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Is There a Correlation between Heart Rate Variability, Cardiac Dysrhythmia and Esophageal Reflux Exposure?

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ABSTRACT

Background and Aim

Autonomic modulation of cardiac activity can be regarded as the efferent response of the CNS integration of various viscerosensory signals from different peripheral organs, including the gastrointestinal wall. The aim of this study was to determine a potential relation between the distal esophagus acid exposure in patients with GERD and the occurrence of cardiac dysrhythmia within this category of patients.

Material and method

Twenty patients (9 women and 11 men, mean age 59,42±13,21 years), hospitalized in the Emergency County Hospital, Cluj-Napoca, Romania, presenting with symptoms chiefly consisting of atypical heartburn-like chest pain and palpitations, were selected to participate in the study. All the patients were subject to investigations in order to determine the cardiovascular risk factors, to ECG at rest and during effort measurements, echocardiogram, upper digestive endoscopy and simultaneous 24-hr ambulatory ECG and distal esophageal pH monitoring. The measurements revealed no pathological findings in rest ECG, treadmill cardiac stress test or ecocardiography parameters. Lipid fraction values were within normal range in all patients. The presence of heart variability rate (HRV), dysrhythmia and ST segment depression were assessed. At the same time, spectral analysis of the heart rate variability was performed in order to calculate the low-frequency (LF) band, the high-frequency (HF) band and the LF/HF ratio. In the case of each patient a symptomatology index (SI) was determined, recording the ratio between the number of symptomatic events produced by reflux episodes and the total number of symptomatic episodes listed in the symptom diary.

Results

There were no statistically significant differences between patients with and without dysrhythmia, namely ST depression, related to the symptoms recorded in the symptomatology index. As concerns the relation between the LF/HF ratio measured during activity (daylight time) and the distal esophageal acid exposure time (pH<4) there were significant differences between the average of these variables in patients with negative SI (p=0.001). We noticed that there was a statistically significant negative correlation (r=0.809, p=0.001, namely r=0.617, p=0.025) between the LF/HF ratio during activity, namely LF/HF during sleep, and age. The same indirect correlation was also found in the case of distal esophageal acid exposure during activity (r = 0.53, p = 0.02).

In conclusion, the study revealed that, in general, there were no significant correlations between the presence of different arrhythmias and the variables recorded in a 24 hours simultaneous ambulatory ECG and pH monitoring. At the same time, age was indirectly correlated to the LF/HF ratio both during activity and sleep.

Keywords : GERD, cardiac dysrhythmia, heart rate variability

Introduction

The electrophysiological mechanisms underlying dysrhythmias are the altered automatism or the impaired electrical signaling of the cardiac conduction tissue. The autonomic modulation of the heart rate plays a vital role in the emergence of cardiac dysrhythmias. [1][2][3]

There is clinical evidence revealing the part played by the esophagus in generating cardiac dysrhythmias due to its influence on the cardiac autonomic innervation, which can be explained by the fact that many afferent visceral fibers stemming from the distal esophagus make up the afferent neural pathway shared with the heart. Consequently, the signals generated by reflux episodes in the distal esophagus can influence the electrical rhythmic activity of the heart, thus contributing to the occurrence of dysrhythmias.[4][5]

The autonomic nervous system, especially the vagal component, is less susceptible to direct investigation and manipulation. The heart rate variability (HRV) analysis is a non-invasive method employed to evaluate the autonomic cardiac function, which includes two main techniques: time-domain and frequency-domain. The power spectral analysis of the autonomic function consists of a low frequency band (LF), high frequencies band (HF) and a LF/HF ratio [6]. The LF is influenced by sympathetic modulation, while the HF represents a modulatory signal of respiratory driven cardiac vago-efferent drive. The two components are mutually regulated, and their reciprocity defines the sympatethic-vagal balance measured by the LF/HF ratio. [7][8][9]

A few studies [10] suggested the theory that there are people sensitive to acid esophageal stimulation (the Bernstein test), in whose case acid-induced afferent signals coming from the esophageal walls can influence the electrical rhythmic activity of the heart and thus contribute to the emergence of dysrhythmias.

The aim of this study was to establish a possible relation between the distal esophageal acid and alkaline exposure generated by gastro-esophageal reflux and the occurrence of cardiac dysrhythmias.

