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ORIGINAL ARTICLE

The relationship of pain, disability, and kinesiophobia levels with heart rate variability in patients with migraine: A prospective cross-sectional study

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ABSTRACT

Objectives: The study aimed to determine the relationship among pain level, disability, kinesiophobia, and heart rate variability (HRV), which is considered one of the indicators of autonomic nervous system (ANS) activity in patients with migraine.

Patients and methods: The prospective cross-sectional study was completed with a total of 37 female patients (mean age: 34.7±2.1 years; range, 18 to 62 years) with migraine between July 2022 and April 2023. Pain levels were measured with the Visual Analog Scale, headache-related disability was measured with the Migraine Disability Assessment (MIDAS), kinesiophobia levels were measured with the Tampa Kinesiophobia Scale, and HRV measurements were made with the Polar H10 model heart rate monitor.

Results: Sixteen patients with migraine with aura and 21 without aura were identified. Statistically significant, positive, and low-level relationships were found between the participants' daytime pain levels and low frequency peak values, as well as between MIDAS scores and minimum heart rate values ($p<0.05$). There was a statistically significant negative and low-level correlation between kinesiophobia measurement data and maximum heart rate values ($p<0.05$). No significant correlations were found between other parameters of HRV and other outcome measures ($p>0.05$).

Conclusion: Since HRV is considered an indicator of ANS activity, it may be an effective factor on clinical variables in patients with migraine, and there may be a connection between pain, kinesiophobia, and the ANS. Therefore, it could be meaningful to consider these factors in the evaluation and treatment of patients with migraine.

Keywords: Disability, heart rate, kinesiophobia, migraine, pain.

Migraine is an episodic neurological disorder characterized by periodic headaches, usually expressed as unilateral and throbbing pain, and its pathophysiology has not been fully explained. During recurrent headache attacks, many issues such as dizziness, photophobia, phonophobia, and nausea accompany the disease.[1] Migraine, which constitutes 15 to 20% of all headaches, is observed three times more frequently in females than in males, starts in the second and third decades of life, and decreases after middle age.[2] Migraine-related disability is at an advanced level in more than 25% of the patients, and 90% of them have moderate-advanced Migraine Disability Assessment (MIDAS) scores. Attacks negatively affect the patient's work, education, and social life and cause significant loss of labor and productivity due to migraine.[3]

The concept of kinesiophobia, which is defined as the anxiety that develops against activity and physical movement resulting from painful injury and sensitivity to reinjury,[4] is a syndrome

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that can lead to withdrawal from meaningful activities, disability, and undesirable conditions such as depression.[5] Migraine is known as a neurologic disease, but it is also associated with musculoskeletal system problems that may contribute to the development of kinesiophobia, as it shows abnormally high sensitivity to light, sound, odors, and even physical activity during attack periods.[6,7] Another factor that may lead to the development of kinesiophobia in patients with migraine is central sensitization.[8] Cutaneous allodynia has been described in approximately 80% of patients, and chronicization of the disease is a risk factor for kinesiophobia and poor prognosis.[9]

Symptoms observed during migraine attacks suggest autonomic nervous system (ANS) involvement. Symptoms such as sensitivity to sound, light, and odor, nausea, vomiting, and sweating are thought to have an autonomic basis.[10,11] Similar to migraine, autonomic symptoms such as lacrimation, flushing, nausea, photophobia, and phonophobia in cluster headaches support the idea that autonomic influence may be effective in the formation of headaches.[12] Studies showed that migraine was associated with an increased risk of cardiovascular disease.[13,14] Although there are many factors that can affect the outcome of autonomic function tests, such as age, weight, sex, test selection, test criteria, and patient selection, the most commonly used method in clinics is the measurement of heart rate variability (HRV). Heart rate variability quantitatively evaluates the change in heart rate intervals.[15] Decreased HRV in the time domain was reported to be associated with autonomic dysfunction in various disease states. Investigating the role of HRV in migraine may provide a better understanding of the increased risk of cardiovascular disease and autonomic dysfunction in patients with migraine.[16]

Studies on migraine have addressed the concepts of heart rate, kinesiophobia, pain, and disability as separate topics, and their effects on the disease and the sources of the emergence of symptoms were investigated. However, to the best of our knowledge, there exists no study examining the effects of these concepts on each other. In patients with migraine, we believe that the increase in the frequency and severity of symptoms and the increasingly chronic pain condition may lead to kinesiophobia behavior and that these symptoms may be triggering factors for each other. Therefore, this study aimed to determine the relationship between pain level, kinesiophobia, disability, and HRV, which can be considered an indicator of autonomic functions, in patients with migraine.

