Comparison of propagation of atrial excitation with the cardiopotential distribution on the body surface of hypertensive rats

Hipertansif sıçanlarda vücut yüzeyinde kardiyopotansiyel dağılımı ile atriyal uyarım yayılmasının karşılaştırılması

Svetlana Smirnova, Lyudmila Ivanova[1], Arkady Markel[1], Irina Roshchevskaya, Michail Roshchevsky

Laboratory of Comparative Cardiology, Komi Science Centre, Russian Academy of Sciences, Syktyvkar, Komi
[1]Siberian Division, Institute of Cytology and Genetics, Russian Academy of Sciences, Novosibirsk-*Russia Federation*

ABSTRACT

Objective: Arterial hypertension is associated with the risk of developing atrial arrhythmia. This research was aimed at studying the sequence of depolarization along the atrial epicardium and formation of the cardioelectric field on the body surface of hypertensive rats.
Methods: The study was carried out on eleven ISIAH rats (with hereditary stress-induced hypertension). We analyzed spatial-temporal characteristics of body surface potential map (BSPM), time characteristics of electrocardiogram during atrial depolarization, sequence of atrial epicardial depolarization of rats. Statistical analysis was performed using independent samples t-test.
Results: The results indicated that in 27% of hypertensive rats in the pulmonary vein (PV) sleeves, early excitation areas are formed 2.0±0.5 ms after the beginning of depolarization of the sino-atrial node area, in 73% of animals, the area of the PV sleeves is excited 6.5±0.4 ms after the beginning of depolarization. In experimental animals, the beginning of inversion of areas of positive and negative cardioelectric potentials on BSPM does not differ. In 73% of rats, duration of inversion on BSPM was 7.7±1.9 ms, and in 27% - 3.9±0.1 ms (p=0.011). The formation of early activation zones in PV of rats with arterial hypertension testifies to possible wandering focus in the myocardium of PV sleeves. Stress-induced hypertension results in actual risk of atrial arrhythmias, which originate at the base of the PV.
Conclusion: In rats with arterial hypertension, two early depolarization zones are revealed in the sinus node area and in the PV return to the left atrium, projected on BSPM by mutual positions of negative and positive potential zones. *(Anadolu Kardiyol Derg 2012; 12: 195-9)*
Key words: Atrial depolarization, body surface potential map, epicardium, stress-induced arterial hypertension, rats

ÖZET

Amaç: Arteryel hipertansiyon, atriyal aritmi gelişme riski ile bağlantılıdır. Bu araştırma, hipertansif sıçanların vücut yüzeyinde kalp elektrik alan oluşumu ve atriyal epikardiyum boyunca depolarizasyon sırasını çalışmayı amaçlamıştır.
Yöntemler: Çalışma on bir (kalıtsal stres kaynaklı hipertansiyonu) sıçan üzerinde gerçekleştirilmiştir. Sıçanların atriyal epikardiyal depolarizasyon dizisi, atriyal depolarizasyon sırasında elektrokardiyogram II derivasyon zaman özellikleri, vücut yüzeyi potansiyel haritası (VYPH)'nın spasyal-temporal özelliklerini analiz ettik. İstatistiksel analiz, bağımsız örneklem t-testi kullanarak yapıldı.
Bulgular: Sonuçlar, hipertansif sıçanların %27'sinde pulmoner ven (PV) dallarında sino-atriyal düğüm alanının depolarizasyonu başladıktan sonra 2.0±0.5 ms'da erken uyarım alanları oluştuğunu, hayvanların %73'ünde, depolarizasyon başladıktan sonra 6.5±0.4ms'da PV dal alanlarında uyarım olduğunu gösterdi. Deney havyalarında, VYPH'de negatif ve pozitif kardiyopotansiyel alanlarının inversiyon başlangıcı farklı değildir. Sıçanların %73'ünde, VYPH inversiyon süresi 7.7±1.9 ms, %27'inde 3.9±0.1 ms'e alır (p=0.011). Arteryel hipertansiyonlu sıçanların PV'inde erken aktivasyon bölgelerin oluşumu, PV kol miyokardiyumunun olası gezici odaklarını kanıtlar. Stresle oluşan hipertansiyon PV tabanından kaynaklanan atriyal aritmi gerçek riskini oluşturur.
Sonuç: Arteryel hipertansiyonlu sıçanlarda, iki erken depolarizasyon bölgesi sinüs düğüm alanında ve sol atriyum PV dönüşünde ortaya çıkar, pozitif ve negatif potansiyel bölgelerinin karşılıklı konumları ile VYPH'ye yansır. *(Anadolu Kardiyol Derg 2012; 12: 195-9)*
Anahtar kelimeler: Atriyal depolarizasyon, vücut yüzeyi potansiyel haritası, epikardiyum, strese bağlı arteryel hipertansiyon, sıçanlar

