

Increased Cardiovascular and Anxiety Outcomes but Not Endocrine Biomarkers of Stress During Performance of Endoscopic Sinus Surgery

A Pilot Study Among Novice Surgeons

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Objective: To compare psychophysiological responses among novice surgeons during performance of endoscopic sinus surgery (ESS).

Design: Randomized study.

Setting: Academic institution.

Participants: Fifteen novice surgeons.

Main Outcome Measures: The psychophysiological effects of performing ESS were assessed among 15 novice surgeons at 30 minutes before (T-30), at the beginning of (T0), at 15 minutes (T15), and 45 minutes (T45) during, and at 30 minutes after (T+30) surgery. Participants were randomized to perform ESS with a computer-assisted surgery system, to perform ESS without a computer-assisted surgery system, or to be evaluated on a nonsurgical day (control day). Measured were the State-Trait Anxiety Inventory score, Visual Analog Anxiety Scale score, heart rate, blood pressure, and plasma cortisol and prolactin levels.

Results: Anxiety as measured by the State-Trait Anxiety Inventory score was not modified by the experimental conditions. The mean (SEM) Visual Analog Anxiety

Scale score increased ($P < .05$) during ESS at T0 (2.45 [0.32]), T15 (3.46 [0.50]), and T45 (3.17 [0.46]) compared with the control day (1.19 [0.19], 1.32 [0.26], and 1.20 [0.19], respectively). The mean (SEM) systolic blood pressure (in millimeters of mercury) increased ($P < .05$) during ESS at T0 (127 [2]), T15 (126 [3]), and T45 (125 [2]) compared with the control day (120 [3], 119 [4], and 116 [3], respectively). The mean (SEM) heart rate (in beats per minute) increased during ESS but was significant only at T15 (73 [4]) compared with the control day (64 [3]). The mean (SEM) plasma cortisol level (in micrograms per deciliter) increased 29% above baseline during performance of ESS and reached a maximum peak at T45 (12.6 [1.2]) compared with the control day (9.7 [1.1]), while prolactin levels did not change. The Visual Analog Anxiety Scale score, heart rate, blood pressure, and endocrine biomarkers of stress were not significantly modified during performance of ESS with a computer-assisted surgery system.

Conclusion: This study demonstrates for the first time that cardiovascular and anxiety changes during performance of ESS are not associated with increased levels of prototypical endocrine stress hormones.

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THE TERM STRESS WAS USED BY Hans Selye in 1936, who defined it as “the non-specific response of the body to any demand for change.”¹ However, modern concepts of stress are more complex and distinguish at least 2 broad categories of stressors, physical (systemic or reactive) and psychological (emotional or processing), with marked differential brain processing. When events or environmental demands exceed an individual's ability to cope, the ensuing psychological stress response typically includes negative thoughts and emotions.

Investigations of stress often use measures of negative mood that assess symp-

toms of general distress, anxiety, or depression. In addition, much attention has been paid to 2 physiological systems, the hypothalamus-pituitary-adrenocortical axis with the secretion of the glucocorticoid cortisol in humans and the sympathetic adrenomedullary system with the secretion of catecholamines (adrenaline and noradrenaline) and cardiovascular changes (ie, increase in heart rate [HR] and blood pressure [BP]). These 2 systems are important not only because of their involvement in pathologic consequences of stress (ie, depression, cardiovascular alterations, and suppression of the immune system) but also because they seem to reflect the intensity of stressful situations,

STUDY DESIGN

based on results of animal investigations. More precisely, exposure to emotionally stressful situations that differ in intensity has been found to cause gradual increases in plasma levels of corticotropin, glucocorticoids, and adrenaline, with an unclear response of noradrenaline level.² Plasma prolactin level also seems to be a good marker of stress intensity in animals.²

Similarly, exposure to emotional stressors has been reported to increase plasma levels of corticotropin, cortisol, adrenaline, and prolactin in humans exposed to acute laboratory stressors, such as mental arithmetic, Stroop Color-Word Conflict Test, public speaking, examinations, and simulated firefighting,³ as well as to more naturalistic stressors, such as apprehension before surgery,⁴ parachute jumping,⁵ or skydiving.⁶ Although little research has been performed among humans to demonstrate responses in these hormone levels to the intensity of emotionally stressful situations, it was demonstrated that anxiety generated by 2 different examinations among medical students was greater with the more difficult examination and that cortisol level and particularly prolactin level discriminated between the 2 examinations,⁷ corroborating results of animal investigations.