PATIENTS AND METHODS

The prospective cross-sectional study was conducted with 37 female patients with migraine (mean age: 34.7±2.1 years; range, 18 to 62 years) between July 2022 and April 2023. All participants were evaluated at the Ankara Yıldırım Beyazıt University Faculty of Medicine, Department of Neurology. All participants consisted of patients with a definitive diagnosis of migraine by a neurologist. Inclusion criteria were being aged 18 to 65 years, being diagnosed with migraine by a physician at least one year ago, having migraine attacks at least five days a month, and having a history of migraine before the age of 50 years. Exclusion criteria were experiencing headache due to organic or secondary causes (history of subarachnoid or cerebral hemorrhage, hypertension, cerebral embolism, or thrombosis); history of bleeding diathesis or receiving anticoagulant therapy; being pregnant or lactating; history of malignancy; diagnosis of depression or receiving antidepressant therapy; caffeine consumption within the last 4 h; tobacco use within the past 48 h; drug and alcohol use within the past week; taking medication that affects the ANS; recent surgery; and having any medical condition affecting the ANS or immune system (e.g., autonomic neuropathy, pure autonomic failure, rheumatic or autoimmune diseases, and acquired autoimmune failure syndrome). All participants were informed about the study before data collection, and written informed consent was obtained from the participants. The study protocol was approved by the Ankara Yıldırım Beyazıt University Ethics Committee (date: 07.04.2022, no: 06). The study was conducted in accordance with the principles of the Declaration of Helsinki.

In addition to the demographic data of the participants, migraine-related characteristics, such as the date of diagnosis of migraine, the number of medications taken daily for migraine pain, the number of migraine attacks in the last week, the duration of migraine attacks (hours), and the presence of relatives with a family history of migraine were questioned. To avoid possible bias, participants were instructed to complete all the scales independently, except for the heart rate measurement.

Participants' migraine-related pain intensity was measured with the Visual Analog Scale (VAS), disability levels were assessed with the MIDAS, pain-induced kinesiophobia levels were examined with the Tampa Kinesiophobia Scale (TKS), and HRV was determined with the Polar H10 model heart rate monitor (H10, Polar Electro Oy, Kempele, Finland).

The VAS is a subjective, reproducible, easy-to-understand, simple, and effective assessment tool used to determine pain intensity. A 10-cm long horizontal or vertical line was drawn with "0" at one end, indicating no pain, and "10" at the other end, indicating unbearable pain. On this line, participants were asked to mark the point that best represented their perceived pain intensity.[17] The Turkish adaptation, sensitivity, and selectivity study was conducted by Eti Aslan[18] in 1998.

The MIDAS was designed to assess disability related to headache. It was adapted to Turkish, and its validity and reliability was shown. It consists of five questions, and the final score is obtained by calculating the number of days in the last three months when migraine-induced headaches have reduced the time spent at work, school, or home life or have completely prevented these tasks.[19]

The TKS was originally developed by Kori et al.[4] in 1991, and Vlaeyen et al.[20] republished the original scale in 1995 with the permission of the researchers who developed it. The TKS is a 17-item scale developed to measure fear of movement/reinjury. The scale includes parameters of injury/reinjury and fear-avoidance in work-related activities.[20]

Heart rate variability was measured with a Polar H10 heart rate monitor. After completing the assessment form, the electrodes on the Polar H10 Bluetooth chest strap (H10, Polar Electro Oy, Kempele, Finland) were moistened with water at room temperature before being placed on the participant, the sensor was placed on the xiphoid process of the sternum and connected with Velcro on the back of the chest strap. The Polar H10 heart rate receiver was worn on the wrist. The Polar H10 chest strap was automatically connected to the Elite HRV (Elite HRV, Asheville, NC, USA) application when a signal was detected.[21] Heart rate variability was measured in a quiet room under thermoneutral conditions (22 to 24°C and 40 to 60% relative humidity)[22] after the subject had rested for 15 min in a seated position. Recordings were taken in the supine position with spontaneous breathing for 5 min. Data were analyzed with Elite HRV, a smartphone application.[23,24] Heart rate variability analyses were performed in two stages as time or frequency axis analyses. Some important time and frequency axis parameters and their descriptions are shown in Table 1.