Material and method

Twenty patients (9 women and 11 men, mean age

59,42±13,21 years), hospitalized in the Emergency County Hospital, Cluj-Napoca, Romania, presenting with symptoms chiefly consisting of atypical heartburn-like chest pain and palpitations, were selected to participate in the study. All the patients were subject to investigations in order to determine the cardiovascular risk factors, to ECG at rest and during effort measurements, echocardiogram, upper digestive endoscopy and simultaneous 24-hr ambulatory ECG and distal esophageal pH monitoring. The measurements revealed no pathological findings in rest ECG, treadmill cardiac stress test or cardiac ultrasound parameters. Lipid fraction values were within normal range in all patients. In the case of each patient a symptomatology index (SI) was drafted, recording the ratio between the number of symptomatic events produced by reflux episodes and the total number of symptomatic episodes listed in the symptom diary. We believe that both acid (pH<4) and alkaline (pH>7,5) reflux could generate symptomatic episodes, in consequence SI was considered positive for acid or alkaline exposure if SI>50%.

HRV Analysis

Heart variability rate (HRV), presence of dysrhythmia and the ST segment depression were analyzed. Also, a spectral analysis of the heart rate variability was performed in order to calculate the low frequency (LF) band, the high frequency (HF) band and the LF/HF ratio. Frequency-domain analysis was conducted by using a non-parametric method of fast Fourier transformation (FFT). The power spectrum was subsequently converted into standard frequency-domain measurements, including the total variance, LF (0.04-0.15 Hz), HF (0.15-0.40 Hz), LF/HF, and LF%. Variance, LF, HF and LF/HF were logarithmically transformed to correct for the skewness of the distribution. Also, we analyzed the presence of dysrhythmia and ST segment depression.

Ambulatory 24-hr distal esophageal pH monitoring

For pH-monitoring, we used a multi-ionometer device (Gastro-pH, Gadion, Romania) and a antimony probe with a built-in manometry channel (Sandhill,USA) placed in the distal esophagus at 5cm above the low esophageal sphincter (LES). The position of the LES was detected by using one channel manometry. The pH-metry recording was interpreted using GastroPH 2.0 software (Datronix,Romania), which provided the following parameters: % time pH<4 during activity (daylight); % time pH<4 during sleep; % time pH>7,5 during activity; % time pH>7,5 during sleep. Values over 4,2% for acid exposure and 5% for alkaline exposure were considered pathological. The patients included in the study were asked to accurately note down in their 24-hr journal the symptoms occurring during simultaneous monitoring. A direct causal relation between reflux episodes and symptoms was taken into consideration when an acid (pH<4) or an alkaline reflux episode occurred within a 5 minutes interval before or after the symptom episode marked in patient's journal.

Statistical analysis

The SPSS 16.0 software for Windows (Demo Versions) was used to carry out the statistical analysis. In order to evaluate the differences between the qualitative variables a χ^2 test was used. The Kolmogorov-Smirnov test was used to check the normal distribution of continuous numerical variables. The Student (unpaired) or the Anova tests were used to assess the difference between the continuous quantitative variables averages. The Pearson coefficient was used to assess the correlation between the different variables. The value of the p<0.05 was considered significant from a statistical point of view.

Results

The average values of the simultaneous ECG-Holter and pH-monitoring variables are presented in fig.1.

The SI analysis revealed the following: 45% of the patients had a negative SI; among those with positive SI, 20% had acid and 35% alkaline reflux.

The ECG-Holter monitoring revealed premature ventricular beats (PVE) in 45% of the patients, and premature supraventricular beats (PSVE) in a similar percentage. We found no significant differences between the patients with or without PVE, namely PSVE, associated to the existing symptomatology: PVE-without symptomatology 36.4% vs. 55.6%, acid reflux 27.3% vs. 11.1%, alkaline reflux 36.4% vs. 33.3%, p=NS in all cases; PSVE- without symptomatology 36,4 vs 55,6%, acid reflux 18,2 vs 22,2%, alkaline reflux 45,5 vs 22,2%, p-NS.

