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Research Article

Association between Serum Cortisol Levels and Autonomic Nervous System Function during Anesthesia in Adults with Chronic Migraine

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ABSTRACT
Background: Chronic migraine is associated with autonomic dysregulation and altered hypothalamic–pituitary–adrenal activity. The perioperative interaction between cortisol responses and autonomic function remains poorly defined.
Objective: To evaluate the association between serum cortisol concentrations and heart rate variability during general anesthesia in adults with chronic migraine.
Methods: This prospective observational study included 120 adults with chronic migraine undergoing elective surgery at Khawaja Muhammad Safdar Medical College, Sialkot, and Jinnah Hospital, Lahore, from January 2025 to January 2026. Serum cortisol and five-minute electrocardiographic recordings were obtained before induction, after induction, 30 minutes after incision, and near the end of surgery. Autonomic function was assessed using RMSSD, HF-HRV, and SDNN. Associations were examined using correlation analysis and multivariable linear mixed-effects modeling.
Results: Mean age was 39.2 ± 10.4 years, and 72.5% were women. Cortisol decreased after induction from 14.1 ± 4.3 to 11.9 ± 3.8 µg/dL, then increased to 17.4 ± 5.1 µg/dL after incision and 19.2 ± 5.6 µg/dL near surgery completion. RMSSD declined significantly across the same period. Cortisol correlated inversely with RMSSD after incision ($r=-0.46$, $p<0.001$) and near surgery completion ($r=-0.43$, $p<0.001$). Each 1-µg/dL increase in cortisol was independently associated with a 2.1% reduction in RMSSD. Greater headache frequency was also associated with lower RMSSD, suggesting reduced autonomic adaptability with increasing migraine burden.
Conclusion: Higher perioperative cortisol concentrations were independently associated with reduced vagally mediated heart rate variability, indicating coordinated neuroendocrine and autonomic stress responses in adults with chronic migraine.

Keywords: Chronic Migraine, Serum Cortisol, Heart Rate Variability, Autonomic Nervous System, Anesthesia, Rmssd.

INTRODUCTION

Chronic migraine is a disabling neurological disorder defined by headache on 15 or more days per month for over 3 months, with migraine features present on at least 8 days per month[1]. In addition to recurrent headache, chronic migraine is now known to be a disease characterized by abnormalities in sensory processing, hypothalamic function, neuroendocrine function, and autonomic nervous system function. Autonomic symptoms such as nausea, cardiovascular changes, sweating changes, gastrointestinal disturbances, and orthostatic intolerance are common in patients, and autonomic dysfunction could be an important part of the pathophysiology of migraine headaches in general[2,3].

Heart rate variability (HRV) provides a non-invasive method for evaluating cardiac autonomic modulation and has increasingly been applied in migraine research[4]. Several studies have found changes in HRV and disturbances in autonomic reactions in migraine patients, such as reduced vagally-mediated cardiac variability and abnormal autonomic

adaptation. Measurable abnormalities in HRV have been found in recent studies of patients with chronic migraine, and systematic evidence indicates that HRV is disturbed in a variety of standardized tests of autonomic function. These results suggest that patients with chronic migraine might be less autonomously flexible when exposed to an additional physiological stress[5].

The hypothalamic–pituitary–adrenal (HPA) axis, another key player in the physiological stress-response system, may be linked to mechanisms underlying migraine chronification[6]. The main glucocorticoid, cortisol, which is produced as a result of activation of the HPA axis, is affected by pain, psychological stress, sleep, circadian rhythms, inflammation, and pharmacologic interventions. Basal cortisol levels have been inconsistently reported in previous migraine studies, but recent evidence indicates that there could be a dysfunction of cortisol dynamics and hypothalamic stress responses in migraine. Changes in cortisol levels during a controlled physiological challenge can thus yield more information regarding neuroendocrine dysfunction in chronic migraine, rather than resting concentration[7,8].

A unique and relevant scenario where both the autonomic and the neuroendocrine systems are challenged at the same time is that of general anesthesia and surgery[9]. Autonomic suppression and alteration of HRV during induction of anesthesia may alter HRV, while laryngoscopy, surgical incision, tissue injury, nociceptive stimulation, and perioperative hemodynamic changes can activate neuroendocrine stress pathways. It is possible, therefore, that cortisol levels could rise during surgical stimulation and anesthetic drugs could also have a direct effect on sympathetic and parasympathetic control of the cardiovascular system. The interaction of HPA axis activity and autonomic regulation is an interesting physiological model for the investigation of the overlapping responses during the perioperative period[10-13].