In the present work, we measured anxiety changes to evaluate stress response among surgeons. Ostensibly, surgeons are exposed to stressful situations because of constant mental strain and the fast tempo of thought process and action. However, clinical investigations have tended to evaluate procedures based on the advantages and disadvantages for patients or the complication rates of procedures rather than on the potential stress for surgeons, such as that encountered during complicated or high-risk surgical procedures. In studies^{8,9} that evaluated stress among surgeons, autonomic and cardiovascular measures were investigated. To our knowledge, only one study⁹ assessed classic neuroendocrine stress outcomes among surgeons during performance of surgery.

Endoscopic sinus surgery (ESS) has been identified as a source of potential high-risk and fatal complications, such as blindness, cerebrospinal fluid leak, ascending meningitis or brain abscess, and internal carotid artery injury.¹⁰ Therefore, ESS requires high concentration levels among surgeons. Depending on the site of surgery (eg, proximity to the anterior skull base, sphenoid sinus, or posterior ethmoid) or the amount of intraoperative bleeding (ie, reduced visibility), periods of variable and considerable tension during some operative procedures may arise for the surgeon. To date, these potentially stressful situations during ESS have not been evaluated. The use of a computer-assisted surgery system (CAS) during ESS has been shown to be an important aid to surgeons, enabling them to identify and confirm anatomical landmarks that are typically difficult to visualize during ESS.^{11,12}

Therefore, the objective of the present study was to compare the psychophysiological responses among novice surgeons during performance of ESS. We aimed to determine the degree to which high stress levels exist and whether psychophysiological responses differ during performance of ESS with or without CAS.

Fifteen fourth-year surgical residents or nonexpert surgeons in the Department of Otorhinolaryngology, Universitat de Barcelona, Barcelona, Spain, volunteered to participate in the study. For study inclusion, all volunteers had to have a normal score on the State-Trait Anxiety Inventory (STAI). To minimize potential variables, volunteers with a history of hypertension, coronary artery disease, diabetes mellitus, or affective disorder were not enrolled in the study. Because of the few female surgeons at our institution and because evidence on premenstrual syndrome demonstrates that women's normal hormone levels and anxiety sensitivity differ from those of men, women were also excluded from the study.¹³ All participants were right-handed, and each was familiar with ESS procedures, having attended at least 2 anatomical cadaver courses. Approval for this study was obtained from the Hospital Clinic of Barcelona ethics committee, and a signed informed consent form was obtained from all participants.

Preoperative activities were standardized to reduce external influences. Participants had at least 7 hours of rest the night before performing surgery, a light breakfast at 7 AM on the day of surgery, and only minor routine activities to do otherwise. Participants were requested to abstain from sexual intercourse, smoking, and alcohol or coffee consumption on the day before the test. All experimental steps were performed by the same investigator (I.A.) and nurse (S.C.). Experiments were performed at 11 AM to avoid potential influences of circadian rhythms on neuroendocrine biomarkers. Because there was a possibility that anxiety associated with venipuncture could affect the study results, the first blood sample was obtained half an hour after venipuncture. The catheter remained in the left antecubital vein during performance of ESS, covered by long-sleeved surgical scrubs to avoid visual and mental stress during blood sample extraction. The effects of mental strain in performing ESS were assessed at 30 minutes before (T - 30), at the beginning of (T0), at 15 minutes (T15) and 45 minutes (T45) during, and at 30 minutes after (T + 30) performance of ESS. For a nonexpert surgeon, 45 minutes of surgery was considered sufficient to perform basic ESS steps, such as middle meatal antrostomy and removal of anterior ethmoidal cells. All participants were randomized to perform ESS with CAS, to perform ESS without CAS, or to be evaluated on a nonsurgical or control day (surgeons knew that they were not going to operate on the control day).