At the same time, there was no statistically significant difference between the incidence of ST segment depression in 20% of the patients and the SI: 53% of the patients without ST segment depression were SI negative vs. 20% SI positive; acid reflux 20 vs. 20% and alkaline reflux 26.7 vs. 60% with p=NS.

Subsequently we studied the relation between the occurrence of premature ventricular beats, supraventricular, the ST segment depression and the pH-metric parameters. The data are presented in figures 2,3 and 4.

There were no statistically significant differences between patients with and without PSVE in relation to the variables recorded by ECG-Holter or pH-metry monitoring. The same hold true in the case of PVE patients, except for the LF/HF ratio recorded during sleep (p=0.023).

As concerns the LF/HF ratio measured during activity (daytime) associated with acid distal esophageal exposure time (pH<4), there was a significant difference between the average of these variables in patients with negative SI (p=0.01). At the same time, this major difference was also signaled in the presence of the ST segment depression, but only at alkaline exposure (pH>7.5) during sleep (p=0.06).

We noticed that there was a statistically significant negative correlation (r = -0.809, p = 0,001, respectively r = 0.617, p = 0.025) between the LF/HF ratio during activity, namely LF/HF during sleep, and age. The same indirect correlation was found in the case of esophageal acid exposure (pH<4) during activity (r = -0.53, p = 0.02).

We did not identify a relevant correlation between the LF/HF –activity ratio and the pH-metry parameters; on the contrary, the LF/HF-sleep ratio was directly correlated to acid exposure during sleep (pH<4).

Discussions

The term gastrocardiac syndrome was suggested as early as 1952 seeing that eso-gastric irritation stimuli are liable of producing not only chest pain, but also cardiac dysrhythmias [12][13].

It is well-known that there is a rich efferent innervation in the sinoatrial node, liable to generate neurovegetative manifestations. [14]. Consequently, a heart rate increase determined by sympathetic stimulation may be the cause of some arrhythmias.

An elevated vagal activity accompanied by a decrease in heart rate may lead to setting in motion ectopic foci that may contribute in their turn to cardiac arrhythmia.

The autonomic modulation of the cardiac function may be responsible for the transmission of many neurosensory impulses towards different peripheral organs, such as the gastro-esophageal walls. The esophagus and the heart equally share an autonomic innervation, as there are many afferent visceral fibers that originate in the distal esophagus forming the neural afferent way through which esophageal events may influence autonomic cardiac activity. Previous studies had shown that an altered sympathetic-parasympathetic balance was common in patients with reflux esophagitis. [11] In this respect, the HRV analysis is a quite accurate and non-invasive method of evaluating the autonomous cardiac function. It has three spectral components: the high frequency power

spectrum (HF=0.15-0.40) influenced by sympathetic activity, the low frequency power spectrum (LF=0.04-0.15) influenced by vagal activity, and the very low frequency power spectrum (VLF=0.033-0.04). A low HRV can be correlated to a reduced vagal activity or to an increased sympathetic activity that can favor the onset of malignant cardiac arrhythmias. The LF/HF (LF/HF) ratio is regarded as a parameter of the sympathetic-vagal balance.

The studies of Fougas et al., as well as other evidence, suggested that there is a group of people with "hipersensitivity" to acid esophageal stimuli that may trigger certain afferent signals from the esophagus and could be responsible for influencing the electrical activity of the heart leading to dysrhythmias[10].

As emphasized above, previous studies had described and demonstrated the presence of a relation between the central nervous system and the local enteric innervation [14][15][16][17]. To be more specific, the vagus and the afferent spinal nerves bring impulses caused by different mechanical and chemical stimuli from the intestine to the central nervous system [14]. The central nervous system influences the enteric innervation and vice versa, a mutual interference of activities taking place [14]. Thus, many situations were described where different pathological vagal changes have been identified as being the cause of some gastro-intestinal diseases [13][15][16][17][18]. In this context, there were several previous studies which proved that an upset balance between the sympathetic and the parasympathetic nervous system may trigger gastro-esophageal reflux.[19][20].The decrease in the vagal tonus at rest was strongly associated with the increase in esophageal sensitivity [15], correlation which we also determined in this study.

