Breathing on Heart Rate Variability in Patients with Ischemic Heart Disease // Electronics and Electrical Engineering. – Kaunas: Technologija, 2005. – No. 3(59). – P. 33–36.

HRV was assessed in 121 consecutive patients on 3-7 days after admission. Patients were instructed to take 6 deep respirations in 1 minute while changes in heart rate were measured and calculated by an electrocardiographic recorder automatically. The test result was defined as a difference between the shortest and longest heart rate interval: HRV = [60.000/Short R-R interval (msec)] - [60.000/Long R-R interval (msec)], measured in beats per minute. HRV was less than 10 beats/min in 27% of the patients, between 10 to 20 beats/min in 46% of patients, and more than 20 beats/min in 27% of patients. HRV less than 10 beats/min was in 35% of patients with myocardial infarction, 27.6% in patients with coronary artery stenosis and 18.4% in patients without coronary artery stenosis. The value of HRV during deep breathing test was found to be lower in patients with coronary artery stenosis ≥ 50 % comparing to the patients with coronary artery stenosis ≤30% (respectively 14.2±1.0 and 19.6±2.1; p=0.02). That has shown diminished vagal-cardiac activity in patients with coronary artery disease. Ill. 2, bibl. 9 (in English; summaries in Lithuanian, English and Russian).

М. Тамошюнайте, Г. Урбонавичене, А. Вайнорас, Л. Гаргасас, С. Каминскене, И. Блужайте, Х. Рикли. Влияние теста дозированного дыхания на вариабельность сердечного ритма больным с ишемической болезнью сердца // Электроника и электротехника. – Каунас: Технология, 2005. – № 3(59). – P. 33–36.

Вариабельность сердечного ритма (ВРС) была оценена 121 больному на 3-7 день после поступления в стационар. Больные должны были глубоко подышать 6 раз в минуту. Вариабельность сердечного ритма была оценена автоматически, как разница между наименьшем и наибольшем интервалом: ВРС = [60.000/наименьший R-R интервал (mc)] - [60.000/наибольший R-R интервал (mc)], измеренный количеством ударов в минуту. ВРС меньше чем 10 ударов/мин. была установлена у 27% больных, ВРС в интервале между 10 и 20 ударов/мин. была установлена у 46% больных, у 27% больных ВРС была больше чем 20 ударов/мин. ВРС меньше чем 10 ударов/мин. была установлена 35% больных инфарктом миокарда, 27,6% больных которым были диагнозированы гемодинамически значимые сужения коронарных артерий и 18,4% больных, которым были диагнозированы сужения коронарных артерий до 30%. Ил. 2, библ. 9 (на английском языке; рефераты на литовском, английском и русском яз.).