STRESS VARIABLES

STAI Score

The STAI is a self-report scale developed to measure the following 2 separable components: state anxiety, which refers to a transitory emotional state characterized by subjective feelings of tension that may vary in intensity over time, and trait anxiety, which refers to a stable disposition to respond to stress with anxiety and a tendency to perceive a wider range of situations as threatening.¹⁴ The first 20 items of the scale (STAI Y-1) measure state anxiety by asking respondents how they feel right now. The STAI Y-1 evaluates apprehension, tension, nervousness, and worry that increase in response to physical danger and psychological stress. Respondents rate their feelings on a 4-point intensity scale (1 indicates almost never; 4, almost always). The next 20 items of the scale (STAI Y-2) measure trait anxiety by asking respondents how they generally feel. The STAI Y-2 is ideal for screening high school and college students and

military recruits for anxiety problems and for evaluating the immediate and long-term outcomes of psychotherapy, counseling, behavior modification, and drug treatment programs.^{15,16} The STAI has high internal consistency and validity and has been successfully used among surgical populations.¹⁷ The questionnaire was administered only once between 10 and 10:30 AM in the recovery unit adjacent to the operating room. Participants rated themselves on a 4-point frequency scale (1 indicates almost never; 4, almost always). Total scores were obtained by summing the value assigned to each response, with higher scores indicating more severe anxiety symptoms. All participants were asked to complete the STAI questionnaire before each study (ESS with CAS, ESS without CAS, or control day).

Visual Analog Anxiety Scale Score

The Visual Analog Anxiety Scale (VAAS) is a 10-cm numeric measure of anxiety ranging from none (score, 0) to maximum (score, 10).¹⁸ Participants were asked to rate their anxiety from 0 to 10 on the VAAS at T-30, T0, T15, T45, and T+30.

HR and BP

The HR and BP were recorded using an automated sphygmomanometer. They were assessed at T-30, T0, T15, T45, and T+30.

Endocrine Biomarkers of Stress

Blood samples were collected in plastic tubes containing edetic acid and were kept on ice until centrifugation for 10 minutes at 1000g. Obtained plasma was frozen at -80°C until analysis. Plasma cortisol and prolactin levels were determined by radioimmunoassay using commercial solid-phase kits (Coat-A-Count; Diagnostic Products Corporation, Los Angeles, California). All samples were processed using the same assay to avoid interassay variability. Intra-assay coefficients of variation were below 5% for cortisol and below 8% for prolactin, which were within the range of values for the samples analyzed.

STATISTICAL ANALYSIS

Data are given as the mean (SEM). Two-sided Wilcoxon matched-pair signed rank test was used to determine statistically significant differences. Comparison of endocrine biomarkers of stress and cardiovascular and anxiety changes was performed using the Mann-Whitney test. Correlation between variables was assessed using the Spearman product moment correlation coefficient. $P < .05$ was considered statistically significant.

RESULTS

Fifteen male novice surgeons (mean age, 34.0 [1.1] years) were included in the study. Participants were randomized to performed ESS with and without CAS in patients with nasal polyposis. Seven surgeons performed ESS on the right side of patients, while 8 surgeons performed ESS on the left side of patients.

STAI SCORE

Participants had no history of psychiatric disorders, and their mean STAI Y-2 score was 29.5 [0.5], which was within the normal range. Anxiety as measured by the STAI

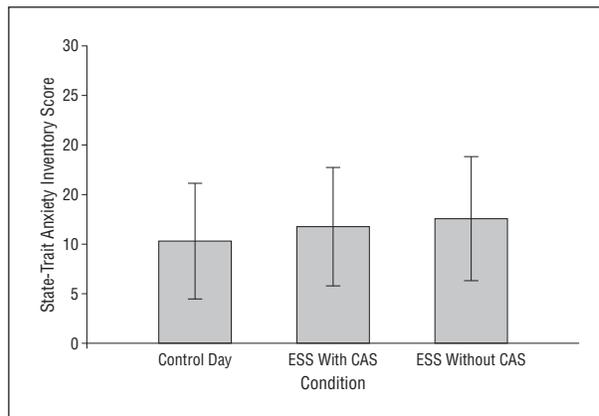


Figure 1. State-Trait Anxiety Inventory scores relative to study condition. CAS indicates computer-assisted surgery system; ESS, endoscopic sinus surgery.