Statistical analysis

The sample size was calculated as a total of 34 patients with migraine, based on a power

TABLE 1
Heart rate variability time and frequency axis parameters[25]

Parameter (Unit)	Definition
Time axis parameters	
Mean RR (ms)	Average RR range
SDNN (ms)	Standard deviation of NN ranges
RMSSD (ms)	Normal is the square root of the mean squared differences of normal ranges and mainly reflects vagal activity.
pNN50 (%)	Percentage of NN intervals with a difference greater than 50 ms
Frequency axis parameters	
VLF (ms^2)	Power spectrum band in the range 0.003-0.04 Hz
LF (ms^2)	0.04-0.15 Hz, reflecting both sympathetic and parasympathetic activity, but generally indicative of sympathetic activity.
HF (ms^2)	It is the region between 0.15 and 0.4 Hz and reflects parasympathetic activity.
LF/HF	Shows the balance between sympathetic and parasympathetic systems

RR: R-R interval' means R wave - R wave interval; NN: Normal-to-normal intervals; RMSSD: Root mean square of the successive difference; pNN50: Percentage of NN intervals that differ by more than 50 milliseconds from the previous interval; VLF: Very low frequency; LF: low frequency; HF: High frequency.

TABLE 2
Data on migraine characteristics of the participants

Variables	Mean±SD	Median	Min-Max
Duration since diagnosis (month)	61.70±87.62	25	6-420
Number of medicines consumed in one day for migraine	1.62±1.87	1	0-10
Number of attacks (last week)	2.27±2.03	2	0-7
Attack duration (h)	24.40±23.08	24	2-72

SD: Standard deviation.

analysis of a similar high-frequency study,[16] with an alpha error probability of 0.05 and a power of 90%.

Data were analyzed using IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Numerical variables were presented as mean ± standard deviation (SD) and median (min-max) values. The normal distributions of all variables were analyzed using the Shapiro-Wilk test and histogram graphs. Spearman correlation analysis was used to examine the relationship between nonnormally distributed data. A p-value <0.05 was considered statistically significant.

RESULTS

Sixteen (43.2%) of the participants had migraine with aura, and 21 (56.8%) had migraine without aura. None of the participants had a history of accident/trauma in the last year, and 16 (43.2%) had a family history of migraine. Data related to other descriptive characteristics of the participants and inquiries about migraine characteristics are shown in Table 2.

According to the results based on the analysis performed to reveal the relationship between HRV measurement parameters and the data obtained from the scales, a statistically significant, positive, and low-level relationship was found between the participants' daytime pain levels and low frequency (LF) peak value and between MIDAS scores and minimum heart rate values (r=0.370, p=0.026; r=0.384, p=0.021, respectively). There was a statistically significant negative low-level correlation between kinesiophobia measurement data and maximum heart rate

TABLE 3
Data on the participants' scale scores, and HRV data

Variables	Mean±SD	Median	Min-Max
Visual Analog Scale (daytime)	7.83±1.87	8	3.70-10
MIDAS	46.91±34.12	39	4-147
Tampa kinesiophobia scale	42.16±13.69	39.5	23-63
Min HR	65.00±12.99	65.50	29.01-91
Max HR	97.38±18.97	94	60.72-157
Average HR	80.86±13.70	77	59-119
RMSSD (ms)	33.32±18.63	28.93	4.50-77.56
SDNN (ms)	51.18±31.60	43.27	13.24-186.91
LN (RMSSD)	3.40±0.72	3.36	1.50-4.95
PNN50 (%)	15.41±18.41	6	0-58
LF power (MS2)	580.79±474.29	433.11	81.23-2764.49
HF power (MS2)	367.02±600.64	220.36	15.30-3675.49
LF/HF Ratio	3.62±2.31	3.23	0.30-7.61
LF peak (Hz)	2.02±10.45	0.13	0.04-63
HF peak (Hz)	0.41±0.23	0.39	0.15-0.91

HRV: Heart rate variability; SD: Standard deviation; MIDAS: Migraine Disability Scale; Min HR: Minimum heart rate; Max HR: Maximum heart rate; RMSSD: Root mean square of the successive difference; SDNN: Standard deviation of normal-to-normal intervals; LN: Natural logarithm; LF: low frequency; HF: High frequency.