Address for Correspondence/Yazışma Adresi: Svetlana Smirnova M.D, 167982, Kommunisticheskaya, 24, Syktyvkar, Komi-*Russia Federation*
Phone: +7 8212 391451 Fax: +7 8212 391451 E-mail: smirnova.sl@mail.ru
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Introduction

In order to research development mechanisms of myocardial hypertrophy of different genesis, experimental animal models such as hereditary hypertensive rats, spontaneously hypertensive rats (SHR line), stress-induced arterial hypertension rats (ISIAH line), and experimentally created specimens are used. An increase of P-wave duration is revealed in the electrocardiogram (ECG) limb leads in hypertensive rats (ISIAH line), (1).

In normotensive rats, the excitation wave spreads along the atrial epicardium from the pacemaker region successively to the right and left atrium (2). In human, arterial hypertension leads to the thickening of the left atrium, a change in conduction velocity of excitation, an increase in P-wave amplitude in the ECG, and stimulates the development of atrial fibrillation (3). The ECG in standard leads is not informative enough for estimating initial phase of atrial depolarization (4). Recordings and analyses of the cardioelectric field on the body surface reveal electrical atrial activity during early depolarization, prior to the formation of the P-wave in the ECG_{II} (5).

The pattern of the sequence of atrial depolarization and regularities of the reflection of excitation on BSPM in hypertensive rats is not described.

This research was aimed at studying the sequence of depolarization along the atrial epicardium and formation of the cardio electric field on the body surface of hypertensive rats.

Methods

Animals

Studies were carried out on three-month-old (n=11), male stress-induced arterial hypertension rats (line ISIAH), anesthetized with urethane (1 mg/kg, im). ISIAH rats were selected for studying the influence of genetic predisposition to emotional stress in forming stable arterial hypertension in the Institute of Cytology and Genetics of the Siberian Division of the Russian Academy of Sciences. Hypertensive ISIAH rats can be good experimental specimens for studying the peculiarities of the heart's electrical activity in hypertension. These are characterized by high arterial pressure: 160-166 mm of mercury in males and 143-149 mm of mercury in females. The signs and symptoms of hypertension in human beings are well reproduced in such rats (6).

During the experiment, the systolic pressure in ISIAH rats formed 190±17 mm of mercury. Heart mass in ISIAH rats was recorded at 1.2±0.07 g; body mass measured 295± 21 g. All animals received care in compliance with the principles of laboratory animal care formulated by the National Society for Medical Research and the Guide for the Care and Use of Laboratory Animals.

Body surface potential mapping and experimental protocol

Body surface potential mappings (BSPM) were simultaneously recorded from 32 subcutaneous needle electrodes (registering surface-0.06 cm^2), uniformly distributed on the torso surface of rat (from the basis of the ears to the last rib). Before opening the thorax, we conducted a tracheotomy, and artificial respiration was also performed. The frequency and depth of breathing were selected individually for each animal. The rats' body temperature was recorded at 37°C. After opening the thorax and cutting the pericardium, by using multipolar electrode with 32 leads (registering surface - 0.004 cm^2) unipolar epicardial electrograms (EG) were recorded from both atria in the same animals.

Electrocardiography

Simultaneous data acquisition was done by means of a custom-designed mapping system (16 bits; bandwidth 0.05 to 1000 Hz; sampling rate 4000 Hz) (7).

Unipolar electrograms and ECGs were recorded in reference to Wilson's central terminal. By unipolar ECGs from the body surface isopotential mappings were constructed. Sequence of spreading of the excitation wave was constructed through the first temporal derivative of epicardial EG. BSMP and sequence of epicardial depolarization were compared relative to *R*-peak in the ECG_{II} in the limb leads.

The beginning of the P-wave was defined as the junction between the isoelectric line and the beginning of the P-wave deflection and the end of the P-wave as the junction between the end of the P-wave deflection and the isoelectric line. The beginning of inversion of BSPM is the beginning of changing mutual positions of zones of positive and negative cardiopotentials. Duration of inversion on BSPM is the time during which the inversion occurs.

