ISSN 0362-1197, Human Physiology, 2021, Vol. 47, No. 1, pp. 23–32. © Pleiades Publishing, Inc., 2021.
Russian Text © The Author(s), 2021, published in Annaly Klinicheskoi i Eksperimental'noi Nevrologii, 2021, Vol. 47, No. 1, pp. 31–42.

Kérdö Autonomic Index: Role of Initial Parameters, Areas, and Limitations of the Use

Yu. E. Vaguine[a, b, *], S. M. Deunezhewa[a, b], and A. A. Khlytina[a, b]

[a] *Sechenov First Moscow State Medical University (Sechenov University), Moscow, 119146 Russia*

[b] *Anokhin Research Institute of Normal Physiology, Russian Academy of Sciences, Moscow, 125315 Russia*

**e-mail: yuvaguine@yandex.ru*

Received February 26, 2020; revised March 14, 2020; accepted June 20, 2020

Abstract—The Kérdö Autonomic Index (KAI) was developed by the Hungarian physician I. Kérdö and was used by Russian physiologists to assess the balance of tone between the sympathetic and parasympathetic nervous systems. KAI gives an indirect characteristic of the vagosympathetic balance in the body without revealing the mechanisms of this balance. It was found that in athletes and patients with hypertension, the correlation between KAI and heart rate (HR) is positive, and between KAI and diastolic blood pressure (BPd) negative, which confirms the ideas of I. Kérdö. A theoretical graphical analysis of the dependence of KAI on its constituent parameters showed that KAI has a decreasing rectilinear dependence on BPd and increasing inverted hyperbolic dependence on HR. KAI reflects vagosympathetic balance in the body to a greater extent in terms of HR and to a lesser extent in terms of BPd. KAI correctly characterizes the vagosympathetic balance in the body of athletes before and after physical activity. The use of KAI to assess vagosympathetic balance in patients with hypertension is not recommended. With high blood pressure in hypertensive patients, KAI values can lead to an erroneous conclusion about the vagosympathetic balance in the body.

Keywords: Kérdö Autonomic Index, vagosympathetic balance, sympathicotonia, vagotonia, heart rate, systolic and diastolic blood pressure

DOI: 10.1134/S0362119720060122

In physiology, many integrated parameters have been developed that make it possible to assess the functional state of various body processes. One of them is Kérdö Autonomic Index (KAI), which is determined by two parameters: diastolic blood pressure (BPd) and heart rate (HR).

For more than ten years, the Hungarian physician I. Kérdö has been developing a theoretical basis for the effectiveness of KAI to assess the balance between the tone of the sympathetic and parasympathetic nervous systems (SNS and PSNS) in the body. Assuming that the KAI directly depends on the predominance of the SNS tone over the PSNS tone and has an inverse relationship with an increase in the PSNS tone compared to the SNS tone, I. Kérdö suggested calculating KAI using the equation $KAI = (1 - BPd/HR) \times 100\%$. KAI has positive values when BP_B is less than HR and negative values when BPd is higher than HR [1].

The Soviet and Russian neurologist A.M. Vein gave the name of I. Kérdö to this autonomic index and described KAI in his monographs as one of the methods for studying the functions of the autonomic nervous system [2, 3]. In subsequent years, KAI was used in various studies to assess the balance between the tone of the SNS and PSNS in the body when the functional state of healthy individuals changes [4–11].

A number of studies have noted a correlation between KAI and diastolic blood pressure (BPd). Thus, in children aged 5–6 years, vagotonia with negative KAI values was recorded [4]. As the children grew older, vagotonia changed to sympathicotonia with positive KAI values in adolescents aged 13–14 years. By the end of puberty, vagotonia re-emerged with negative KAI values [5]. In hyperreactive children, unusual external stimuli elicited a stress response accompanied by a KAI increase [6]. Classes of university students were accompanied by sympathicotonia. The KAI values were greatly increased in the first and last years of study [7], especially during examination sessions [8]. For workers in the north, negative KAI values were most pronounced in April, and in July KAI became positive and reached maximum values [9]. Differences in the Autonomic tone were recorded among workers of the same profession in the north of Russia and in Kazakhstan. Workers in the north were dominated by vagotonics with KAI values $<-10\%$, while workers in the south were dominated by normotonics with KAI values $\pm 10\%$ and sympathotonics with KAI values $>10\%$ [10].

The KAI-based Autonomic status of the subjects was investigated before studying the effect of olfactory stimuli. In three groups of subjects (normotonics, sympathotonics and vagotonics), differences in heart rate were noted, while differences in systolic pressure (BPs) and BPd were not revealed [11].

The study of KAI proved to be effective in sports medicine as well [12]. In our laboratory, we also repeatedly used KAI in a comprehensive assessment of the stress of body functions during physical exertion of athletes to the limit of physical capabilities [13–15].

Despite the fact that KAI is one of the indicators of vagosympathetic balance in the body [16–19], it is only an indirect indicator. It is known that the KAI-forming hemodynamic HR and BPd parameters change with a shift in the vagosympathetic balance in the body, but they can also change with the time course of other functional processes in the body. Despite the fact that we, like other researchers, studied KAI to assess the state of those examined, it is important to have more compelling reasons for using KAI as an estimate of the vagosympathetic balance of the body.

Until now, the contribution of each of the KAI parameters to its value remains unexplored. The values of the correlation coefficient between the KAI values and the initial parameters have not been investigated for any group of individuals. In addition, the area of application of the KAI, as well as its information content in various functional states of the body, remained unexplored.

In this regard, it was expedient to perform a graphical analysis of the dependence of KAI on its constituent parameters separately and during interaction, as well as to calculate the values of the correlation coefficient between KAI and baseline parameters in healthy people in different functional states and in patients with blood pressure disorders.

METHODS

The study of KAI in healthy individuals was carried out at the Anokhin Research Institute of Normal Physiology (Moscow, Russia). A group of healthy individuals included 25 regularly training beginners (age, 20–22 years; height, 161–172 cm; body weight, 55–82 kg). None of the athletes had a medical prescription for limiting physical activity. All subjects followed the instructions not to train on the study day and one day before the study, as well as to adhere to the normal eating pattern.

