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## ASSESSMENT OF AUTONOMIC NERVOUS SYSTEM BALANCE IN HEALTHY YOUNG ADULTS USING HEATED TOBACCO PRODUCTS

**Abstract.** This article investigates the impact of heated tobacco product (HTP) use on the autonomic balance in healthy young individuals. The authors highlight the growing prevalence of HTP consumption among youth and question the claims regarding their reduced harm compared to conventional cigarettes. The aim of the study was to assess the state of the autonomic nervous system (ANS) in HTP users using the following tools: the Wayne questionnaire, the Kerdo autonomic index (KAI), the Hildebrandt index (Q), and the clinostatic-orthostatic test. The study involved 92 participants (66 HTP users and 26 individuals who had never smoked). The results revealed statistically significant differences in the objective detection of autonomic dysfunction between HTP users and the control group. Notably, 57.6% of HTP users exhibited signs of autonomic impairment according to clinical assessment, compared to only 15.4% in the control group ( $p < 0.0001$ ). Additionally, female HTP users reported a higher level of subjective symptoms than their male counterparts ( $p < 0.0001$ ). The Kerdo index showed a predominance of parasympathetic regulation among HTP users ( $-6.7 \pm 18.56$ ), in contrast to the control group, where the sympathetic type prevailed ( $1.5 \pm 8.82$ ),  $p = 0.033$ . Excessive parasympathetic activation was identified in 45.4% of HTP users, compared to 15.4% in the control group. Conversely, sympathetic predominance (sympathicotonia) was more common among non-smokers (57.7% versus 36.4%, respectively;  $p = 0.025$ ). The Hildebrandt index (Q) indicated discoordination in autonomic regulation of the cardiorespiratory systems in 24% of HTP users (especially among women), compared to 12% in the control group. Disruption of autonomic balance was found to be three times more frequent in female HTP users and six times more frequent in males than in their respective control subgroups. The

clinostatic-orthostatic test revealed a higher average pulse rate in HTP users at the first test stage (86 vs. 79 beats per minute,  $p = 0.033$ ), which may reflect specific features of ANS reactivity in this population. Overall, 70% of HTP users demonstrated parasympathetic hypertonia, and 85% showed decreased sympathetic tone. These findings suggest significant alterations in autonomic regulation among young HTP users, underlining the need for further research to evaluate the long-term effects of alternative smoking methods on the body's adaptive capacities.

**Keywords:** smoking, autonomic nervous system, HTP, autonomic dysfunction, Kerdo index, Hildebrandt index, autonomic regulation, young smokers, parasympathictonia, sympathictonia, heated tobacco products.

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## СТАН ВЕГЕТАТИВНОГО БАЛАНСУ У ЗДОРОВИХ МОЛОДИХ ОСІБ - КУРЦІВ ТВЕН

**Анотація.** У статті досліджено вплив вживання тютюнових виробів для електричного нагрівання (ТВЕН) на стан вегетативного балансу у здорових молодих осіб. Автори акцентують увагу на поширеності використання ТВЕН серед молоді та сумнівності тверджень щодо їхньої меншої шкідливості порівняно з традиційними сигаретами. Метою дослідження було вивчення стану автономної нервової системи у користувачів ТВЕН з використанням таких інструментів: опитувальник Вейна, вегетативний індекс Кердо (ВІК), індекс Хільдебранта (Q), кліноортостатична проба. У дослідженні взяли участь 92 особи (66 – курці ТВЕН, 26 – особи, які ніколи не курили). Отримані результати свідчать про статистично значущі відмінності в об'єктивному виявленні вегетативної дисфункції серед курців ТВЕН у порівнянні з контрольною групою. Зокрема, 57,6 % курців мали ознаки вегетативних порушень за оцінкою лікаря, проти лише 15,4 % у групі контролю ( $p < 0,0001$ ). При цьому жінки-курці мали вищий рівень суб'єктивної симптоматики порівняно з чоловіками ( $p < 0,0001$ ). Вегетативний індекс Кердо продемонстрував переважання парасимпатичного типу регуляції ВНС серед курців ТВЕН ( $-6,7 \pm 18,56$ ), на відміну від групи контролю, де домінував симпатичний тип ( $1,5 \pm 8,82$ ),  $p = 0,033$ . Надмірна активація ПНС була притаманна 45,4 % курців проти 15,4 % у контрольній групі, а симпатикотонія частіше зустрічалася серед осіб, які не курили (57,7 % проти 36,4 % відповідно,  $p = 0,025$ ). Індекс