Although there is increasing evidence that cortisol regulation and autonomic function are disrupted in migraine, their relationship under general anesthesia has not been sufficiently studied. Identifying patients with impaired autonomic modulation in the context of heightened perioperative cortisol responses may help in understanding which other patients could be vulnerable to physiological stress in the perioperative period and may help identify those that need more attention during perioperative monitoring 14,15. The present study aimed to assess the relationship between serum cortisol level and autonomic nervous system function during general anesthesia in adult patients with chronic migraine, using HRV-derived parameters as objective markers of cardiac autonomic regulation. We hypothesized that increased serum cortisol levels during surgery would be correlated with decreased vagally mediated HRV, especially root mean square of successive RR-interval differences and high-frequency HRV.

MATERIALS AND METHODS

The study was a prospective observational study carried out at Khawaja Muhammad Safdar Medical College, Sialkot, Pakistan, and Jinnah Hospital, Lahore, Pakistan, between January 2025 and January 2026. Adult chronic migraine sufferers were recruited from patients in whom elective surgery under general anesthesia was planned. All 120 participants meeting the criteria for assessment were recruited using consecutive sampling. The study was conducted in line with the principles of the Declaration of Helsinki and approved by the appropriate institutional ethical review committees prior to commencement of patient recruitment. All participants signed written informed consent before entering the study.

Patients between 18 and 60 years of age with a diagnosis of chronic migraine, based on the International Classification of Headache Disorders, third edition guidelines, were eligible. Chronic migraine was defined as headache occurring on at least 15 days per month for more than three months, with migraine features present on at least eight days per month. The patients included were those who were ASA physical status I/II and were scheduled for elective non-cardiac surgery under general anesthesia with an anticipated duration of anesthesia of at least 60 minutes. Patients with known ischemic heart disease, clinically significant cardiac arrhythmias, cardiac pacemaker, uncontrolled hypertension, diabetes mellitus complicated with autonomic neuropathy, thyroid dysfunction, adrenal disorders, severe renal or hepatic disease, major neurological disorders other than migraine, pregnancy, chronic systemic corticosteroid use, active systemic infection, and emergency surgical procedures were excluded. Technically suboptimal electrocardiographic recordings, as well as incomplete serial cortisol measurements and major intraoperative events which precluded

completion of the study protocol, were further excluded.

The number of patients was fixed at 120. This number was deemed adequate for the ability to detect a clinically meaningful moderate association between the serum cortisol concentration and the heart rate variability parameters, with a two-sided significance level of 5%, and also to accommodate the possibility of some observations being unanalyzable because of incomplete blood sampling or poor-quality ECG recordings. The eligible patients who sought care in a consecutive manner during the study period were recruited until the desired sample size was obtained.

A thorough clinical evaluation was made prior to the surgery. Demographic data such as sex, age, body weight, stature, and BMI were documented. Migraine details consisted of duration of migraine and regularity of migraine (number of headache days per month), presence or absence of aura, typical intensity of the headache, use of preventive migraine medication, use of acute migraine medication, and occurrence of headache the morning of surgery. Medical history, concomitant medications, smoking habits, comorbidities, and previous anesthetic exposure were also noted. Patients were encouraged to observe standard institutional guidelines for fasting, and caffeinated drinks, nicotine, and strenuous exercise were avoided the morning of surgery when possible to prevent the potential effects of these on autonomic activity and cortisol secretion.

There is considerable variation in serum cortisol levels throughout the day, and whenever possible patients were prioritised for morning lists. Patients were placed in a quiet room in the supine position for at least 10 minutes before induction of anesthesia. Heart rate, systolic and diastolic blood pressure, mean arterial pressure, oxygen saturation, and electrocardiographic rhythm were taken as baseline. The first heart rate variability recording and baseline serum cortisol sample were taken prior to the administration of sedative or anesthetic medication.