To create physical tension, the subjects performed the exercise stress test rotating the bike pedals. The pedaling speed was 70–75 rpm, which corresponded to a virtual movement speed of 7 km/h, which the athletes tracked according to the speedometer readings on the handlebars of the bicycle. The resistance to rotation of the bike pedals was set at 60 W. The resistance was then increased stepwise by 10 watts every minute. Athletes exercised on the bicycle to the limit of their physical capabilities.

Before and after the end of exercise, the athletes had an ECG recorded in the second standard lead with the subsequent calculation of the heart rate for 1 min. At the same time, BPs and BPd were measured on the brachial artery with an electronic tonometer using the Korotkov method by wrapping the tonometer cuff around the left upper arm.

The study of KAI in patients was carried out in municipal clinical hospital no. 1, Ministry of Health of the Kabardino-Balkarian Republic (Nalchik). We examined 27 patients (with the ages varying between 59 and 86 years) diagnosed as having aortic and coronary atherosclerosis, grade 3 arterial hypertension, grade 4 health risk. In the course of drug treatment, patients received from six to twelve pharmacological agents. The main one was bisoprolol, which belongs to the group of selective blockers of β1-adrenergic receptors of the heart and causes a negative chronotropic effect by slowing down the heart rate and reduces blood pressure. The period of hospital treatment was 11.0 ± 0.3 days. The heart rate and blood pressure in the subjects of this group were recorded on admission and on discharge from the hospital.

Statistical analysis of the results was performed using a parametric package for processing the results obtained with the Microsoft Statistica 8 software. For each group of those examined, the arithmetic means and standard deviations ($M \pm \sigma$) were calculated for each parameter studied. The differences between the parametric means were assessed by Student's t test. The differences between the parameter means were statistically significant at $p < 0.05$.

The presence of correlations between the recorded parameter values was assessed using the parametric method by the linear correlation coefficient (r) values, which could vary between 0 and 1.0. The correlations between the studied parameters were statistically significant ($p < 0.05$) at the r values higher than the critical value. The critical value of statistically significant r values was calculated by the Student's t test value and the number of compared parameter pairs in two samples of the parameters studied.

The correlation coefficient values were calculated using 50 recorded parameters in twenty-five athletes both before and after the load. In 27 patients, the correlation coefficient values were calculated using fifty-four recorded parameters both before and after treatment.

The functions of the recorded and calculated study results from other parameters were examined graphically.

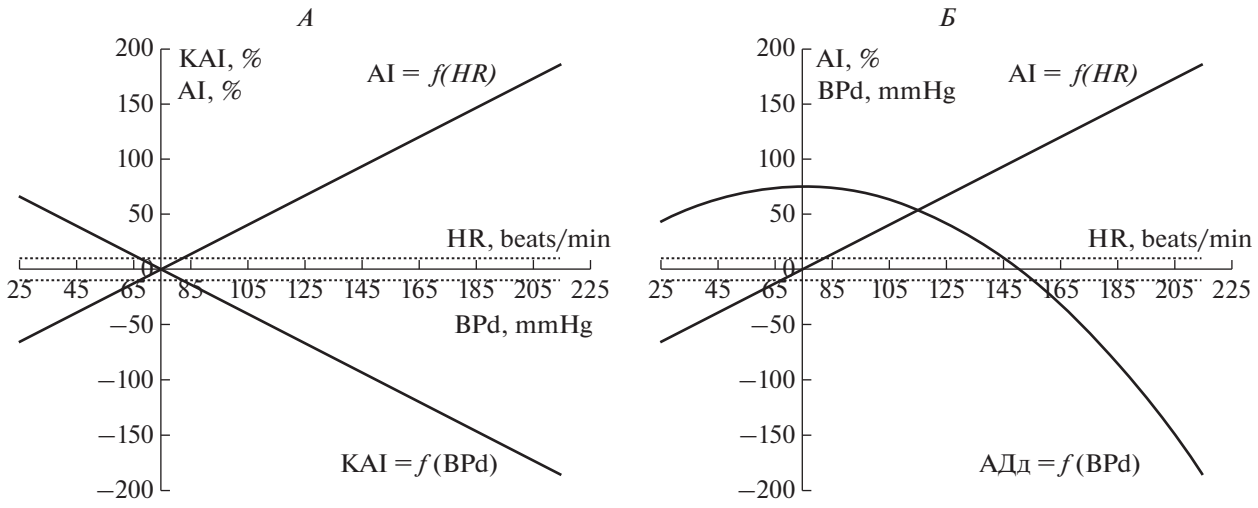

Fig. 1. Dependence of Kérdö Autonomic index (KAI) on diastolic blood pressure (BPd), Autonomic index (AI) on heart rate (HR), and BPd on HR. (a) A graph of a direct decreasing BPd dependence of KAI at a constant HR = 75 beats/min and a graph of a direct increasing HR dependence of AI at constant BPd = 75 mmHg. KAI = *f*(BPd) is the BPd function of KAI. AI = *f* (HR) is the HR function of AI. (b) Repetition of the graph of HR dependence of AI at constant BPd = 75 mmHg and a graph of decreasing inverted hyperbolic HR dependence of BPd with a rectilinear HR dependence of AI. AI = *f*(HR) is the HR function of AI. BPd = *f*(HR) is the HR function of BPd. Two dashed horizontal straight lines are at the KAI and AI values +10 and −10%.

RESULTS

Results of the theoretical analysis of BPd and HR dependence of KAI. Various rearrangements of the body's functional state in comparison with functional rest lead to changes in heart rate and diastolic blood pressure. With sympathicotonia, HR increases, and BPd decreases. With vagotonia, HR decreases, and BPd increases. Changes in HR and BPd have an opposite effect on the calculated KAI value.

For visual clarity, these dependencies were analyzed graphically. The origin of the constructed coordinate system was the zero value for the ordinate and the value 75 for the abscissa (Figs. 1a, 1b).

