

# Non-Invasive Stress Estimation in Simulative Endoscopy Setting: Literature Review

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## Abstract

One of the most common stressors is so-called “occupational stress.” It is defined as the sum of physical, mental and physiological responses to work in situations where the workload or stress associated with it intensifies for an extended period of time. It is a gradual process in which individual cognitive assessments of occupational stressors generate adverse health events and may lead to burnout. Since it has become a major problem in the medical field, studying, measuring and limiting it have been set as goals for the future.

We present a literature review on the topic of measuring stress using non-invasive means, such as cardiac indices measured through different devices, electrodermal activity, skin temperature, and salivary biomarkers. A virtual reality simulation could be used in conducting such experiments in order to provide a standardized environment with set variables for researchers to discern the most precise indices to be used in a real-life setting.

## Keywords

cardiac indices, salivary biomarkers, stress measurement, virtual reality simulators,

## INTRODUCTION

Stress is a biological and psychological reaction that people experience as they encounter challenges in life. Stress can be defined as a stability imbalance that occurs when a person perceives a situation or a task to be above their physical or mental resources.<sup>[1]</sup> Stressors can be divided into two major categories - physical (systemic or reactive) and psychological (emotional or processing).<sup>[2]</sup> One of the most common stressors is the so called “occupational stress”. It is defined as the sum of physical, mental and physiological responses to work in situations where the workload or stress associated with it intensifies for an extended period of time. It is a gradual process, in which individual cognitive assessments of occupational stressors generate adverse health

events and may lead to burnout.<sup>[3]</sup> Occupational stress has become an endemic problem in healthcare, with its prevalence among healthcare professionals ranging from 30% to 87%, depending on the country.<sup>[4]</sup>

For decades now, medical professionals have been trying to understand, quantify and measure the stress that medical doctors experience in their daily practice. Several objective and subjective stress indicators have been researched. While objective indicators are measured using different devices or bodily fluids, the subjective ones are in the form of tests. Saliva is a promising diagnostic alternative to blood in objective measurement of physiological and psychological stress.<sup>[5]</sup> Stress can be measured in the everyday medical practice as well as in a simulative setting. In contrast to the uniqueness of everyday work cases, virtual reality

simulation provides a certain standardization of situations that allows performances to be collated among and within participants, thus allowing us to quantify stress levels on different levels of experience.<sup>[6]</sup>

In the paper, we aim to review the literature on the subject of different stress indicators and their use in measuring stress in both real-life medical practice and virtual reality simulation.

## MATERIALS AND METHODS

A literature search up to July 2020 was carried out, including the following data bases: Medline, Google Scholar and Web of Science. The key phrases of this search were “salivary stress biomarkers/markers”, “stress-measuring devices”, “virtual simulation”, “endoscopy simulation”, “electro-dermal activity”, “skin temperature”, and “stress assessment tests”. 263 articles were found. Case reports, case series, and animal studies were excluded from analysis. Only articles written in English language were considered eligible. All articles were initially screened for title and abstract, and 52 eligible articles for full text reading were subsequently selected, of which 32 were included in this paper.

### Stress indices

On the subjective side of stress measurement, there are the stress-assessing tests with their most commonly used representatives: the Trier Social Stress Test (TSST) and the State Trait Anxiety Inventory (STAI). TSST is used to assess the stress response in human subjects that are placed in investigative setting. It is known to reliably increase hypothalamic-pituitary-adrenal axis activation.<sup>[7]</sup> It consists of an interview and solving mathematical problems for a limited amount of time.<sup>[8]</sup> The meta-analysis of Dickerson and Kemeny examining the tests and conditions that result in cortisol activation concludes that TSST is an appropriate tool for inducing and further studying of stress hormones.<sup>[9]</sup> STAI is a subjective tool for evaluating the quantity and quality of the stress that certain circumstances or case in the clinical practice induces. The questionnaire is completed at baseline and immediately after the challenge, and it is established that the higher the score, the greater the stress experienced. STAI is often combined and compared to other stress indices.<sup>[10]</sup>