The data processing was carried out using the software of our development (7).

Statistical analysis

Data were analyzed using Statistica software version 6.0 for Windows statistical package (StatSoft, Inc., Tulsa, OK, USA). All results were expressed as mean±standard deviation. Statistical analysis was performed using an independent samples t-test. Differences were considered to be statistically significant if the p value was <0.05.

Results

Body surface potential distribution

BSPM in the cranial zone of positive potentials, which occupy the largest section, were conducted on the ventral and dorsal sides of body surfaces, and BSPM in the caudal zone of negative potentials - on the dorsal side (Fig. 1A, Table 1) in 73% of the rats with arterial hypertension before the P_{II}-wave deflection appeared. The positive BSPM zone shifts caudally, while the negative zone shifts cranially. Inversion occurs. Changes in mutual positions of positive and negative zones terminate when the initial stages of the P_{II} -wave are shaped. During ascending

and descending phases of the P_{II} -wave, the BSPM zone of positive cardiopotentials occupies the caudal part, whereas the zone of negative cardiopotentials takes up the cranial part of the body surface, and this location does not change up to the end of atrial depolarization.

On BSPM of 27% of ISIAH rats before the beginning of the P_{II}-wave, the zone of positive potentials is formed cranially, the zone of negative potentials-caudally. It coincides with the beginning of atrial depolarization. Mutual positions of BSPM positive and negative potentials occur before the beginning of the P_{II} -wave as well as in 73% of ISIAH rats (Fig. 2A, Table 2).

In 27% of ISIAH rats, the positive potential zone of BSPM is located laterally left on the dorsal and ventral sides, whereas the negative potential zone is located laterally right. During the ascending and descending phases of the P_{II} -wave, the zone positions do not change any more. The positive potential area of BSPM is situated caudally, whereas the negative potential area is located cranially.

Epicardial depolarization

In 73% of rats, the excitation wave spreads along the epicardium from the sinus node region, located in the superior vena cava (SVC) (Fig. 1B, Table 2). From the sinus node, the depolarization wave, rounding the SVC, passes to the right atrium (RA); first, it activates the upper part of the appendage, and then the front spreads evenly, depolarizing the middle and lower parts of the RA appendage on the ventral side. After the ventral surface has been activated, the excitation wave passes to the dorsal side, where the upper part of the appendage is depolarized first in the inferior vena cava, and then in the middle and lower parts. The excitation wave spreads to the left atrium (LA) over the left auricle to the upper and lower parts of the interatrial septum. Auricular excitation terminates on the dorsal side of the LA.

In 27% of hypertensive rats, early excitation areas are formed simultaneously along the epicardium in the PV sleeves (or 2 ms later), and in the sino-atrial node area simultaneously (Fig. 2B- Table 2). From the early activation area on the epicardium of PV sleeves, the excitation wave spreads to the left atrial appendage and interatrial septum, and meets with the depolarization front, moving from the right atrium. We can observe heterogeneous propagation of the excitation wave in the PV sleeves of the left atrium.

Table 1. Time characteristics of BSPM and ECG_{II} of rats of ISIAH line during atrial depolarization

Variables (ms)	Groups of rats		*p
	73% of rats (8/11)	27% of rats (3/11)	
Beginning of inversion on BSPM	66.8±5.7	68.5±6.1	0.685
Duration of inversion on BSPM	7.7±1.9	3.9±0.1	0.011
Beginning of P-wave ECG_{II}	59.1±7.2	64.5±6.0	0.284
Peak of P-wave ECG_{II}	53.8±7.0	58.0±5.6	0.378
End of P-wave ECG_{II}	46.5±7.0	51.7±6.8	0.298
Total duration of P-wave ECG_{II}	16.7±4.5	14.2±0.7	0.383

Data are presented as mean±SD

*independent samples t-test

BSPM - body surface potential mapping, ECG - electrocardiogram, ISIAH - stress-induced arterial hypertension rats