BPd dependence of KAI at constant HR was analyzed using the usual equation: KAI = (1 – BPd/75) × 100%, where 75 is the average HR in beats/min of a healthy individual at rest with the duration of each cardiac cycle 0.8 s. The BPd function of KAI was linear decreasing (Fig. 1a). KAI was positive at BPd < 75 mmHg; equal to zero at BPd = 75 mmHg; became negative at BPd >75 mmHg. Consequently, the ideas of Kérdö about the decreasing rectilinear BPd dependence of KAI at a constant HR = 75 beats/min in a healthy individual proved to be correct.

Direct HR dependence of KAI assumed by Kérdö could only hold if HR is the fraction numerator in the KAI equation. Therefore, we changed the equation for calculating the KAI by transferring HR from the denominator to the numerator of the fraction. In addition, a unity was subtracted but not added to the fraction. The result of calculation was not KAI, but a different integrated indicator, which we named the "autonomic index" (AI) by analogy with KAI, and it was calculated using the equation: AI = (HR/BPd – 1) × 100%. The HR function of AI at constant BPd = 75 mmHg was expressed by the equation: AI = (HR/75 – 1) × 100%, where 75 is the average BPd value in mmHg in a healthy individual. The ordinate axis, with the AI values plotted on it, crossed the abscissa axis with HR values at HR = 75 beats/min of a healthy individual (Figs. 1a, 1b). The HR function of AI was linear increasing. AI had negative values at HR < 75 beats/min; was equal to zero at HR = 75 beats/min; and became positive at HR > 75 beats/min. Consequently, when the KAI equation was converted to the AI equation, a rectilinear HR increase led to AI increase, which could be evidence of the correctness of Kérdö's ideas about the effect of HR on KAI.

In this regard, the HR dependence of BPd was analyzed with a rectilinear increasing HR dependence of AI. The BPd values were calculated according to the equation: BPd = (1 – AI/100) × HR, which was derived by mathematical transformation of the AI equation. The HR dependence of BPd was represented by an inverted hyperbola (Fig. 1b). At HR > 150 beats/min, BPd was less than zero, which is physiologically impossible. Therefore, at HR ≥ 150 beats/min, the physiological significance of KAI measurement was lost. Consequently, the HR dependence of KAI could not be rectilinear as Kérdö believed.

Further, the BPd dependence of KAI was analyzed at various constant HR values. The BPd dependence of KAI was represented graphically in the form of a family of curves at different HR values (Fig. 2). The ordinate axis, with the KAI values plotted on it,

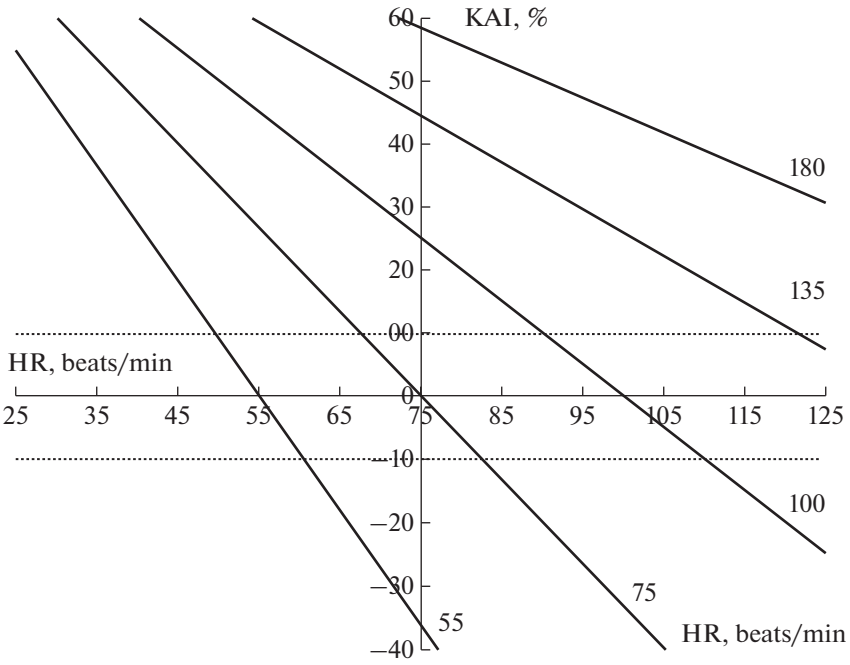

Fig. 2. Family of linearly decreasing curves of diastolic blood pressure (BPd) dependence of Kérdö Autonomic Index (KAI) at a heart rate (HR) of 55, 75, 100, 135, and 180 beats/min. The two dashed horizontal lines are at the KAI values +10 and −10%.

crossed the abscissa axis with the BPd values at BPd = 75 mmHg in a healthy individual. The BPd dependence of KAI, with a constant HR, was a linear decreasing function. With a BPd increase, the KAI value decreased at any constant HR values.

With a HR of lower than 100 beats/min, the KAI values could be positive and negative, and with HR higher than 100 beats/min, the KAI values were predominantly positive. The KAI values became positive when BPd was lower than HR and negative when BPd was higher than HR. At KAI values higher or lower than ±10%, BPd was less or more than HR by 10%. Consequently, the assumption of Kérdö about the inverse linear BPd dependence of KAI was confirmed at various constant HR values.

We then investigated the HR dependence of KAI. For this, we graphically analyzed the dependence of KAI and the result (P) of dividing HR by BPd on HR at constant BPd = 75 mmHg. The ordinate axis with P and KAI values crossed the abscissa axis with HR values at HR = 75 beats/min in a healthy individual (Fig. 3a). In the KAI equation, HR is the denominator of the BPd/HR fraction; therefore, the graph of HR dependence of P was a decreasing hyperbole. The P values gradually approached zero and did not become negative.

The KAI versus HR graph was an increasing inverted hyperbola, because KAI was the difference between 1.0 and P (Fig. 3a). At HR <75 beats/min, KAI increased from negative values to zero. At HR > 75 beats/min, the increase in KAI gradually approached the maximum level.