As concerns the theory that the acid exposure of the distal esophagus may trigger arrhythmias [14], we found no significant correlation between the occurrence of premature ventricular or supraventricular beats and the variables recorded during 24-hr Holter ECG and/or pH-metry monitoring. Still, there was an exception – the presence of a correlation in the case of patients with premature ventricular beats – LF/HF ratio during sleep (p=0.023), data in agreement to other studies [14]. Contrary to Tougas's study, there was no significant correlation between the patients with symptomatic acid exposure (positive SI) and the occurrence of Holter ECG modifications (EV, ESSV, ST segment depression).

As we noticed in this study, the LF/HF ratio in the daytime was poorly correlated to the pH-metry parameters, whereas the same ratio measured during the night was directly and significantly correlated to the pH<4, which confirmed the presence of a vagal hyperactivity induced by acid exposure during this period [14].

Another aspect that should be emphasized was the indirect significant correlation between the LF/HF ratio, pH<4 time and age. The average age of our patients was approximately 60 years. The data, very little in fact, in the literature in the field reveal that arrhythmias occurring as a result of digestive pathology in general and esophageal in particular are more frequent in young people, thus stressing out the "functional" pathogeny with this category of patients [24][25].

In most cases, average age and elderly patients rather display degenerative (organic) and not functional mechanisms. Another possible explanation could be that esophageal sensibility decreases with age and/or because a long history of distal esophageal acid exposure is associated with concurrent destruction of mucus sensors in old subjects.

We would like to emphasize that the present study has a major shortcoming, namely the small number of patients. However, in this context we should not overlook the fact that simultaneous Holter ECG/24h and esophageal pH-monitoring are hard to carry out as patients are most reluctant to comply with. Therefore, we still believe that the results concerning the presence of a correlation between the heart rate variability – cardiac dysrhythmia – and the gastro-esophageal reflux detected by pH-monitoring may contribute to enrich the extremely little data accessible worldwide (according to the information in the literature in the field).

In conclusion, our study revealed no significant correlation between the occurrence of different arrhythmias and the variables recorded during a 24-hr ECG and pH monitoring. On the contrary, we discovered that there is an indirect correlation between age and the LF/HF ratio both during activity and sleep, correlation that also occurred during acid exposure pH<4 measurements, but only in daytime.

pathophysiologic perspective. Curr Gastroenterol Rep. 2008 Jun;10(3):200-7.Colucci RA, Silver MJ, Shubrook J. Common types of supraventricular tachycardia: diagnosis and management. Am Fam Physician. 2010;82(8):942-52. Review.

21. Lombardi F, Tarricone D, Tundo F, et al. Autonomic nervous system and paroxysmal atrial fibrillation: a study based on the analysis of the RR intervals change before, during and after paroxysmal atrial fibrillation. Eur Heart J 2004; 25: 1242–8.

22. Bettoni M, Zimmerman M. Autonomic tone variations before the onset of paroxysmal atrial fibrillation. Circulation 2002; 105: 2753–9.

23. Coumel P. Neural aspects of paroxysmal atrial fibrillation. In: Falk RH, Rodrid PJ, eds. Atrial Fibrillation: Mechanisms and Management. New York: Raven Press, 1992: 109–25.

24. Brembilla-Perrot B. Age-related changes in arrhythmias and electrophysiologic properties. Card Electrophysiol Rev 2003; 7: 88–91.

25. Botek M, Stejskal P, Krejci J, Jakubec A, Gaba A. Vagal Threshold Determination. Effect of Age and Gender. Int J Sports Med. 2010 Sep 10. [Epub ahead of print].