A uniform general anesthesia protocol was used in all patients to minimize any differences in the autonomic and neuroendocrine response that could be due to anesthesia used. Standard monitoring was performed intraoperatively, consisting of continuous electrocardiography, non-invasive blood pressure measurement, pulse oximetry, capnography and temperature monitoring. If possible, depth of anaesthesia monitoring was used. General anesthesia was induced with intravenous propofol (1.5–2.5 mg/kg) and fentanyl (1–2 μg/kg), and an adequate non-depolarizing neuromuscular blocker was used for intubation. Once the airway has been secured, anesthetic maintenance was provided with sevoflurane in an oxygen-air mixture, the concentration of which was adjusted according to clinical needs and anesthetic level.

To prevent variability in autonomic measurements due to changes in ventilation and arterial carbon dioxide, mechanical ventilation was standardized to keep the end-tidal carbon dioxide at approximately 35 to 40 mmHg. There was maintenance of oxygen saturation levels above 94% and a normal physiologic range of temperature. Opioid administration ensured additional doses were given as clinically indicated based upon surgical stimulation and hemodynamic response. Hypotension was defined as a mean arterial pressure < 65 mmHg and/or a decrease of > 20% from the pre-induction mean arterial pressure and was treated with intravenous fluids and vasoactive agents as per institutional practice. Bradycardia and tachycardia were treated if clinically relevant. For each participant, the total anesthetic time, surgical time, opioid use, volume of intravenous fluid infusions, estimated blood loss, and use of vasopressors or other vasoactive drugs were measured.

Cortisol levels were determined at four predetermined perioperative time points. The first sample (T0) was taken at the beginning of the experiment, around 15-20 minutes before anaesthetic induction, and used as a baseline measurement. The second sample (T1) was taken around 10 minutes after anesthesia and prior to making the surgical cut to check the pure effect of the anesthesia. The third sample, T2, was collected 30 minutes after the surgical incision in order to evaluate the neuroendocrine response to the surgical stimulation. The T3 sample was drawn at the end of surgery (last 10 minutes) before awakening from anesthesia. At each time point, 3-5 mL of venous blood was obtained in a standard manner using aseptic technique.

Blood samples were left to clot and the serum separated by centrifugation. The serum was separated, placed in labeled tubes, and analyzed using standard laboratory procedures. Samples not analysed immediately were kept under recommended laboratory conditions until biochemical testing was done. A validated

electrochemiluminescence immunoassay was used for the determination of serum cortisol concentration. The same laboratory methodology was used for all the samples, minimizing inter-assay variation. When possible, laboratory staff were not informed of the concomitant autonomic tests.

Heart rate variability analysis was used to evaluate the function of the autonomic nervous system by means of continuous electrocardiographic recordings. Five-minute ECG segments were chosen at the time nearest possible to the serum cortisol measurement. Recordings were made at baseline (before induction), after induction (before incision), 30 minutes after incision, and near the end of surgery (before emergence). Segments of the ECG with excessive artifacts, ectopic beats, electrical interference, or unstable rhythm were excluded or corrected following standard HRV processing procedures. Recordings were only included where there were enough normal-to-normal RR intervals to allow reliable analysis.

Both time and frequency domain HRV parameters were considered. The most important autonomic parameter was the root mean square of successive differences between normal RR intervals (RMSSD), which primarily indicates short-term vagal/parasympathetic modulation of heart rate. SDNN (standard deviation of normal-to-normal RR intervals) was used as a measure of overall short-term heart rate variability. High-frequency power was also used as a supplementary index of vagally mediated cardiac autonomic activity for the frequency domain analysis. Low-frequency power and the low-frequency-to-high-frequency ratio were merely measured as exploratory variables and were not interpreted as direct quantitative measures of sympathetic-parasympathetic balance due to the cardiovascular and respiratory factors affecting their physiological interpretation.

The main study result was the relationship between serial serum cortisol levels and RMSSD during general anesthesia. Secondary outcomes comprised: association of serum cortisol and high-frequency HRV and SDNN; serum cortisol changes at different perioperative time points; autonomic parameter changes during anaesthetic and surgical stimulation; and the association between migraine severity and perioperative autonomic changes. The principles of migraine burden measurement were mainly based on the monthly headache frequency and chronic migraine duration.

The data were recorded in the computer database and verified for completeness and accuracy prior to analysis. SPSS software was used for statistical analyses. Normality of continuous variables was evaluated by distribution plots and appropriate tests of normality. Normally distributed variables were reported as mean ± standard deviation, and non-normally distributed variables as median with interquartile range. Categorical data were displayed as frequencies and percentages.