The graphical HR dependence of KAI represented a family of curves at various constant BPd values (Fig. 3b). The ordinate axis, with the KAI values plotted on it, crossed the abscissa axis with the HR values at HR = 75 beats/min in a healthy individual.

The HR dependence of KAI increased at any BPd values. However, KAI is not directly proportional to HR. At low HR values, the KAI values increased rapidly. At high HR values, the increase in KAI values slowed down, and the KAI value approached the maximum level.

There were positive and negative KAI values at any BPd values. The KAI values became positive when HR was higher than BPd and negative when HR was lower than BPd. With the KAI values higher or lower than ±10%, the HR value was higher or lower than the BPd value by 10%.

Consequently, the HR dependence of KAI was not linear, as Kérdö believed, but an increasing inverted hyperbolic one. With a HR increase from 35 to 115 beats/min, KAI increased rapidly, but at high HR values, the increase in KAI slowed down. At the same time, the increase in KAI could theoretically continue mainly due to the BPd increase lagging behind the HR.

Thus, BPd and HR influenced the KAI value in a different way. With an increase in BPd, the KAI value decreased in direct proportion to the BPd increase, with HR being invariable. With increasing HR, the

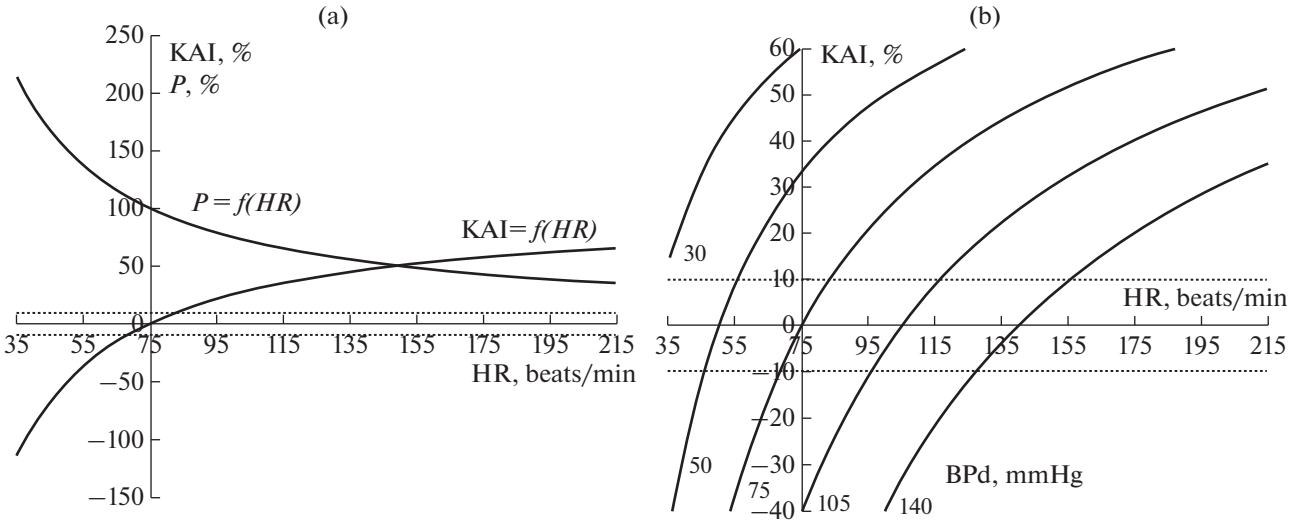

Fig. 3. HR dependence of Kérdö Autonomic Index (KAI) and the result (P) of dividing diastolic blood pressure (BPd) by heart rate (HR). (a) A graph of an increasing inverted hyperbolic HR dependence of KAI and a graph of a decreasing hyperbolic HR dependence of P at BPd = 75 mmHg. (b) A family of ascending inverted hyperbolic KAI versus HR curves at BPd = 30, 50, 75, 105, and 140 mmHg. The two dashed horizontal lines are at the KAI values +10 and –10%.

KAI value increased disproportionately. With an increase in HR up to 75 beats/min, KAI increased rapidly, but when the HR increase was over 75 beats/min, KAI increased slowly. In this case, KAI could increase mainly due to a delayed BPd increase as compared to HR.

Results of practical research. KAI in healthy and ill individuals. Examination of athletes before and after exercise gave the following results. Before exercise, the HR varied between 71 and 114 beats/min, which after exercise increased to 82–140 beats/min. Mean HR values before and after exercise were significantly different. BPs before exercise varied between 100 and 141 mmHg; after loading, between 98 and 145 mmHg. BPd before exercise was 55 to 88 mmHg; after loading, from 59 to 94 mmHg. The BPs and BPd means before and after exercise did not differ significantly. Before loading, KAI ranged from –9 to 38.6%, and after loading it increased to 1.2–49.6%. The KAI means before and after exercise were significantly different (Table 1).

It is known that with a simultaneous BPd and HR increase, the KAI values can be positive and negative. When HR is higher than BPd, the KAI value becomes positive. When HR is lower than BPd, the KAI value becomes negative. Conventionally, it is believed that when the HR value is 10% higher than the BPd value, the SNS tone prevails. When the HR value is 10% lower than the BPd value, the PSNS tone prevails [2, 3].

For visual clarity, the relationship between HR and BPd was analyzed graphically for each athlete and each patient. The origin of the coordinate system we constructed was 75 mmHg for the abscissa and 75 beats/min for the ordinate (Figs. 1a, 1b).

Before the load, twelve athletes had KAI within ±10%, and in thirteen athletes it was above 10%, which was possibly due to prestart sympathicotonia. After physical exertion, KAI in three athletes remained within the normal range, and in twenty-two athletes it increased by more than 10%. The maximum KAI value for one athlete reached 49.6% (Fig. 4a).