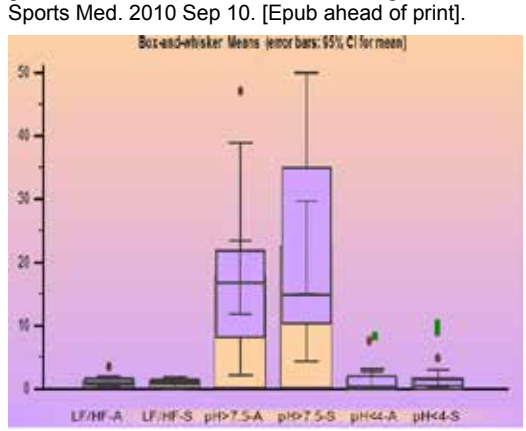

Fig.1. The relationship between pH and Holter ECG parameters

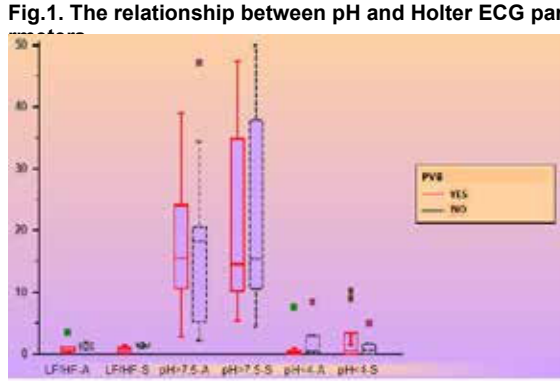

Fig 2.The relationship between pH parameters and premature ventricular beats

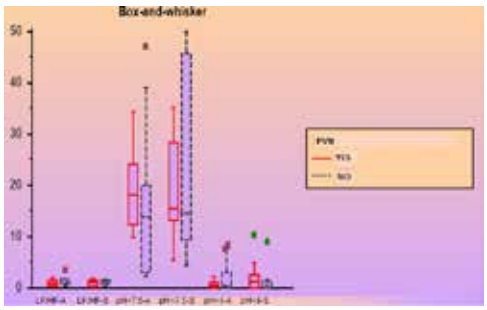

Fig 3.The relationship between pH parameters and premature supravetricular beats

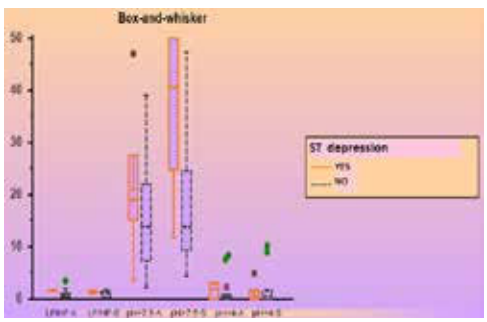

Fig 4.The relationship between pH parameters and ST segment depression

		LF/HF-A	LF/HF-S	pH<4-A	pH<4-S	pH>7.5-A	pH>7.5-S	VÅRSTA
LF/HF-A	Pearson Correlation	1	.380	-.013	.007	.088	.074	-.809**
	Sig. (2-tailed)		.181	.966	.980	.766	.801	.001
LF/HF-S	Pearson Correlation	.380	1	.357	.216	-.241	-.223	-.617*
	Sig. (2-tailed)	.181		.210	.459	.407	.443	.025
pH<4-A	Pearson Correlation	-.013	.357	1	.237	.037	.258	-.530*
	Sig. (2-tailed)	.966	.210		.315	.878	.273	.020
pH<4-S	Pearson Correlation	.007	.216	.237	1	.436	.251	-.378
	Sig. (2-tailed)	.980	.459	.315		.055	.287	.111
pH>7.5-A	Pearson Correlation	.088	-.241	.037	.436	1	.477*	-.082
	Sig. (2-tailed)	.766	.407	.878	.055		.034	.740
pH>7.5-S	Pearson Correlation	.074	-.223	.258	.251	.477*	1	-.199
	Sig. (2-tailed)	.801	.443	.273	.287	.034		.413
**. Correlation is significant at the 0.01 level (2-tailed).								