Хільдебранта (Q) свідчив про дискоординацію вегетативного забезпечення кардіореспіраторних систем у 24 % курців ТВЕН (особливо серед жінок), проти 12 % в контрольній групі. Порушення балансу вегетативного забезпечення у жінок-курців було втричі частішим, а у чоловіків — у шість разів частішим, ніж серед відповідних підгруп контролю. Клиноортостатична проба показала вищу середню частоту пульсу у курців на першому етапі тесту (86 проти 79 уд./хв.,  $p = 0,033$ ), що також може свідчити про особливості реактивності ВНС у цієї категорії осіб. Загалом, 70 % курців мали гіпертонус ПНС, а 85 % — зниження тонуусу СНС. Результати свідчать про суттєві особливості вегетативної регуляції у молодих курців ТВЕН, що потребує подальших досліджень для оцінки довготривалих наслідків впливу альтернативних форм куріння на функціональні резерви організму.

**Ключові слова:** куріння, вегетативна нервова система, ТВЕН, вегетативна дисфункція, індекс Кердо, індекс Хільдебранта, автономна регуляція, молоді курці, парасимпатикотонія, симпатикотонія, електронні тютюнові вироби.

**Introduction.** The tobacco industry markets heated tobacco products (HTPs) as a less harmful alternative to conventional cigarettes, often citing a 90–95% reduction in toxicity. However, this claim remains scientifically unsubstantiated. Recent studies have shown no significant differences in most biomarkers of potential health harm between HTP users and conventional cigarette smokers. The European Respiratory Society has stated that HTPs are harmful, potentially addictive, and should not be recommended as an alternative to traditional tobacco products. Moreover, data on the health effects of HTPs remain limited [1].

The World Health Organization (WHO) maintains that all forms of tobacco use, including HTPs, are detrimental to health. Tobacco is inherently toxic and contains carcinogenic substances, even in its unprocessed form. Consequently, under the WHO Framework Convention on Tobacco Control and national legislation, HTPs should be subject to the same regulatory measures as all other tobacco products [2].

A study by Kim DK et al. reported increased parasympathetic nervous system tone among users who switched from conventional cigarettes to HTPs [3]. When comparing the effects of HTPs and conventional cigarettes on the autonomic nervous system (ANS), it was observed that regular HTP users did not exhibit elevated sympathetic activity, likely due to the nicotine content in HTPs [3,4]. Furthermore, novice cigarette smokers demonstrated a greater impact on ANS tone than novice HTP users, presumably due to the combustion of non-nicotine components in conventional cigarettes [5].

In addition, tobacco smoke, nicotine, acrolein, and reactive oxygen species activate afferent vagal nerve fibers rich in capsaicin-sensitive receptors, which are associated with autonomic responses in HTP users [6,7]. Other components of tobacco smoke—such as heavy metals, polycyclic aromatic hydrocarbons, volatile organic compounds (e.g., acrolein), gases (e.g., carbon monoxide), and particulate matter—may independently influence autonomic balance [8,9].



**Materials and Methods.** The state of autonomic regulation in healthy young individuals from the main group ( $n = 66$ , HTP users) and the control group ( $n = 26$ ; individuals who had never smoked) was assessed using the following tools:

- the Wayne questionnaire, which made it possible to evaluate both subjective and objective autonomic symptoms by scoring, allowing for the detection of autonomic disorders even in individuals without active complaints;
- the Kerdo autonomic index (KAI);
- the Hildebrandt index (Q), which enabled the assessment of coordination between the cardiovascular and respiratory systems and the analysis of intersystem cardiorespiratory correlations;
- the clinostatic-orthostatic test.

Statistical data analysis was performed using R Commander (<https://www.r-project.org/>) and MedCalc Statistical Software trial version 23.2.1 (<https://www.medcalc.org/download/>). Considering the normal distribution of quantitative data in the groups (as determined by the Shapiro–Wilk test), parametric characteristics and analytical methods were applied. Results were considered statistically significant at  $p < 0.05$  for all tests.