Examination of patients before and after treatment gave the following results. Before treatment, the HR ranged from 52 to 118 beats/min, which after treatment decreased to 62–78 beats/min. BPs before treatment was 110 to 210 mmHg and after treatment decreased to 110–180 mmHg. BPd before treatment was 70 to 120 mmHg and after treatment decreased to 70–90 mm Hg. The HR, BPs, and BPd means before and after treatment were significantly different. Before treatment, KAI varied between –73.1 and 30%; after treatment, between –36.4 and 12.5%. The mean KAI values were not significantly different (Table 2).

Before treatment, in 2 patients the KAI was within ±10%, in 21 patients it was less than 10%, and in 4 patients it was higher than 10%. After a course of drug treatment, in 5 patients KAI was within ±10%; in 22 patients it was less than 10% and in 1 patient it exceeded 10%. The minimum KAI value in one patient before treatment was –73.1%; in another patient after treatment, –36.4% (Fig. 4b).

Calculation of the values of the correlation coefficient between KAI and cardiovascular parameters gave the following results. In athletes and patients with hypertensive disease, statistically significant values of the correlation coefficient (r) were ≥+0.28 and

Table 1. Heart rate (HR, beats/min), systolic blood pressure (BPs, mmHg), diastolic blood pressure (BPd, mmHg) and Kérdö Autonomic Index (KAI, %) in athletes before and after bicycle exercise

Name	Before load				After load			
	HR	BPs	BPd	KAI	HR	BPs	BPd	KAI
Abr-v	114	100	70	38.6	126	98	74	41.3
Al-v	78	122	55	29.5	117	105	59	49.6
Al'-v	85	130	74	12.9	108	118	62	42.6
Ark-n	71	126	70	1.4	82	107	76	7.3
Ast-n	78	122	85	–9.0	106	134	78	26.4
Bak-v	74	117	66	10.8	109	114	64	41.3
Bas-n	80	134	76	5.0	104	124	75	27.9
Bob-v	87	114	79	9.2	95	126	78	17.9
Vakhr-v	102	110	75	26.5	109	110	62	43.1
Grab-v	86	130	78	9.3	119	120	74	37.8
Dem-n	79	139	66	16.5	121	120	68	43.8
Dzhem-v	75	109	62	17.3	98	113	72	26.5
Er-n	110	141	68	38.2	126	145	70	44.4
Zel-v	82	117	75	8.5	101	143	86	14.9
Mar-v	92	118	77	16.3	101	125	74	26.7
Mon-v	81	118	66	18.5	98	131	94	4.1
Myl-v	78	123	78	0.0	107	119	82	23.4
Naz-v	82	129	74	9.8	107	136	74	30.8
Omel'-k	85	117	62	27.1	117	115	78	33.3
Pavl-ch	85	118	61	28.2	106	117	70	34.0
Pokr-i	78	126	74	5.1	83	126	82	1.2
Sor-n	87	132	85	2.3	140	110	77	45.0
St-r	91	134	80	12.1	110	133	77	30.0
Shug-v	81	139	86	–6.2	130	118	77	40.8
Yus-v	87	101	88	–1.1	89	119	68	23.6
$M \pm \sigma$	85.1 ± 2.1	122.6 ± 2.2	73.2 ± 1.7	13.1 ± 2.6	108.4 ± 2.8	121.0 ± 2.3	74.0 ± 1.6	30.3 ± 2.7
Significant differences	*			*	*			*

≥+0.27, respectively, at $p < 0.05$ with a direct increasing dependence of one parameter on another. With a direct decreasing dependence of one parameter on another, statistically significant values of the correlation coefficient (r) were ≤ –0.28 and ≤ –0.27, respectively, at $p < 0.05$.

In athletes and hypertensive individuals, KAI depended directly on HR ($r = 0.82$ and $r = 0.69$) and inversely on BPd ($r = –0.57$ and $r = –0.55$). This corresponded to the ideas of Kérdö about HR and BPd dependence of KAI.

In addition, we analyzed the correlation between the BPs and BPd values, as well as between KAI and BPd. In athletes, there was no correlation between the BPs and BPd values. In patients, the correlation between the BPs and BPd values was statistically significant ($r = 0.78$). This was due to the simultaneous BPs and BPd decrease during patient treatment (Table 2).

The BPs values could not affect the KAI values in any way, because BPs is not included in the equation for KAI calculation. However, the relationship between KAI and BPs could be statistical instead of functional. Therefore, it made sense to determine the value of the correlation coefficient between KAI and BPs. In athletes, there was no correlation between the KAI and BPs values. In patients, the KAI value inversely correlated with the BPs value ($r = –0.39$). This was due to positive correlation ($r = 78$) between the BPs and BPd values in hypertensive individuals.