The most common cardiac stress marker is heart rate variability (HRV). It is traditionally calculated by digital processing of electrocardiograms (ECG). The amount of time between consecutive heartbeats usually fluctuates so slightly that these fluctuations can only be measured with specific devices. HRV portrays those variations in consecutive R-R intervals. In recent times, with the technological development of modern devices for measuring cardiac indices, HRV has become a very sensitive indicator for dysregulation of the autonomic tone.<sup>[11]</sup> The accumulation of chronic stress has been associated with a predominance

of sympathetic activity, resulting in reduced HRV and reduced parasympathetic modulation.<sup>[12]</sup> In a systematic review regarding HRV as an index of work stress, emergency physicians’ data analysis showed that subjects had a higher intraoperative HR and a low expression of HRV.<sup>[13]</sup>

Eccrine glands on the hairy skin are activated by heat, as opposed to the ones found on the glabrous skin of the hands and feet, which are triggered by deep respiration, mental stress, and tactile stimulation. As these processes are dictated by autonomic stimuli, the result in shifts of electrodermal conductivity and electrodermal activity (EDA) is measured. The so called “emotional sweating” has been studied in order to be used in the assessment of sympathetic function and limbic activity.<sup>[14]</sup>

In the Villanueva et al. study, the electrodermal activity of students was measured before and after an exam session. The session consisted of writing a self-report on one’s academic achievements, accompanied by an interview. Before, during the sessions, and shortly after them, the students wore devices that estimated EDA, and salivary biomarkers (cortisol, estradiol, progesterone, testosterone, and DHEA-S) were collected. Both methods showed that stress elevation was unrelated to the exam type, but EDA increased during both emotional activation and recollection of data.<sup>[15]</sup>

Moreover, acute stress induces thermogenesis on the base of sympathetic nervous system (SNS) activation. Studies show that the hyperthermia is proportional to the intensity of the stressor.<sup>[16]</sup> Initially, the measurement of skin temperature was performed via contact devices. Nowadays, infrared thermography (IRT) offers a non-contact way of assessing skin temperature that presents an alternative to conductive devices, ensuring maximum comfort for test subjects.<sup>[17]</sup> In a test study with fifteen male participants, Engert et al. used IRT and established stress markers (HR, HRV, finger temperature, sAA, and sC) to assess stress during the cold pressor test and the TSST. In the study, thermal imaging of the face was performed and was found to correlate with mood changes rather than with stress. A weak correlation between IRT results and the other stress markers was established.<sup>[18]</sup>

### Salivary stress biomarkers

Saliva is a promising diagnostic fluid in stress measurement for many reasons, the main one being that its collection is noninvasive and causes no additional distress to the subjects. It can be collected at short intervals of time. Moreover, obtaining saliva does not require trained health care professionals or specific medical equipment and is estimated to be almost 50% cheaper than blood collection.<sup>[5,19]</sup> Salivary levels of cortisol, alpha-amylase, secretory immunoglobulin A and chromogranin A have been associated with stress state.

Salivary cortisol (sC) is the most studied stress marker of the above-mentioned and is widely considered as a valid indicator of free cortisol and the hypothalamus-pituitary-adrenocortical-axis.<sup>[20]</sup> Research indicates that the increase in sC

levels occurs 5 minutes after the increase in plasma cortisol, peaking 31 to 40 minutes after stressor onset. Furthermore, there is a strong correlation between sC levels and plasma cortisol concentrations.<sup>[21]</sup> In a study of 38 army nurses exposed to a combat, casualty simulation data showed that an increase in cortisol levels was observed for the majority of the army nurses, who showed an average increase of 136% for cortisol over baseline levels. In this study, salivary cortisol remained elevated over baseline levels 30 minutes after the conclusion of the task.<sup>[22]</sup> Moreover, medical students' salivary cortisol levels showed elevation during an ambulatory and in hospital patient consultation.<sup>[23]</sup>