Table 1. Current correlations between pH parameters and HRV

REFERENCES

1. Saoudi N, Cosio F, Waldo A, et al. A classification of atrial flutter and regular atrial | tachycardia according to electrophysiological mechanisms and anatomical bases. Eur Heart J 2001; 22: 1162–82. | 2. Pop Dana, Zdrenghea D în Zdrenghea D (sub red). Compendiu de electrocardiografie clinică .Clusium. Cluj-Napoca.2011 | 3. Chen YJ, Chen SA, Tai CT, et al. Role of atrial electrophysiology and autonomic nervous system in patients with supraventricular tachycardia and paroxysmal atrial fibrillation. J Am Coll Cardiol 1998; 32: 732–8. 15 | 4. Fallen EL, Kamath MV, Tougas G, et al. Afferent vagal modulation. Clinical studies of visceral sensory input. Auton Neurosci 2001; 90: 35–40. | 5. Berthoud HR, Neuhuber WL. Functional and chemical anatomy of the afferent vagal system. Auton Neurosci 2000; 85: 1–17. | 6. Moulopoulos SD. Heart rate variability and autonomic nervous system. Eur J Int Med. 2006;16:1-2. | 7. Bootsma MC, Swenne C, van Bolhuis H,et al. Heart rate and heart rate variability as indexes of sympathovagal balance.Am J Physiol 1994; 266: 1565–71. | 8. Goldberger JJ. Sympathovagal balance:how should we measure it? Am J Physiol 1999; 276: 1273–80. | 9. Kamath MW, Fallen EL. Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function. Crit Rev Biomed Eng 1993; 21: 245–311. | 10. Tougas G, Kamath M, Watteel G, et al. Modulation of neurocardiac function by esophageal stimulations in humans. Clin Sci 1997; 92: 167–74. | 11. Wood JD, Alpers DH, Andrews PLR. Fundamentals of neurogastroenterology.Gut 1999; 45 (Suppl. II): II6–16. | 12. Jervell O, Lodoen O. The gastrocardiac syndrome. Acta Med Scand Suppl 1952; 266: 595–9. | 13. Tougas G, Spaziani R, Hollerbach S, et al.Cardiac autonomic function and esophageal acid sensitivity in patients with noncardiac chest pain. Gut 2001; 49: 706–12. | 14. Cuomo R, De Giorgi F, Adinolfi L, Sarnelli G. et al.Oesophageal acid exposure and altered neurocardiac function in patients with GERD and idiopathic cardiac dysrhythmias. Aliment Pharmacol Ther 24, 361–370. | 15. Lee YC, Wang HP, Lin LY, Chuang KJ, Chiu HM, Wu MS, Chen MF, Lin JT. Circadian change of cardiac autonomic function in correlation with intra-esophageal pH. Gastroenterol Hepatol. 2006;(8):1302-8. | 16. Chen CL, Orr WC. Autonomic responses to heartburn induced by esophageal acid infusion. J Gastroenterol Hepatol 2004; 19: 922–6. | 17. Lee YC, Wang HP, Lin LY, et al. Heart rate variability in patients with different manifestations of gastroesophageal reflux disease. Auton Neurosci 2004; 116: 39–45. | 18. Cunningham KM, Horowitz M, Riddel PS, et al. Relations among autonomic nerve dysfunction, esophageal motility, and gastric emptying in gastro-esophageal reflux disease. Gut 1991; 32: 1436–40. | 19. Chakraborty TK, Ogilvie AL, Heading RC, et al. Abnormal cardiovascular reflexes in patients with gastroesophageal reflux. Gut 1989; 30: 46–9. | 20. Long JD, Orlando RC. Nonerosive reflux disease: a pathophysiologic perspective. Curr Gastroenterol Rep. 2008 Jun;10(3):200-7.Colucci RA, Silver MJ, Shubrook J. Common types of supraventricular tachycardia: diagnosis and management. Am Fam Physician. 2010;82(8):942-52. Review. | 21. Lombardi F, Tarricone D, Tundo F, et al. Autonomic nervous system and paroxysmal atrial fibrillation: a study based on the analysis of the RR intervals change before, during and after paroxysmal atrial fibrillation. Eur Heart J 2004; 25: 1242–8. | 22. Bettoni M, Zimmerman M. Autonomic tone variations before the onset of paroxysmal atrial fibrillation. Circulation 2002; 105: 2753–9. | 23. Coumel P. Neural aspects of paroxysmal atrial fibrillation. In: Falk RH, Rodrid PJ, eds. Atrial Fibrillation: Mechanisms and Management. New York: Raven Press, 1992: 109–25. | 24. Brembilla-Perrot B. Age-related changes in arrhythmias and electrophysiologic properties. Card Electrophysiol Rev 2003; 7: 88–91. | 25. Botek M, Stejskal P, Krejci J, Jakubec A, Gaba A. Vagal Threshold Determination. Effect of Age and Gender. Int J Sports Med. 2010 Sep 10. [Epub ahead of print]. |