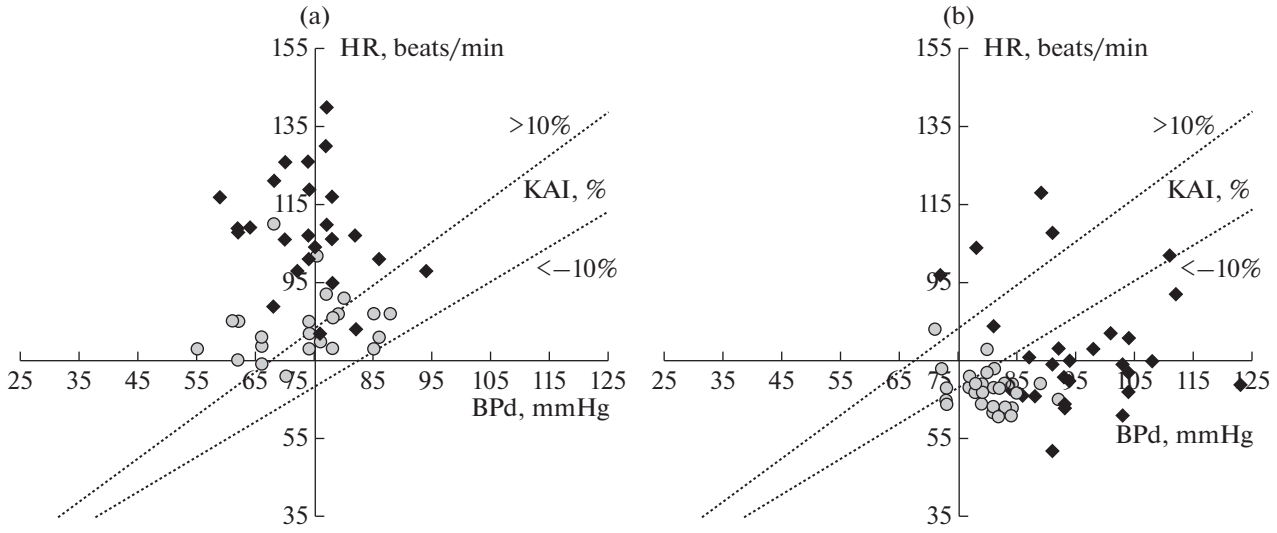

Fig. 4. Diastolic blood pressure (BPd) dependence of heart rate (HR) in athletes and patients with hypertensive disease. (a) BPd dependence of HR in athletes. The HR and BPd values of each athlete are marked with light markers before exercise and dark markers after exercise. (b) BPd dependence of HR in patients with hypertensive disease. The HR and BPd values in each patient before treatment are plotted with dark markers; after a course of drug treatment, with light markers. Two dotted ascending straight lines characterize BPd dependence of HR at KAI = +10 and –10%. Markers of the HR versus BPd values plotted on the graph between these straight lines, characterize the KAI values from –10 to +10%; those above the upper straight line characterize the KAI values >10%; those below the lower curve, the KAI values <–10%.

DISCUSSION

Theoretical analysis of BPd and HR dependence of KAI. KAI is calculated with the equation: KAI = (1 – BPd/HR) × 100%. But it is possible to calculate the Autonomic index (AI) for other relationships between HR and BPd: AI = (1 – HR/BPd) × 100%, AI = (BPd/HR – 1) × 100%, AI = (HR/BPd – 1) × 100%.

In this case, the results obtained will also characterize the balance between the tone of the SNS and PSNS. However, these indices cannot be compared with the KAI values.

When calculating the AI using the first equation, the main parameter that determines KAI is the quotient of BPd by HR. In this case, the functional meaning of these parameters is lost. The physiological meaning of the quotient of two different cardiovascular parameters disappears, and its measurement units are absent. The result of division shows how much the BPd value is higher or lower than HR.

It is generally accepted that in a healthy human, BP = 120/80 or 110/70 mmHg; i.e., BPd is 75 mmHg on average. In a healthy individual at rest, the duration of each cardiac cycle is, on average, 0.8 s, in which the HR is 75 beats/min. At these BPd and HR values, the quotient is equal to 1. With an increase or decrease in BPd and HR by the same quantity, the BPd/HR fraction remains equal to 1.

In his research Kérdö substantiated this proposition [1]. To order to determine the value of the BPd/HR fraction in healthy individuals, 1250 people were examined. Of these, 1000 individuals were apparently healthy (aged 9 to 65 years) and 250 patients were afflicted with mild mental disorders without organic diseases (aged 17 to 75 years). The average quotient of BPd by HR in healthy individuals was 1.035 ± 0.15 and in patients with mental disorders 1.036 ± 0.25.

The KAI equation determines to what degree the BPd and HR values differ from the same values of these parameters in a healthy individual at rest. For convenience of assessing KAI, the result obtained is converted to percentages when multiplied by 100%.

Our mathematical analysis of the correlation between KAI and the initial parameters showed the difference in BPd and HR dependence of KAI. The graphical presentation of BPd and HR dependences of KAI made it possible to understand the patterns of KAI formation visually, which facilitates the understanding of these patterns. The relationship between KAI and BPd is inversely proportional. The higher BPd, the lower KAI is. The HR dependence of KAI is increasing, not directly proportional. With an increase in HR, KAI increases rapidly at first, but this increase then slows down, and the KAI values approach a plateau.

Kérdö linked an increase in KAI to sympathicotonia and a decrease to vagotonia. In order to substantiate the initial assumptions, 100 subjects were examined in the supine position with the subcutaneous injection of 1 mL of epinephrine. Epinephrine caused an increase in heart rate within one hour, starting at two minutes. BPd decreased slowly over 1 hour, starting at 15 minutes. The KAI gradually increased to

Table 2. Heart rate (HR, beats/min), systolic blood pressure (BPs, mmHg), diastolic blood pressure (BPd, mmHg) and Kérdö Autonomic index (KAI, %) in patients with hypertensive disease before and after treatment

Case history code	Before treatment				After treatment			
	HR	BPs	BPd	KAI	HR	BPs	BPd	KAI
0182*F*	74	170	90	−21.6	68	125	80	−17.6
0281*F*	78	190	90	−15.4	68	130	90	−32.4
0379*F*	100	120	80	20.0	74	120	70	5.4
0477*M*	84	120	80	4.8	66	110	70	−6.1
0574*F*	70	190	120	−71.4	64	130	80	−25.0
0677*M*	60	200	100	−66.7	64	120	80	−25.0
0786*F*	118	180	90	23.7	68	180	80	−17.6
0868*F*	72	180	100	−38.9	70	130	80	−14.3
0977*F*	78	210	100	−28.2	78	180	80	−2.6
1078*F*	100	110	70	30.0	80	110	70	12.5
1176*F*	74	190	90	−21.6	66	130	80	−21.2
1258*F*	70	180	90	−28.6	62	130	80	−29.0
1379*M*	81	150	100	−23.5	70	130	80	−14.3
1465*M*	64	170	90	−40.6	64	130	80	−25.0
1582*F*	82	200	100	−22.0	64	130	80	−25.0
1676*F*	76	160	90	−18.4	66	130	85	−28.8
1779*F*	74	180	100	−35.1	67	120	70	−4.5
1871*F*	74	190	90	−21.6	62	130	80	−29.0
1977*F*	67	170	100	−49.2	66	130	90	−36.4
2064*F*	66	150	90	−36.4	64	130	70	−9.4
2167*M*	70	170	90	−28.6	60	120	80	−33.3
2259*F*	52	160	90	−73.1	68	130	80	−17.7
2380*F*	92	180	110	−19.6	68	130	80	−17.7
2467*F*	75	180	110	−46.7	70	120	80	−14.3
2576*M*	100	190	110	−10.0	72	130	80	−11.1
2677*F*	60	160	90	−50.0	68	120	80	−17.7
2781*M*	108	160	90	16.7	70	120	80	−14.3
$M \pm \sigma$	78.5 ± 3.0	170.7 ± 4.7	94.4 ± 2.0	−24.9 ± 5.2	67.7 ± 0.9	129.4 ± 3.0	79.1 ± 1.0	−17.4 ± 2.2
Significant differences	*	*	*		*	*	*	