Normally distributed data were assessed using repeated-measures analysis of variance, and if the distributional assumptions were not met, then an appropriate non-parametric repeated-measures test was used to examine the changes in each variable at each of the four perioperative time points. When a significant difference between times was detected, post-hoc comparison was done between each of the individual times. Pearson correlation coefficient was used for normal variables, and the Spearman rank correlation coefficient for non-normal variables to calculate the relationships between serum cortisol concentrations and HRV parameters.

Since the measurements were made in the same participant multiple times during surgery, linear mixed-effects modeling was applied for the primary multivariable analysis. Serum cortisol concentration was used as the primary independent variable, and participant identification as a random effect, to account for repeated observations within individuals, in a model with log-transformed RMSSD as the dependent variable. The potential confounding factors were: age, sex, body mass index, frequency of headaches per month, length of migraine history, baseline cortisol level, baseline HRV, intraoperative mean arterial pressure, heart rate, cumulative opioid use, anesthetic time, surgical time, and vasoactive drug use. HRV variables that had skewed distributions were log-transformed prior to regression analysis. Results from regression analysis were presented with 95% confidence intervals. All statistical tests were two-sided, and a p-value < 0.05 was taken as statistically significant.

RESULTS

A total of 126 patients who had chronic migraine and were to undergo elective surgery were evaluated during the study period for eligibility. Six patients were excluded before enrollment because of significant cardiac arrhythmia, endocrine disease, chronic corticosteroid therapy, or inability to obtain an

adequate baseline electrocardiographic recording. Thus, the final analysis comprised 120 patients, who all underwent the predetermined perioperative sampling of cortisol and the autonomic assessment.

Baseline Characteristics

The mean age of the participants was 39.2 ± 10.4 years, and 87 (72.5%) were women. The mean body mass index was 26.8 ± 4.1 kg/m². Sixty-seven patients (55.8%) had ASA physical status II, and fifty-three patients (44.2%) had ASA physical status I. The mean headache frequency was 21.5 ± 4.6 days per month, and the median duration of migraine was 9.0 years. 34 (28.3%) had migraine with aura, and 70 (58.3%) participants were on migraine prevention. Preoperatively, 30.8% (37 patients) had headache. As seen in Table 1, the mean time of anesthesia was 113.6 ± 30.7 minutes.

Table 1. Baseline Demographic and Clinical Characteristics of Participants

Variable	Total, n=120
Age, years	39.2 ± 10.4
Female sex	87 (72.5%)
Male sex	33 (27.5%)
BMI, kg/m²	26.8 ± 4.1
ASA physical status I	53 (44.2%)
ASA physical status II	67 (55.8%)
Migraine duration, years	9.0 (6.0–14.0)
Monthly headache days	21.5 ± 4.6
Migraine with aura	34 (28.3%)
Preventive migraine therapy	70 (58.3%)
Headache on morning of surgery	37 (30.8%)
Baseline heart rate, beats/min	76.8 ± 10.6
Baseline mean arterial pressure, mmHg	91.7 ± 10.3
Duration of surgery, min	88.4 ± 28.9
Duration of anesthesia, min	113.6 ± 30.7

Data are presented as mean ± standard deviation, median (interquartile range), or n (%).

Perioperative Changes in Serum Cortisol

Serum cortisol concentrations differed significantly across the four perioperative measurement points ($p<0.001$). Mean cortisol decreased from 14.1 ± 4.3 µg/dL at T0 to 11.9 ± 3.8 µg/dL at T1 following induction of anesthesia. After surgical stimulation, cortisol increased substantially to 17.4 ± 5.1 µg/dL at T2 and reached 19.2 ± 5.6 µg/dL at T3. Pairwise analysis demonstrated significant reductions between T0 and T1 and significant increases between T1 and both T2 and T3 (all $p<0.001$).

Autonomic indices demonstrated the opposite overall pattern. Median RMSSD decreased from 32.4 ms at baseline to 24.0 ms after induction and 18.7 ms following surgical incision, followed by a modest increase to 20.5 ms toward the end of surgery. HF-HRV and SDNN demonstrated comparable reductions. These serial changes are summarized in Table 2.