**Results and Discussion.** According to our data, the proportion of respondents reporting subjective complaints—such as a tendency for facial flushing or pallor during emotional stress; discolouration of fingers or toes; sensations of palpitations, skipped or stopped heartbeats; subjective feelings of numbness or coldness in extremities; excessive sweating; gastrointestinal disturbances; shortness of breath; disorientation (including episodes of fainting or near-fainting); headaches (diffuse, unilateral, or global, with pressing or pulsating characteristics); reduced work capacity and fatigue; and sleep disturbances (difficulty falling asleep, shallow or non-restorative sleep, frequent awakenings, morning fatigue)—did not differ significantly between the main group and the control group. This suggests that the baseline autonomic status, as measured by the Wayne questionnaire, was comparable across groups.

The presence of autonomic dysfunction based on self-assessment using the Wayne questionnaire (score  $>15$  points) was demonstrated by 72.7% of HTP users and 69.2% of never-smokers ( $p = 0.813$ ), with mean scores of 18.4 (9.33) and 22.6 (14.22), respectively ( $p = 0.163$ ). In contrast, the objective clinical assessment showed a score exceeding 25 points—indicating autonomic dysfunction—in 57.6% of HTP users compared to just 15.4% of the control group ( $p < 0.0001$ ). Regardless of sex, the average score assessed by clinicians was significantly higher in the HTP group at 23.0 (11.65), compared to 12.5 (8.19) in the control group ( $p = 0.0001$ ).

It should be noted that the prevalence of autonomic dysfunction based on subjective self-assessment did not differ significantly between men and women in either group: 65% of men in the main group versus 80% in the control group ( $p = 0.363$ ), and 84% of women versus 62.5%, respectively ( $p = 0.102$ ). However, among female HTP users, scores above 15 were more common than among their male counterparts ( $p = 0.08$ ). The mean self-assessed score was significantly higher in

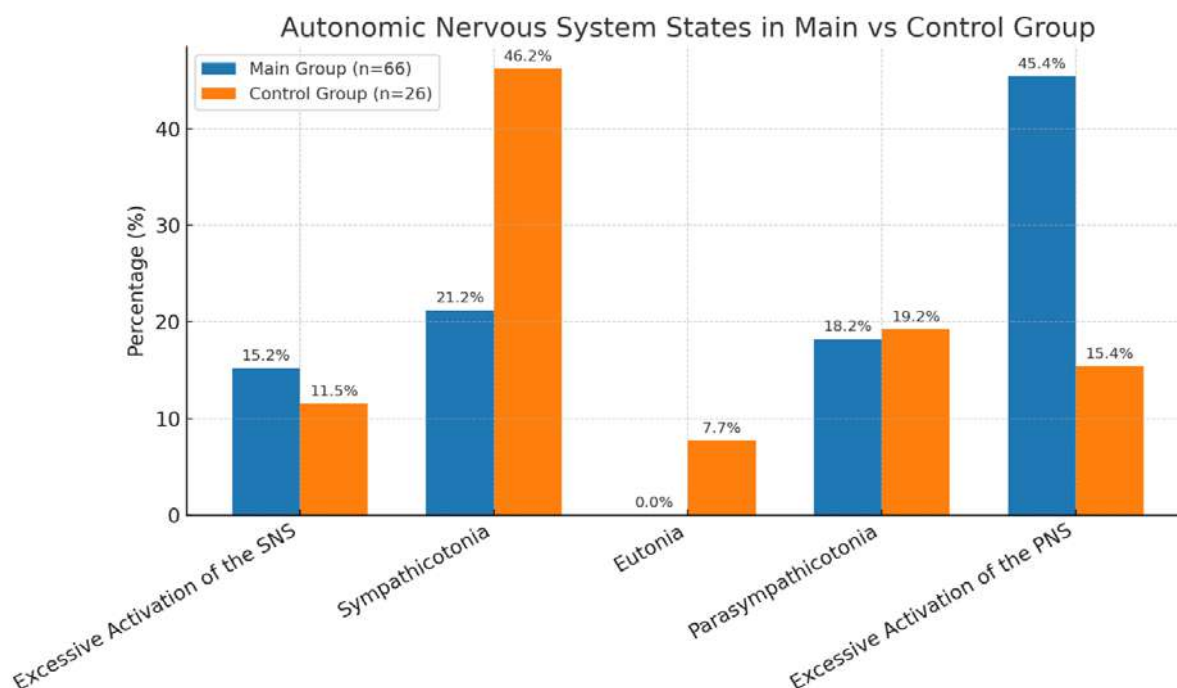
healthy young female HTP users compared to males (31.2 (14.93) vs 17.1 (10.70),  $p < 0.0001$ ).