36%. This served as evidence of the sympathicotonic effect of adrenaline on the cardiovascular parameters.

Adrenaline is known to have a higher affinity for β-adrenergic receptors in comparison with α-adrenergic receptors. Therefore, adrenaline increases the HR by stimulating β1-adrenergic receptors in the heart, and decreases BPd by exciting β2-adrenergic receptors in the vessels.

In the same subjects, a decrease in sympathetic influences on hemodynamic parameters was induced by Kérdö by subcutaneous administration of 1 mL of hydergine, which has an adrenolytic and vasodilating effect. The HR decreased over 1.5 h starting at 30 min. BPd did not change. KAI decreased insignificantly within 1 h; and after 1.5 h, to −24%. This result was interpreted as evidence of a decrease in sympathicotonia at negative KAI values [1].

The studies by Kérdö showed that HR changes more rapidly, and BPd changes are delayed. Therefore, KAI reflects sympathicotonic and vagotonic changes in the body, to a greater extent according to changes in HR and, to a lesser extent, according to changes in BPd.

Despite these studies, there is no experimental evidence of a direct effect of SNS and PSNS on KAI. When KAI was calculated, the action of other hormones that increase or decrease systemic blood pressure and the cardiac function was not taken into account. The processes of myogenic regulation of the constancy of blood flow in organs and the effect of

blood pooling on blood circulation were not taken into account.

Kérdö believed that with sympathicotonia, HR increases and BPd decreases. An increase in HR leads to an increase in cardiac output and systolic pressure. At the same time, the average blood pressure remains constant due to a decrease in peripheral vascular resistance and BPd. With vagotonia, the heart rate decreases, which is accompanied by a decrease in cardiac output, and to maintain the average pressure and blood flow, BPd increases due to an increase in vascular resistance [1].

It can be suggested that such a mechanism of self-regulation of average pressure occurs with insignificant changes in HR and BPd in healthy individuals. But a different process of blood pressure regulation is also possible. This is the Anrep effect or phenomenon, in which an increase in peripheral vascular resistance increases BPs, BPd, and the average BP without changing the HR and stroke volume [20].

In addition, it is known that a simultaneous increase in HR, BPs, and BPd occurs during physical and mental work, emotional stress, and hypertension. A decrease in HR, BPs, and BPd occurs during rest, deep sleep, collapse, and hypotension.

The theoretical analysis performed by us showed that KAI is an integrated parameter that depends on HR and BPd, the interaction of which in the equation for KAI calculation is complex. In certain functional states of the body, KAI adequately reflects vagosympathetic balance and can be a reliable criterion for changes in the vagosympathetic balance of the body [2, 3, 12].

Assessment of vagosympathetic balance in athletes and patients with hypertension by the KAI value. In our study of the cardiovascular functions of athletes, characteristic changes in the KAI were recorded during physical activity to the limit of their physical capabilities. In some of the athletes, KAI was increased already in the pre-start state, which could be associated with the motivation to achieve high sports results during physical activity. After exercising on the bicycle, KAI increased in most athletes and equaled more than 10%, which reflected an increase in the tone of the sympathetic nervous system. The results obtained were consistent with our earlier studies of KAI during exercise [13–15].

There are no data in clinical journals on the use of KAI to assess the balance between SNS and PSNS tone in patients with blood pressure disturbances. We found only one clinical article in which KAI was used to divide the examined patients into groups according to the value of the vagosympathetic balance of the body. It was established that sympathicotonia, which was established by high KAI values, at 70% is a concomitant factor of the onset of chronic prostatitis in men [19].

Due to the lack of literature data on changes in KAI in patients with blood pressure changes, we conducted a study of KAI in such patients. It was found that negative KAI values prevailed in hypertensive patients before and after treatment. In accordance with the theoretical ideas about KAI, this was the evidence of vagotonia. But at the same time, the patients had high blood pressure before treatment, which is the main sign in favor of the diagnosis of hypertension. Negative KAI values are due to high BPd value, which exceeds the HR value. After treatment, BPs decreased, which was the main indicator of treatment success. The HR also decreased, but BPd remained higher than HR. Therefore, the KAI values remained negative. In many patients with hypertension, BPd was higher than HR. This could erroneously be confused with vagotonia.

Therefore, the KAI adequately reflects a change in the vagosympathetic balance in humans with a change in HR without a significant change in BPd. When BPd changes, but HR values remain unchanged, the analysis of the KAI value may lead to an erroneous conclusion about the vagosympathetic balance. KAI should be one of the components of a comprehensive examination of healthy and sick individuals when studying the vagosympathetic balance in the human body.

CONCLUSIONS

(1) Kérdö Autonomic Index (KAI) developed by the Hungarian physician Kérdö was used by Russian physiologists to assess the balance of tone between the SNS and PSNS. KAI provides an indirect characteristic of vagosympathetic balance in the body without revealing the mechanisms of this balance.

(2) In athletes and patients with hypertension, the correlation between KAI and HR is positive, and between KAI and BPd negative, which confirms the ideas of Kérdö.