Salivary chromogranin A (sCgA) has been known to greatly react to psychosomatic as well as academic assessment stress.<sup>[24]</sup> Kanamaru et al. found a rapid increase in sCgA levels in 14 airplane pilots from before a cognitive test, within the test, and 20 minutes after its start. They found that sCgA secretion increased in the anticipation of the task, remained high during, and was still elevated after it.<sup>[25]</sup> On the other hand, Nomura et al. found that sCgA concentration increased during arithmetic tasks and decreased shortly after them, thus illustrating the value of sCgA as a biomarker for a short-term cognitive stress.<sup>[26]</sup>

Salivary immunoglobulin A (sIgA) levels are known to show inconsistent results when it comes to stress reactions. A study analyzed the sC and sIgA levels in saliva and cardiac indices heart rate and systolic blood pressure in three groups of oral surgeons (senior, experts and junior) while they performed operations of different levels of difficulty. sIgA variations were not significant in any of the groups examined and did not show collinearity with the sC or the cardiac indices.<sup>[2]</sup>

Salivary alpha-amylase (sAA) is the least studied of the aforementioned biomarkers. In a study of 30 male subjects being submitted to TSST and speaking in front of an audience, sAA was found to correlate with plasma catecholamine levels. Results showed sAA to be sensitive to psychological stress and to have positive relationship with the sympathetic activity.<sup>[27]</sup>

## Endoscopy simulation

Simulation training is a well-established method that provides standardized environment with set variable for educational purposes as well as for research.<sup>[28]</sup> It is assumed that a high-fidelity simulator can replicate real-life cases and duplicate the stress experienced by the operators. This way, trainees can experience multiple critical situations and perform diagnostic and therapeutic techniques as many times as needed without the risk of harming the patient, resulting in lower stress levels after their training.<sup>[29,30]</sup> There are four types of endoscopic simulators: mechanical, ex vivo animal tissue models, live animal-based models, and virtual reality (VR) computer simulators.<sup>[31]</sup> In our literature review, we focus solely on the virtual reality computer simulators. Although, the majority of clinical trials revolving around the validity of virtual simulation as an education method,

are performed in the field of surgery, there are a number of studies that incorporate endoscopy training.

VR simulators provide objective measures of performance, such as procedural completion and other endpoints such as the extent to which the lumen was visualized. Additionally, a summary describing several other performance parameters including the total time of the examination, recognition of pathologic findings, the amount of air insufflation, the degree of patient discomfort, the use of a virtual attending physician, and ability to perform retroflexion or other therapeutic maneuvers is presented at the end of the procedure. This allows for customization of benchmarks to define competency assessment.<sup>[32]</sup>

## CONCLUSION

The goal of understanding and quantifying stress in order to find the means to reduce it has been around for decades. With the technology advancement, the means for measuring it have increased exponentially. The cardiac indices, electrodermal activity, and salivary biomarkers show great potential in this field. Moreover, the simulative setting presents a standardized environment in which stress can be caused and used to improve the performance of certain individuals in a safe way. To truly comprehend the level of stress that medical professionals encounter on a daily basis, more research involving sizable subject cohorts is required.

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# Неинвазивная оценка стресса в условиях имитационной эндоскопии: обзор литературы

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## Резюме

Одним из наиболее распространённых стрессоров является так называемый „профессиональный стресс“. Он определяется как сумма физических, психических и физиологических реакций на работу в ситуациях, когда связанная с ней рабочая нагрузка или стресс усиливаются в течение длительного периода времени. Это постепенный процесс, в ходе которого индивидуальная когнитивная оценка факторов профессионального стресса приводит к неблагоприятным последствиям для здоровья и может привести к выгоранию. Поскольку это стало серьёзной проблемой в области медицины, его изучение, измерение и ограничение были поставлены в качестве целей на будущее.

Мы представляем обзор литературы по теме измерения стресса с использованием неинвазивных средств, таких как сердечные показатели, измеряемые с помощью различных устройств, электродермальная активность, температура кожи и биомаркеры слюны. При проведении таких экспериментов можно использовать моделирование виртуальной реальности, чтобы предоставить исследователям стандартизированную среду с заданными переменными, позволяющую исследователям определить наиболее точные показатели, которые будут использоваться в реальных условиях.

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## Ключевые слова

сердечные показатели, биомаркеры слюны, измерение стресса, симуляторы виртуальной реальности,

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