Clinically assessed scores exceeding 25 on the Wayne questionnaire were observed in 55% of men and 61.5% of women in the main group, whereas in the control group these values were seen in only 20% of men and 12.5% of women. The mean scores for men in the HTP group were 22.9 (9.75) compared to 13.4 (7.87) in the control group ( $p = 0.006$ ), and for women—23.1 (14.29) versus 11.8 (8.85), respectively ( $p = 0.008$ ).

Therefore, based on objective assessment by clinicians using the Wayne questionnaire, both male and female HTP users exhibited autonomic dysfunction. In particular, healthy young female HTP users had more pronounced and severe autonomic disturbances (1.8 times higher) than women in the control group according to their self-assessments.

According to our findings, pronounced autonomic disorders were identified in 27.3% of participants from the HTP group (including 4 men and 14 women) and in 7.7% (2 women) from the control group ( $p = 0.011$ ).

At the second stage of the autonomic regulation assessment, we evaluated the results of the Kerdo autonomic index (KAI) in both groups. The distribution of KAI scores among healthy young individuals, depending on their smoking status, is visually presented in Figure 1.



*Fig. 1. Distribution structure of the Kerdo Autonomic Index (KAI) in healthy young individuals depending on HTP smoking status*

According to the obtained results, a predominance of the parasympathetic type of autonomic nervous system (ANS) regulation was demonstrated in the HTP user group based on the mean KAI level, regardless of sex. Specifically, the average KAI

values in the main group were below zero ( $-6.7 \pm 18.56$ ), compared to  $1.5 \pm 8.82$  in the control group ( $p = 0.033$ ).

Discrete analysis of KAI results in the main group, shown in Figure 1, revealed that a purely parasympathetic type of ANS regulation was present in 63.6% of cases, with excessive parasympathetic activation observed in nearly half (45.4%). In contrast, the sympathetic type of regulation was found in 36.4% of individuals, with excessive sympathetic activation recorded in 15.2%.

In the control group, one in three individuals (34.6%) exhibited parasympathetic-type regulation, of whom 15.4% had excessive parasympathetic activation. Eutonia (balanced ANS tone) was identified in 7.7% of cases, while sympathetic-type regulation was noted in 57.7%, including 11.5% with excessive sympathetic activation.

Thus, based on KAI data, young individuals differed significantly in the proportion of sympathicotonia depending on their HTP smoking status. Sympathicotonia was significantly more prevalent among never-smokers (nearly every second individual in the control group compared to every fifth in the HTP group;  $p = 0.025$ ), whereas excessive parasympathetic activation occurred significantly more frequently among HTP users (every second individual in the HTP group versus every seventh in the control group;  $p = 0.002$ ).

The average value of the Hildebrandt index (Q) in the main group was  $4.4 \pm 0.72$ , compared to  $4.3 \pm 0.60$  in the control group ( $p = 0.6812$ ), with no index Q values below 2.8 observed in this study. According to our findings, there was a statistically significant difference in the average Hildebrandt index scores depending on sex in both the main and control groups (Figure 2).