Table 2. Perioperative Changes in Cortisol, Heart Rate Variability, and Hemodynamic Parameters

Parameter	T0: Baseline	T1: Post-induction	T2: 30 min post-incision	T3: End of surgery	p value
Serum cortisol, µg/dL	14.1 ± 4.3	11.9 ± 3.8	17.4 ± 5.1	19.2 ± 5.6	<0.001
RMSSD, ms	32.4 (24.8–41.5)	24.0 (18.0–31.8)	18.7 (13.6–25.9)	20.5 (14.8–28.7)	<0.001
HF-HRV, ms²	414 (264–636)	253 (158–403)	169 (103–287)	195 (119–320)	<0.001
SDNN, ms	39.5 (30.6–49.8)	30.1 (22.9–39.2)	24.6 (18.2–32.9)	26.8 (19.8–35.9)	<0.001
Heart rate, beats/min	76.8 ± 10.6	67.9 ± 9.1	72.8 ± 9.8	71.0 ± 9.5	<0.001

Mean arterial pressure, mmHg	91.7 ± 10.3	75.4 ± 8.8	78.6 ± 9.5	77.9 ± 9.0	<0.001

T0, before induction; T1, after induction before incision; T2, 30 minutes after incision; T3, before emergence; RMSSD, root mean square of successive RR-interval differences; HF-HRV, high-frequency heart rate variability; SDNN, standard deviation of normal-to-normal intervals.

Association between Serum Cortisol and Autonomic Function

Serum cortisol showed an inverse relationship with vagally mediated HRV throughout the perioperative period, with the strongest associations observed during and after surgical stimulation. At baseline, cortisol was weakly inversely correlated with RMSSD (r=−0.24, p=0.008). The association strengthened after induction (r=−0.29, p=0.001), reached its greatest magnitude 30 minutes after incision (r=−0.46, p<0.001), and remained significant toward the end of surgery (r=−0.43, p<0.001). HF-HRV also demonstrated significant inverse correlations with serum cortisol at T2 (r=−0.39, p<0.001) and T3 (r=−0.37, p<0.001). Similarly, SDNN was negatively associated with cortisol after incision and near the end of surgery. The correlations between cortisol and individual HRV measures are presented in Table 3.

Table 3. Correlation between Serum Cortisol and Heart Rate Variability Parameters

Time point	RMSSD, r	p value	HF-HRV, r	p value	SDNN, r	p value
T0	−0.24	0.008	−0.20	0.028	−0.18	0.048
T1	−0.29	0.001	−0.25	0.006	−0.23	0.011
T2	−0.46	<0.001	−0.39	<0.001	−0.35	<0.001
T3	−0.43	<0.001	−0.37	<0.001	−0.32	<0.001

The change in cortisol following surgical stimulation was also associated with the magnitude of autonomic suppression. The increase in serum cortisol from T1 to T2 correlated inversely with the corresponding change in RMSSD (r=−0.41, p<0.001), indicating that patients with a greater cortisol response to surgical stimulation generally experienced a greater reduction in cardiac vagal modulation.

Multivariable Association between Cortisol and RMSSD

In the linear mixed-effects model incorporating repeated measurements from all four time points, serum cortisol remained independently associated with lower RMSSD after adjustment for potential confounding variables. Each 1 µg/dL increase in serum cortisol was associated with a 2.1% reduction in RMSSD after adjustment for age, sex, body mass index, monthly headache frequency, migraine duration, mean arterial pressure, opioid exposure, and duration of surgery (adjusted β=−0.021, 95% CI −0.028 to −0.014; p<0.001).

Increasing age and greater monthly headache frequency were also independently associated with reduced RMSSD. Mean arterial pressure showed a modest positive association with RMSSD, whereas sex, body mass index, migraine duration, cumulative opioid exposure, and surgical duration were not independently associated with the primary autonomic outcome, as shown in Table 4.

Table 4. Multivariable Linear Mixed-Effects Analysis of Factors Associated with Intraoperative RMSSD

Predictor	Adjusted β	95% CI	p value
Serum cortisol, per 1 µg/dL	−0.021	−0.028 to −0.014	<0.001
Age, per year	−0.006	−0.010 to −0.002	0.003
Female sex	0.038	−0.037 to 0.113	0.320
BMI, per kg/m²	−0.004	−0.012 to 0.004	0.337
Monthly headache days	−0.015	−0.026 to −0.004	0.008
Migraine duration, per year	−0.003	−0.008 to 0.002	0.235
Mean arterial pressure, per 10 mmHg	0.036	0.011 to 0.061	0.005
Cumulative opioid exposure	−0.017	−0.050 to 0.016	0.311
Surgical duration, per 30 min	−0.020	−0.046 to 0.006	0.132

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Relationship with Migraine Burden

Patients with higher chronic migraine burden had more significant autonomic changes under anesthesia. Participants experiencing 25 or more headache days per month had lower RMSSD following surgical incision compared with those experiencing 15–19 headache days per month (16.9 [12.4–23.7] ms vs 21.8 [16.0–29.6] ms; p=0.009). They also demonstrated a greater mean increase in cortisol between T1 and T2 (6.4 ± 3.7 μg/dL vs 4.3 ± 3.2 μg/dL; p=0.012). No significant differences in cortisol–HRV associations were observed according to sex or presence of migraine aura.