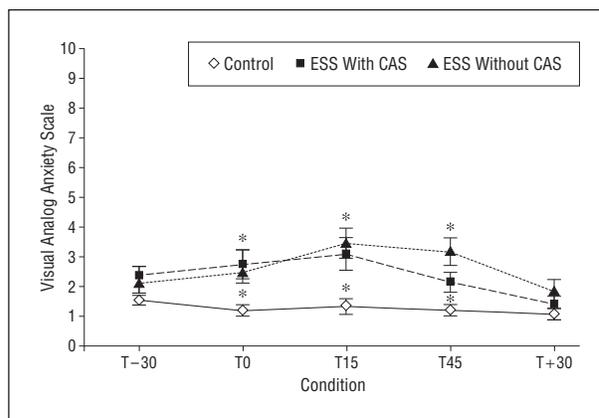


Figure 2. Visual Analog Anxiety Scale scores were assessed at 30 minutes before (T-30), at the beginning of (T0), at 15 minutes (T15) and 45 minutes (T45) during, and at 30 minutes after (T+30) surgery. CAS indicates computer-assisted surgery system; ESS, endoscopic sinus surgery. * $P < .05$ compared with the control (nonsurgical) day.

Y-1 score was not modified by the 3 experimental conditions (**Figure 1**). Baseline STAI Y-1 and STAI Y-2 scores were significantly correlated ($r=0.6$, $P < .03$).

VAAS SCORE

The mean VAAS score increased ($P < .05$) during ESS at T0 (2.45 [0.32]), T15 (3.46 [0.50]), and T45 (3.17 [0.46]) compared with the control day (1.19 [0.19], 1.32 [0.26], and 1.20 [0.19], respectively) These results are shown in **Figure 2**.

BP AND HR

The mean systolic BP (in millimeters of mercury) increased 6% above baseline ($P < .05$) during ESS at T0 (127 [2]), T15 (126 [3]), and T45 (125 [2]) compared with the control day (120 [3], 119 [4], and 116 [3], respectively) (**Figure 3A**). The mean diastolic BP (in millimeters of mercury) increased 7% above baseline during ESS at T0 (81 [2]), T15 (83 [2]), and T45 (82 [3]) compared with the control day (76 [2], 77 [3], and 76 [2], respectively) (**Figure 3B**). The mean HR (in beats per

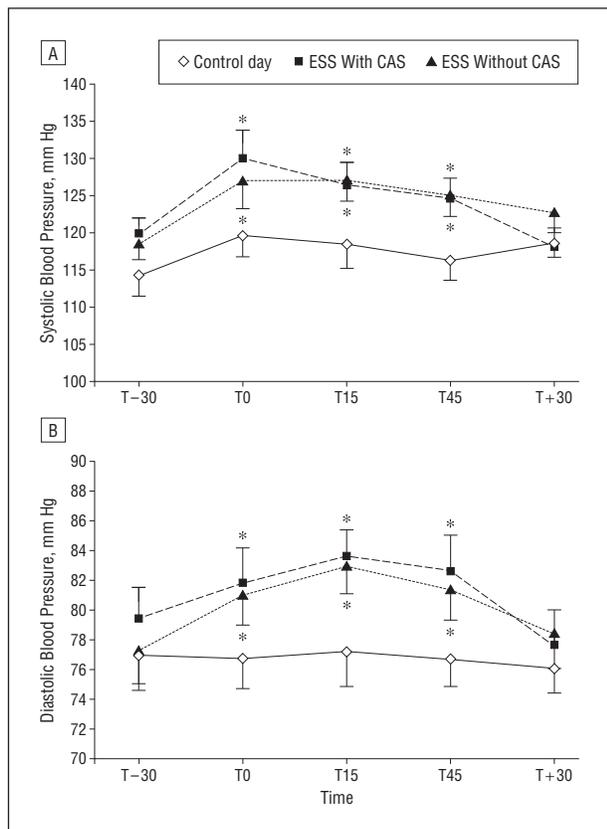


Figure 3. Systolic (A) and diastolic (B) blood pressures. Abbreviations are explained in Figure 2. * $P < .05$ compared with control (nonsurgical) day.