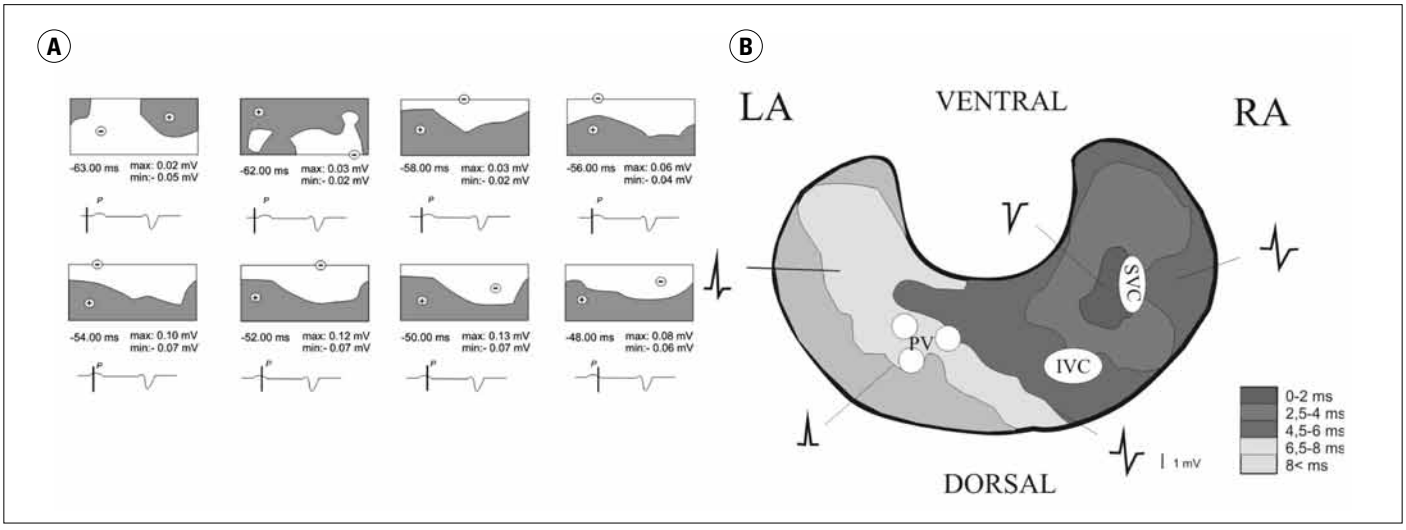

Figure 1. Isopotential body surface map of the rat of ISIAH line (73%) during atrial depolarization. (A) Shaded areas are positive areas of BSPM; «+» and «-» - locations of positive and negative extrema; ECG in the II lead with the time marker (vertical line)
Sequence of spreading of the excitation wave on atrial epicardium of ISIAH rats (73%). (B) Near each map there are original electrograms registered in the areas marked with pointers

BSPM - body surface potential mapping, ECG - electrocardiogram, ISIAH - stress-induced arterial hypertension rats, IVC - inferior vena cava, LA - left atrium, PV - pulmonary veins, RA - right atrium, SVC - superior vena cava