(3) Theoretical analysis showed that BPd and HR have different effects on the KAI value. KAI has a decreasing rectilinear BPd dependence and an increasing inverted hyperbolic HR dependence. KAI reflects vagosympathetic balance in the body, to a larger extent in terms of HR and to a lesser extent in terms of BPd.

(4) The practical use of KAI confirms that KAI is recommended for use to characterize the vagosympathetic balance in the body of healthy individuals when their functional state changes. KAI creates the basis for assessing the tone of the SNS and PSNS without analyzing the mechanisms of sympathicotonia or vagotonia.

(5) The use of KAI to assess vagosympathetic balance in patients with hypertension is not recommended. Many hypertensive individuals have negative KAI values when their blood pressure is high, which can be misinterpreted as vagotonia.

COMPLIANCE WITH ETHICAL STANDARDS

All procedures performed in studies involving human participants were in accordance with the biomedical ethics principles formulated in the 1964 Helsinki Declaration and its later amendments and approved by the local bioethics commission of the Anokhin Research Institute of Normal Physiology, Russian Academy of Sciences (Moscow, Russia).

INFORMED CONSENT

Informed written consent was obtained from all individual participants involved in the study and signed by them after being explained the potential risks and advantages, as well as the essence of the future study.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest connected with the publication of this article.

REFERENCES

1. Kérdö, I., Ein aus Daten der Blutzirkulation kalkulierter Index zur Beurteilung der Autonomicn Tonuslage, *Acta Neuroveg.*, 1966, vol. 29, no. 2, p. 250.
2. *Vegetativnye rasstroistva: klinika, lechenie i diagnostika (Autonomic Disorders: Clinics, Therapy, and Diagnostics)*, Vein, A.M., Ed., Moscow: Med. Inf. Agentstvo, 2000.
3. Vein, A.M., Solov'eva, A.D., and Kolosova, O.A., *Vegetososudistaya distoniya* (Vegetovascular Dystonia), Moscow: Meditsina, 1981.
4. Krivolapchuk, I.A., Factor structure of the functional state of five- and six-year-old children, *Hum. Physiol.*, 2014, vol. 40, no. 5, p. 513.
5. Krivolapchuk, I.A. and Chernova, M.B., The factor structure of the functional state of boys aged 13–14 years, *Hum. Physiol.*, 2017, vol. 43, no. 2, p. 157.
6. Ilyukhina, V.A., Krivoshchapova, M.N., and Manzhosova, G.V., Characteristics of the cerebral mechanisms controlling the level of wakefulness, the maturity of cognitive functions, and adaptive responses in children with attention deficit hyperactivity disorder and healthy children of the same age, *Hum. Physiol.*, 2011, vol. 37, no. 2, p. 148.
7. Buduk-ool, L.K., Aizman, R.I., and Krasilnikova, V.A., The time required for adapting to academic load for students living in a climatically uncomfortable geographic region, *Hum. Physiol.*, 2009, vol. 35, no. 4, p. 484.
8. Poborsky, A.N., Yurina, M.A., Lopatskaya, Zh.N., and Deryagina, E.Yu., The level of anxiety and state of autonomic regulation depending on the predicted examination grades in students living under unfavorable environmental conditions, *Hum. Physiol.*, 2009, vol. 35, no. 4, p. 416.
9. Solonin, Yu.G., Markov, A.L., Boyko, E.R., et al., Functional indices in participants of the satellite study on the Mars-500 project in the Russian north during different seasons, *Hum. Physiol.*, 2014, vol. 40, no. 6, p. 634.
10. Solonin, Yu.G., Markov, A.L., Boyko, E.R., et al., Comparison of the results of satellite studies of the Mars-500 experiment in Syktyvkar and Almaty, *Hum. Physiol.*, 2015, vol. 41, no. 3, p. 311.
11. Avilov, O.V. and Sudakov, K.V., Effects of olfactory stimuli on students with different tones of the autonomic nervous system, *Hum. Physiol.*, 2008, vol. 34, no. 6, p. 709.
12. Graevskaya, N.D. and Dolmatova, T.I., *Sportivnaya meditsina: kurs lektsii i prakticheskikh zanyatii* (Sports Medicine: Lectures and Practice), Moscow: Sovetskii Sport, 2004.
13. Fudin, N.A., Klassina, S.Ya., and Vaguine, Yu.E., Rhythmic thermal impacts as a means of restoring persons engaged in physical training and sport after intensive physical activity, *Vestn. Nov. Med. Tekhnol.*, 2013, vol. 20, no. 4, p. 74.
14. Fudin, N.A., Klassina, S.Ya., Vaguine, Yu.E., and Pigareva, S.N., Physiology of the impact of hypoventilation breathing on the cardiorespiratory and muscular human system during physical work until failure, *Sport. Med.: Nauka Prakt.*, 2016, vol. 6, no. 3, p. 22.
15. Fudin, N.A. and Klassina, S.Ya., Influence of hypoventilation breathing on cardiorespiratory indices of the persons with different initially dominant Autonomic tone during physical work until failure, *Vestn. Nov. Med. Tekhnol.*, 2017, vol. 24, no. 3, p. 128.
16. Sudakov, K.V., Andrianov, V.V., Vaguine, Yu.E., et al., *Normal'naya fiziologiya: uchebnik* (Normal Physiology: A Manual), Moscow: GEOTAR-Media, 2012.
17. Andrianov, V.V., Badikov, V.I., Bunina, T.P., et al., *Normal'naya fiziologiya: praktikum* (Normal Physiology: Practical Manual), Moscow: Med. Inf. Agentstvo, 2016.
18. Sudakov, K.V., Andrianov, V.V., Vaguine, Yu.E., and Kiselev, I.I., *Fiziologiya cheloveka: atlas dinamicheskikh sistem* (Human Physiology: Atlas of Dynamic Systems), Moscow: GEOTAR-Media, 2018.
19. Zaitsev, D.N. and Govorin, A.V., The markers of endothelial dysfunction in patients with chronic prostatitis, *Arterial'naya Gipertenziya*, 2015, vol. 21, no. 4, p. 436.

Translated by E. Babchenko

SPELL: 1. OK