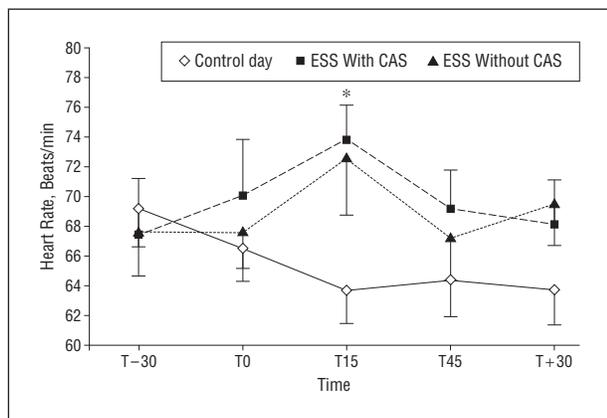


Figure 4. Heart rates. Abbreviations are explained in Figure 2. * $P < .05$ compared with control (nonsurgical) day.

minute) increased during ESS but was significant only at T15 (73 [4]) compared with the control day (64 [3]). The mean HR increased 16% above baseline at T15 (**Figure 4**).

ENDOCRINE BIOMARKERS OF STRESS

The mean plasma cortisol level (in micrograms per deciliter) increased 29% above baseline during performance of ESS and reached a maximum peak at T45 (12.6 [1.2]) compared with the control day (9.7 [1.1]) (to convert cortisol level to nanomoles per liter, multiply by 27.588)

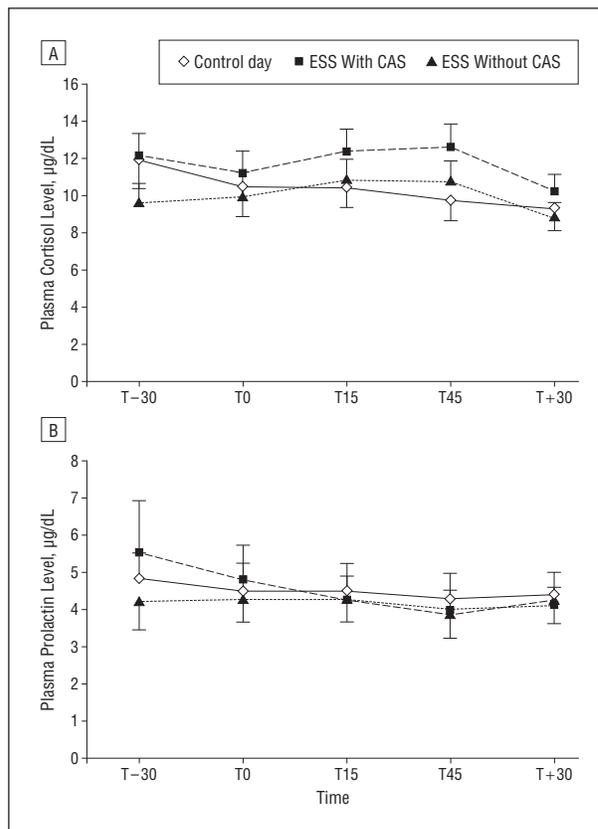


Figure 5. Plasma cortisol (A) and prolactin (B) levels. Abbreviations are explained in Figure 2. To convert cortisol to nanomoles per liter, multiply by 27.588; to convert prolactin to picomoles per liter, multiply by 43.478.

(**Figure 5A**), while the mean plasma prolactin level did not change (**Figure 5B**). The mean VAAS score, HR, BP, and endocrine biomarkers of stress were not significantly modified during performance of ESS with CAS.