TABLE 4
Correlation analysis table showing the relationship between the data obtained from the scales and HRV measurements

Clinical parameters	Average HR	Min HR	Max HR	LF power	LF peak	RMSSD
VAS (daytime)						
r	-0.075	−0.072	−0.142	0.370*	0.073	−0.155
p	0.663	0.675	0.409	0.026	0.673	0.366
MIDAS						
r	0.123	0.384*	0.114	0.043	−0.074	−0.146
p	0.473	0.021	0.506	0.804	0.667	0.395
TKS						
r	−0.155	0.018	−0.332*	0.012	0.109	−0.110
p	0.367	0.919	0.048	0.945	0.528	0.522
Number of medicines consumed in one day for migraine						
r	0.071	−0.042	0.019	0.016	0.067	−0.058
p	0.680	0.809	0.914	0.926	0.697	0.738
Number of attacks (last week)						
r	0.041	0.094	−0.070	0.140	0.129	−0.090
p	0.814	0.585	0.687	0.416	0.454	0.603
Attack duration (h)						
r	−0.035	−0.008	−0.040	0.039	−0.041	−0.195
p	0.840	0.464	0.918	0.821	0.814	0.255

HRV: Heart rate variability; Min HR: Minimum heart rate; Max HR: Maximum heart rate; LF: low frequency; RMSSD: Root mean square of the successive difference; VAS: Visual Analog Scale; MIDAS: Migraine Disability Scale; TKS: Tampa kinesiophobia scale; * Significant at 0.05 level; r: Spearman correlation coefficient.

values. There was no statistically significant correlation between the other parameters of heart rate measurement and the data of pain, migraine-related disability, and kinesiophobia measurements, as well as between the data obtained from these scales, except for the heart rate ($p>0.05$; Table 4).

DISCUSSION

In this study, which evaluated the relationship between pain, disability and kinesiophobia levels, and HRV in patients with migraine, it was revealed that the increase in pain intensity and LF power values, the decrease in maximum heart rate values of kinesiophobia, and the increase in minimum heart rate values of migraine-related disability were related to each other.

In two studies investigating autonomic functions in patients with migraine, sympathetic hyperfunction and hypofunction were shown.[26,27] In the study by Shechter et al.,[11] diastolic blood pressure measured at rest was higher compared to that of the control group, and it was reported that this may be secondary to sympathetic hyperactivity or reflex response to sympathetic hypoactivity. In the same study, lower values indicating parasympathetic hypofunction were found in RR interval variability, and symptoms indicating ANS dysfunction were observed in patients with migraine. Gass and Glaros[28] found decreased variability in HRV indices in the migraine and tension-type headache group compared to the control group, and this was associated with decreased parasympathetic system activity. Studies examining HRV parameters in headache found significantly lower NN50 (number of pairs of successive normal-to-normal intervals that differ by more than 50 milliseconds) and pNN50 (percentage of normal-to-normal intervals that differ by more than 50 milliseconds from the previous interval) compared to healthy controls, consistent with lower vagal activity indexed by root mean square of the successive difference (RMSSD) and high frequency (HF).[28,29] In one study examining the RMSSD parameter, RMSSD was found to be higher in headache patients, while in another study, RMSSD was found to be lower in those with migraine among groups of patients with

various types of headaches, including tension-type headache.[29,30] Although these results provided evidence for the physiological context between migraine and vagal activity, it was emphasized that it was difficult to make clear interpretations. This may be due to the large number of factors that may influence both vagal activity and migraine disease activity and symptoms. As in these studies, in our study, we examined the factors that we thought to be associated with the ANS in patients with migraine.