The results overall showed a clear temporal relationship between the rise in serum cortisol level and the decrease in cardiac vagal activity during surgical stimulation. In adults with chronic migraine, the most robust negative correlations were seen following incision and remained through surgery, suggesting that the perioperative neuroendocrine stress response is inversely related to autonomic nervous system function.

DISCUSSION

The current study found a strong inverse correlation of serum cortisol levels with ANS function in chronic migraine in adults under general anesthesia[1]. RMSSD, HF-HRV, and SDNN were reduced, and serum cortisol was reduced after induction and increased significantly after surgical stimulation. The highest correlation was found between cortisol and HRV following surgical incision, and this correlation was still significant towards the end of surgery, indicating that a higher level of neuroendocrine stress was correlated with a lower level of cardiac vagal modulation[2,3].

The cortisol curve seen is typical for the effect of anesthesia and surgery. Under general anesthesia, hypothalamic–pituitary–adrenal functions may be initially suppressed, whereas the neuroendocrine stress pathways may be stimulated due to the effects of the surgical incision and tissue damage[4]. This co-occurrence of decreases in HRV parameters suggests that parasympathetic regulation of the heart decreases during periods of increased physiological stress. After adjusting for demographic, migraine-related, hemodynamic, and anesthetic factors, the important negative association between cortisol and RMSSD was still present, suggesting that there is an independent association between endocrine stress response and autonomic regulation[5].

Autonomic dysfunction is now known to be a significant element in chronic migraine. Increased activation of trigeminovascular and hypothalamic pathways, chronic pain, chronic disruption of sleep, and repeated physiological stress may lead to loss of autonomic adaptability[6,7]. For the current study, those who had higher headache frequency per month showed lower RMSSD post-incision and larger increases in cortisol. The result indicates that the more migraines increase, the more the stress-system regulation is disturbed[8,9].

The relevance of RMSSD and HF-HRV was particularly important, as both are mainly vagally mediated cardiac activity[10]. Their constant reduction in surgical stimulation, coupled with the growing cortisol levels, points to a coordinated activation of neuroendocrine stress pathways and a decrease in the influence of the parasympathetic system. The higher correlation coefficient after incision as opposed to baseline also suggests that the dynamic response to stress of surgery may better illustrate the autonomic abnormality than resting measurements alone[11].

These results could have implications in the perioperative setting. Traditional methods of measuring blood pressure and heart rate only detect large changes in hemodynamics and cannot detect more subtle changes in the autonomic control of these variables[12]. This means that HRV assessment may offer extra physiological data on the response of individuals to anesthesia and surgical stimulation. The current results, however, do not support the use of routine cortisol or HRV monitoring clinically, and additional research is required to assess if monitoring these parameters provides a predictive tool for postoperative pain, migraine exacerbation, hemodynamic instability, opioid requirement, or a delay in recovery[13,14].

There are some drawbacks to take into account. The design is only correlational, so it does not guarantee that the rise in cortisol causes the decline in autonomic activity[15,16]. Circadian variability, anesthetic level, ventilation, medication, surgery intensity, and psychological stress can also affect cortisol and HRV. Further, the lack of a non-migraine control group makes it difficult to identify the specificity of the association to chronic migraine. However, the prospective data and serial measurements at standardized peri-operative time points and multivariable adjustment add to the robustness of the results[17-20].

CONCLUSION

Serum cortisol levels are independently linked to a decrease in vagally mediated HRV in adults with chronic migraine who are undergoing GA. Increased cortisol and reduced autonomic modulation were observed with surgical stimulation, and the magnitude of changes was greater in those patients with higher migraine burden. Such results indicate a coordinated neuroendocrine and autonomic stress response while under anesthesia, and should be the basis for additional controlled studies to see if this has any clinical relevance.

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