COMMENT

To our knowledge, this is the first study to evaluate neuroendocrine responses among surgeons during performance of ESS. The main findings were significantly increased anxiety and sympathetic activity, as evaluated by the VAAS score, HR, and BP, with no significant alterations in well-characterized neuroendocrine biomarkers of stress, such as cortisol and prolactin levels. In addition, no differences were observed when ESS was performed with vs without CAS. The increase in sympathetic activity during performance of ESS may be related to general activation rather than to a high level of stress. The present data are compatible with the fact that surgeons are trained to activate sympathetic activity when faced with the demands of surgery, without allowing the situation to progress beyond their perceived capacities.

Novice surgeons were studied in the following 3 conditions: during performance of ESS with CAS, during performance of ESS without CAS, and on a nonsurgical day. When the 3 were compared, the 2 ESS conditions were associated with increased anxiety (as measured by the VAAS score) compared with the control condition immediately before and during performance of surgery. In-

creases of 6% to 7% in diastolic and systolic BPs were observed. The HR also increased up to 16% in both ESS conditions but only at T15 with a subsequent decline, despite continuing the surgery. Plasma cortisol levels increased 29% and reached maximum peaks at T45 compared with the control day, while plasma prolactin levels did not change.

In animal investigations, plasma levels of glucocorticoids and prolactin have been found to be good biological markers of stress intensity when measured at appropriate times with respect to the start of a stressful situation.² Similarly, among medical students anxiety-provoking situations, such as the immediate anticipation of an examination, increased plasma cortisol, prolactin, and glucose levels, with the prolactin level increase discriminating between the difficulty levels of 2 examinations.⁷ Heightened anxiety and increased cortisol and prolactin secretion occurred immediately before exposure to the situation. In another study¹⁹ comparing cardiovascular and hypothalamus-pituitary-adrenocortical responses to 2 different tasks (mental arithmetic and public speaking), both responses were greater for public speaking, again suggesting a similar relationship with stress intensity.

A possible explanation for the present results is that cardiovascular variables are more sensitive than cortisol and prolactin levels to low-intensity stressful situations. However, confirmation of this hypothesis would require studying emotionally stressful conditions of a similar nature but with graded intensity. In analyzing the existing studies in which cardiovascular responses to stressors have been evaluated together with cortisol or prolactin levels, both types of responses were correlated with cognitively demanding tasks,^{20,21} phobic anxiety,²² and parachute jumping.⁵ However, in studies^{23,24} involving mental arithmetic or public speaking stressors, increased HR and diastolic and systolic BPs were observed, with no changes in cortisol or prolactin levels, suggesting a lower sensitivity of neuroendocrine markers to stress. Richter et al⁵ reported increased HRs 30 minutes before a first-time tandem parachute jump and increased epinephrine levels during the jump, which normalized 20 minutes later. Using a continuous blood sampling technique, the authors demonstrated stress-induced increases in plasma concentrations of epinephrine, norepinephrine, cortisol, growth hormone, prolactin, and thyrotropin during and after the jump. Chatterton et al⁶ studied young men in their first skydiving jump and found that plasma luteinizing hormone levels were not suppressed and that anxiety and stress measures, as well as stress ratings of the event, rose to high levels just before the jump. Although testosterone levels remained low in their study, serum cortisol, prolactin, and growth hormone levels increased greatly after the rise in psychological measures of stress, reached peak values before or shortly after landing, and declined significantly within the next hour. Therefore, we cannot rule out that under our conditions the intensity of stress was sufficient to increase anxiety (as measured by the VAAS score) and cardiovascular variables but that they were of insufficient intensity to activate cortisol and prolactin release. Alternatively, anxiety (as measured by the VAAS

score) and cardiovascular variables may reflect physical and mental effort rather than stress.