Although migraine is generally considered a neurological disease, it is also a musculoskeletal disease that can cause fear or avoidance behavior from movement (kinesiophobia).[7] The number of studies investigating kinesiophobia in patients with migraine is quite limited. Different results were obtained from studies on this subject. It was shown that kinesiophobia behavior may develop in patients due to reasons such as the belief that physical activity increases the intensity of pain during a migraine attack, fear of falling, and the instinct to protect themselves in patients with vestibular symptoms.[31,32] To our knowledge, this is the first study in the literature to examine kinesiophobia and HRV in patients with migraine. Studies examining the relationship between these two variables in different groups are also quite limited. Weak to moderate correlations were found between HRV parameters and perceived level of disability and kinesiophobia in patients with chronic musculoskeletal pain.[33,34] In this recent study, it was found that the maximum heart rate of the participants decreased as their level of kinesiophobia increased. This is an interesting outcome because kinesiophobia, which has been shown to be associated with pain in many studies, might cause sympathetic activation, or these two conditions might mutually affect each other. However, the low level of the relationship we found and the fact that we did not find any study examining the relationship between kinesiophobia and heart rate in patients with migraine reduced the generalizability of this result. In our study, no significant relationship was found between kinesiophobia levels and the other factors examined. Benatto et al.[31] found that 53% of 89 patients with migraine exhibited kinesiophobia, which was associated with higher severity levels of cutaneous allodynia but not with cutaneous allodynia or migraine pain characteristics. In another study examining HRV and pain sensitivity in patients with chronic low back pain, no significant relationship was found between participants' pain sensitivity and HRV parameters.[35]

Another important result in our study was that as the pain intensity of the participants increased, LF power values also increased. The LF power parameter is an important indicator of the activation of the sympathetic nervous system. Although the results obtained in our study reflected a consistent relationship with this definition, some studies provided evidence that LF reflected parasympathetic activity. Studies emphasized that when the parasympathetic component of HRV was high, there was a reduction in pain or improvement in the management of painful conditions (e.g., pain tolerance).[36,37] It was reported that the inhibitory vagal effect on pain could be associated with these results.[36] Appelhans and Luecken[37] found a negative relationship between sympathetic activity and pain sensitivity, but not between HF and pain. According to the authors, LF has a complex relationship with arterial baroreflex, a homeostatic mechanism mediated by the ANS whose components also mediate an endogenous pain inhibitory pathway.

Migraine is the main type of headache that causes disability due to its physical and psychological effects on patients, with symptoms accompanying migraine during attacks.[38] Pain, kinesiophobia, and autonomic dysfunction, as well as accompanying symptoms, may be factors leading to disability. Although the role of pain in the development of disability is predictable, there is insufficient literature and evidence to explain the relationship between ANS and disability. In one of the rare studies examining this issue, Shechter et al.[11] examined ANS function in migraine and found that the low RR variation in patients with migraine might be due to sympathetic or parasympathetic hypofunction. In this study, it was stated that the presence and degree of ANS dysfunction might be related to the degree of disability. It was also emphasized that patients with migraine with headache attacks might be more prone to ANS hypofunction, which might predispose to the development of disability.[11] In this recent study, we found that minimum heart rate values increased as the level of migraine-related disability of the participants increased. This result supported the relevant literature and showed that sympathetic function increased in a correlated manner with disability. However, this interpretation did not provide complete clarity about ANS dysfunction because we did not find

associations between the LF, HF, and RMSSD values of HRV, which provide clearer information about the sympathetic and parasympathetic balance of the ANS and migraine-related disability levels.

There were some limitations to this study. It is a known fact that the ANS can be affected by many factors. For this reason, it was not possible to state that there was a causal relationship between the components, and they were definitely affected by each other. In addition, in contrast to the monthly questionnaires about headache in the literature, our weekly questionnaires were another limitation. Another limitation of the study was that all participants were female. We had difficulty in reaching male patients with migraine. In addition, the lack of a control group with similar characteristics can also be considered a limitation. Studies with larger samples with a sufficient number of participants of both sexes are needed. The fact that menstrual periods, which may be an effective factor in triggering migraine attacks, was not questioned in our study also constitutes a limitation.

In conclusion, this study evaluated the relationship between pain, kinesiophobia, disability levels, and HRV in patients with migraine, and the main finding of this study was that there was a low level of statistical and clinical correlation between the heart rate and other parameters thought to be associated with the disease. Since HRV as an indicator of ANS activity may be an effective factor on clinical variables in patients with migraine, and given the potential connection between pain, kinesiophobia, and the ANS, it can be said that it would be meaningful to consider these factors in the evaluation and treatment of patients with migraine.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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