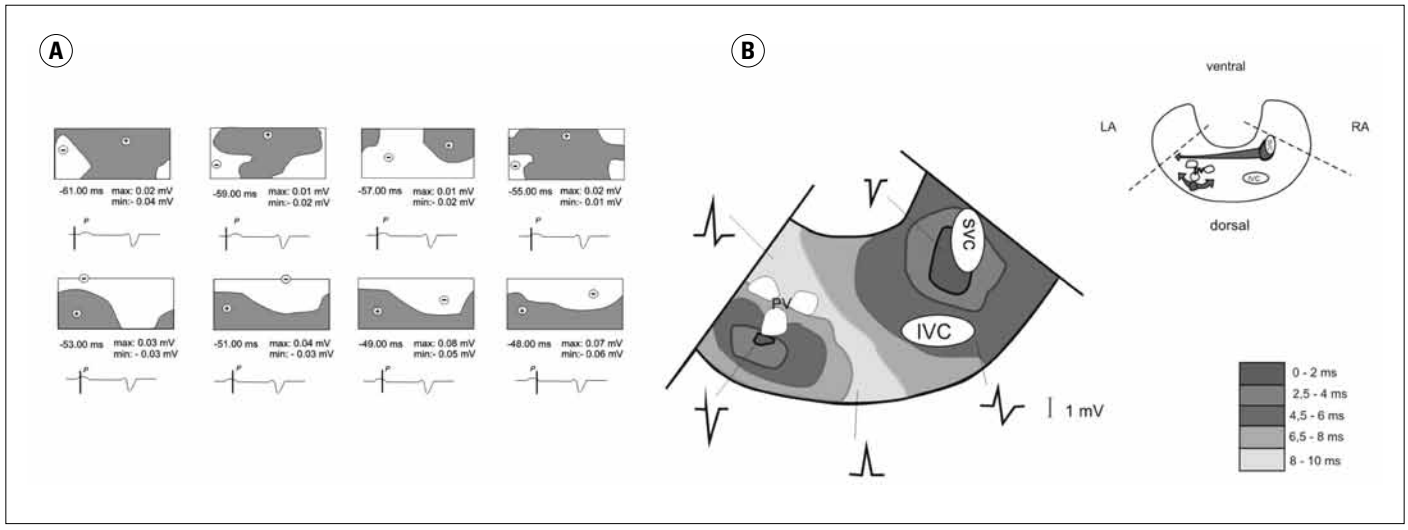

Figure 2. Isopotential body surface map on the rat's body surface (27%) during initial atrial activation. (A) Shaded areas are positive potentials; «+» and «-» - locations of positive and negative extrema; ECG in the II lead with the time marker (vertical line)
Sequence of spreading of the excitation wave on atrial epicardium of ISIAH rats (27%). (B) Near each map there are original electrograms registered in the areas marked with pointers.
ECG - electrocardiogram, ISIAH - stress-induced arterial hypertension rats IVC - inferior vena, LA - left atrium, PV - pulmonary veins, RA - right atrium, SVC - superior vena cava

Table 2. Form of epicardial EG and time of depolarization in the area of the sinus node and the area of pulmonary veins drain into the left atrium in rats of ISIAH line

Number of rats	EG in the area of the sinus node	EG in the area of falling pulmonary veins to the left atrium	Sinus node depolarization, ms	Depolarization of the area of falling pulmonary veins to the left atrium, ms*
73% of rats (8/11)			0	6.5±0.4
27% of rats (3/11)			0	2.0±0.5

Data are presented as mean±SD
*independent samples t-test (p<0.001)
EC - electrogram, ISIAH - stress-induced arterial hypertension rats

Discussion

On the body surface of 27% of stress-induced arterial hypertension rats (line ISIAH) during atrial depolarization after inversion, the zone of positive cardiopotentials is situated laterally left on the dorsal and ventral sides, whereas the zone of negative cardiopotentials is located laterally right. It reflects the formation of two early activation zones on the epicardium in the sino-atrial node area and in PV return to the left atrium.

In normotensive rats, the excitation wave along the epicardium spreads successively from the sino-atrial node area, located in the upper vena cava. The excitation wave moves from the right to the left atrium in the posterior part of the interatrial septum (5). Histologically speaking, internodal conduction tracts are shown in the composition of the interatrial septum (8, 9). In 73% of hypertensive rats, the excitation wave spreads from the right to the left atrium along the anterior and posterior part of the interatrial septum. The propagation of the excitation wave along the epicardium from the right to the left atrium in normotensive and hypertensive rats (5) is probably connected with the position of predominant conduction tracts.

In 27% of hypertensive rats, early excitation areas are formed on the epicardium in the PV sleeves. This results in changes to the total picture of excitation propagation along the atria. In normotensive rats, the excitation wave spreads unidirectionally along the epicardium in pulmonary venous return to the left atrium (5).

Studies of intracellular action potentials in PV sleeves have revealed that cells can act as an independent accessory pacemaker, whose effects will not spread to adjoining muscular cardiomyocytes (10). Pacemaker-like cells in PVs can result in wandering focus and atrial fibrillation (11). Clinical studies have shown the direct dependence between the increase in the size of the left atrium under hypertrophy and the risk of developing paroxysmal fibrillation in human beings (12, 13).

The formation of early activation zones in PVs of rats with arterial hypertension testifies to possible wandering focus in the

myocardium of PV sleeves. Stress-induced hypertension results in actual risks of atrial arrhythmias, which originate at the base of the PVs.

The formation of early activation zones in PVs of rats with arterial hypertension testifies to possible wandering focus in the myocardium of PV sleeves. Stress-induced hypertension results in actual risks of atrial arrhythmias, which originate at the base of the PVs.

Study limitations

The most important limitation of our study was the sample size. We would perform our experiments in a larger population to increase the statistical power of the study.

Conclusion

In rats with arterial hypertension, two early depolarization zones are revealed in the sinus node area and in the PV return to the left atrium, projected on body surface potential mappings by mutual positions of negative and positive potential zones.

Conflict of interest: None declared.

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