Cardiovascular activation observed in the present study during performance of ESS is in accord with the findings of previous studies^{8,9} using different types of surgical interventions. Therefore, surgical performance is a potential source of stress for surgeons, although the degree of stress is greatly influenced by experience.²⁵ For instance, increases in HR and urinary adrenaline level during performance cataract surgery were inversely related to the degree of experience when the respondents were classified as inexperienced, intermediate, or experienced surgeons, with the response of the latter remaining almost unchanged throughout the procedure.⁸

Similarly, although changes in HR or salivary cortisol level were not observed among a group of cardiologists during cardiac catheterization,⁹ less experienced invasive cardiologists (n=6) had significantly higher mean STAI scores (38.4 vs 31.7), baseline salivary cortisol levels (0.51 vs 0.33), and HR changes (50.1 vs 27.4 beats/min) during procedures compared with more experienced invasive cardiologists (n=3), suggesting high levels of stress before performance of surgery. High serum cortisol levels have been reported in some surgeons during procedures, providing objective evidence of a high arousal state that may have long-term negative effects. For example, Swedish surgeons demonstrated a 2:1 greater risk of dying from ischemic heart disease than general practitioners; overall mental strain was greater among the surgeons, as was the inability to relax after work, perceived work tempo, and total number of work hours.²⁶ Therefore, it is important to determine factors that influence the degree of stress that surgeons may experience in their practice. Specific types of surgery with a higher demand of skill and anatomical knowledge and surgical procedures associated with potentially severe complications, such as ESS, may produce higher stress levels compared with simpler surgical procedures. To reduce the effect of training and experience, only novice surgeons were included in the present study. Navigational systems used during ESS are believed to reduce stress by facilitating identification and confirmation of anatomical landmarks, minimizing disorientation.¹² This study aimed to assess stress variables among residents performing ESS with and without CAS. Our data showed no difference in any endocrine biomarker of stress between the 2 procedures, despite the surgeons not having had significant experience in using CAS.

Little is known about the degree to which the mental effort is required to perform ESS and how this can contribute to anxiety and cardiovascular variables (HR and BP). In our study, these responses increased significantly during performance of surgery, especially when participants removed nasal polyps from ethmoidal cells reaching the skull base. However, neuroendocrine biomarkers (cortisol and prolactin levels) showed no significant changes at any time. Fatigue, difficulty of surgery, and type of anesthesia are proposed as possible causes of sympathetic arousal in the surgeon,²⁷ and endoscopic and laparoscopic techniques require greater concentration levels than open surgery, increasing mental stress.²⁸

A limitation of our study is that we did not evaluate HR variability. This is the best method of assessing mental strain and is more sensitive than measurement of HR alone.²⁹

In conclusion, our study demonstrates for the first time that cardiovascular and anxiety changes during performance of ESS are not associated with increased levels of prototypical endocrine stress hormones, such as cortisol and prolactin levels, suggesting low levels of stress during performance of the surgical procedure. Cardiovascular and anxiety alterations may reflect physical and mental effort rather than stress per se, but further study is needed to delineate both types of variables. The extent to which cardiovascular changes during an intervention in the absence of other classic neuroendocrine changes may affect the health of surgeons is unclear.

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Author Contributions: Drs Armario and Bernal-Sprekelsen contributed equally to this work, with senior responsibilities. Drs Alobid, de Pablo, Mullol, Parramon, and Armario had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Alobid, de Pablo, Mullol, Centellas, Parramon, Armario, and Bernal-Sprekelsen. *Acquisition of data:* Alobid, Centellas, and Carrasco. *Analysis and interpretation of data:* Alobid, de Pablo, Mullol, Parramon, Carrasco, and Armario. *Drafting of the manuscript:* Alobid, Mullol, Centellas, Carrasco, and Armario. *Critical revision of the manuscript for important intellectual content:* Alobid, de Pablo, Mullol, Parramon, Armario, and Bernal-Sprekelsen. *Statistical analysis:* Alobid. *Obtained funding:* Alobid, Mullol, Centellas, and Armario. *Administrative, technical, and material support:* Alobid, Mullol, Centellas, and Carrasco. *Study supervision:* Alobid, de Pablo, Mullol, Parramon, Armario, and Bernal-Sprekelsen.

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