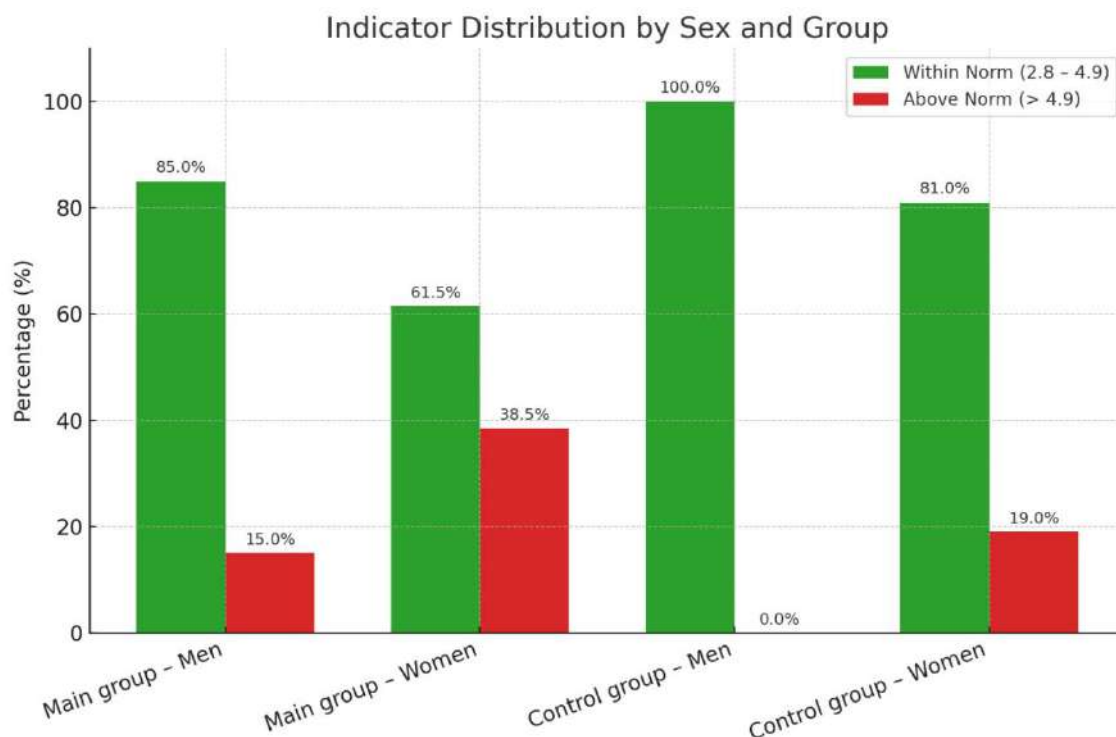


Fig. 2. Distribution structure of Hildebrandt index values (normal or above normal) in healthy young individuals from the main and control groups



Ranking the Hildebrandt index results (normal and above normal) among participants allowed for the identification of individuals with discoordination of autonomic regulation of the respiratory and cardiovascular systems based on  $Q > 4.9$  (Figure 2). This condition was observed in 24% of cases in the main group versus 12% in the control group ( $p = 0.15$ ), with a predominance of females in both the main (15.2% of the subgroup) and control (11.5% of the subgroup) groups.

It is worth noting that the proportion of individuals in the main group who exhibited autonomic imbalance in cardiorespiratory regulation was significantly lower—by a factor of three among women and six among male HTP users—compared to those with normal Hildebrandt index levels ( $p = 0.03$ ).

According to the results of the clinostatic-orthostatic test, comparison of pulse rate across all five test stages (standing, lying after 1 minute, lying after 5 minutes, standing after 1 minute, standing after 3 minutes) showed a significant difference only in the initial standing position. The average pulse rate in HTP users was significantly higher ( $p = 0.033$ )—86 (14.9) beats per minute compared to 79 (9.1) beats per minute in the control group.

Our findings indicate that 70% of participants in the HTP group exhibited parasympathetic hypertonia, and 85% demonstrated reduced sympathetic tone. When evaluating the reactivity of the sympathetic and parasympathetic branches of the ANS among HTP users, no statistically significant differences were found in the distribution of reactivity levels (low, medium, or high), suggesting that HTP use did not affect the distribution structure of ANS reactivity levels among the studied youth.

Thus, the state of autonomic balance in healthy young HTP users differs in certain aspects from their peers who have never smoked, which highlights the need for further research into the effects of alternative smoking products on the body's adaptive capacities and potential long-term consequences.

**Conclusions.** The proportion of autonomic dysfunction based on the Wayne questionnaire did not significantly differ between sexes in terms of subjective assessment (65% of men in the HTP group vs. 80% in the control group,  $p = 0.363$ ; and 84% of women vs. 62.5%,  $p = 0.102$ ). However, the severity of autonomic dysfunction, as measured both by self-assessment and clinician evaluation, was significantly higher in female HTP users compared to their male counterparts. In the HTP group, regardless of sex, parasympathetic dominance in ANS regulation was confirmed (mean KAI:  $-6.7$  (18.56) vs.  $1.5$  (8.82) in the control group,  $p = 0.033$ ), with men showing a significantly lower average KAI ( $-13.4$  (17.25)) compared to female HTP users ( $+3.5$  (15.88);  $p = 0.0002$ ). Autonomic regulation disturbances in the direction of sympathicotonia, based on the Hildebrandt index ( $Q > 4.9$ ), were identified in 24% of HTP users and 12% of the control group, with a predominance of females in both the main group (15.2%) and the control group (11.5%). According to the results of the clinostatic-orthostatic test, most healthy young HTP users (70%) exhibited parasympathetic hypertonia and 85% had reduced sympathetic tone.

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