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A systematic review of biological changes in surgeons' acute stress levels during surgery

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ABSTRACT

Background: While a degree of stress facilitates learning and task performance, excessive stress in surgeons may lead to poor patient outcomes, with maladaptive stress as a risk factor for surgeon burnout or self-harm through mechanisms including substance abuse, and suicide. We aim to systematically review publications investigating how measures of surgeons' acute biological stress change during surgery.

Methods: Medline, Embase, Cochrane library, and The United States, Australian, and European clinical trials registries were searched using the terms stress; surgeon; cortisol; skin conductance; and heart rate. Studies had to report at least one measure of biological stress related to surgery or simulated surgical exercise and have been published between January 1996 to June 2022.

Results: Twenty-eight studies with a total of 433 participants met inclusion criteria with cortisol, heart rate, heart rate variability, and electrodermal activity being reported. Salivary cortisol was measured in four studies with conflicting directional changes reported. Mean heart rate increased in nine studies (by 6-22 beats/minute), however the impact of the physical work of surgery was not reported. Heart rate variability, as measured by low-frequency to high-frequency ratio, was significantly increased in three of six studies. One study measured electrodermal activity reporting significant increase in skin conductance in a simulation setting.

Conclusion: While some biological measures appear able to detect changes in acute stress in surgeons (particularly heart rate), appropriate measures of stress during non-stressful and stressful surgery are yet to be fully identified. Importantly, there are no current pathways for identifying surgeons at risk of burnout or self-harm and this is a critical unmet research need.

Introduction

'Stress' is a common occurrence in many areas of medicine [1] with physicians exposed to a number of systemic workplace stressors [2,3]. Although some stressors likely affect medical specialties equally, surgeons are subject to intraoperative stressors such as bleeding, operative complications, and equipment problems [4] which may cause high physiological and psychological stress states [5–7]. Despite ongoing work on reducing overall physician stress and burnout [8,9], the difference in workplace stressors may explain the higher rates of burnout amongst surgeons compared to non-surgical physicians [10,11]. Acute stress is necessary to facilitate task performance and learning [2,12], however, very frequent or extreme stress negatively affects cognitive processes, such as memory and attention, and performance of complex motor skills [13,14]. These maladaptive responses then impact patient safety in addition to increased surgeon burnout, job turnover, early retirement, depression, substance abuse, and suicide [10,14–17].

Recognising the threshold between stress states that facilitate or impair surgeons' performance is vital to programs of surgeon wellbeing. Changes in cortisol [18], urinary interleukins [19] and heart rate [20] have been measured in health professionals and may reflect a response to working conditions. Currently, there is little clarity about which biological measures detect intraoperative stress in surgeons, and how acute stress affects surgical performance.

The primary aim of this review is to assess how surgeons' acute stress levels change during surgery, as reflected by biological measures, with

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secondary aims to identify factors that influence surgeons' acute stress levels during surgery.

Methods

The protocol for this systematic review was published with PROSPERO (CRD42020156960). A literature search was performed using Medline, Embase, and the Cochrane library for relevant articles using the terms: ["stress" OR "anxiety"] AND ["doctor" OR "surgeon"] AND ["cortisol" OR "skin conductance" OR "heart rate variability" OR "heart rate"]. Studies were limited to publication from January 1996 to October 2021. The United States Clinical Trials (https://clinicaltrials.gov), Australia and New Zealand Clinical Trial registry (www.anzctr.org.au), and European Clinical Trials registries (https://www.clinicaltrialsregister.eu) were searched for current trials using the same terms. Results were screened for duplicates and the abstracts of appropriate titles were further screened by two authors (AB, SS) to identify full articles for inclusion in the review. Discrepancies in article inclusions for the review between the two authors were resolved by a third author (JA). The reference list of all full text articles was further screened for any additional articles not previously identified.

Inclusion criteria included publications in English, conducted in surgeons, and reporting at least one physiological measure of stress during live or simulated surgery. Both comparative and non-comparative studies were considered. Exclusion criteria were those not in humans or not defining the conditions where stress was measured.

Data were collected on a pre-specified template. Timing of biological sample collection referenced to the surgical procedure or simulation was recorded and notation made where multiple measures were collected at different time intervals. Where a comparative study was assessed, biological measures were recorded by their respective intervention or comparator group. Included studies were assessed for risk of bias using the Cochrane risk of bias tool [21] for randomised trials and the Newcastle-Ottawa scale [22] for non-randomised studies.

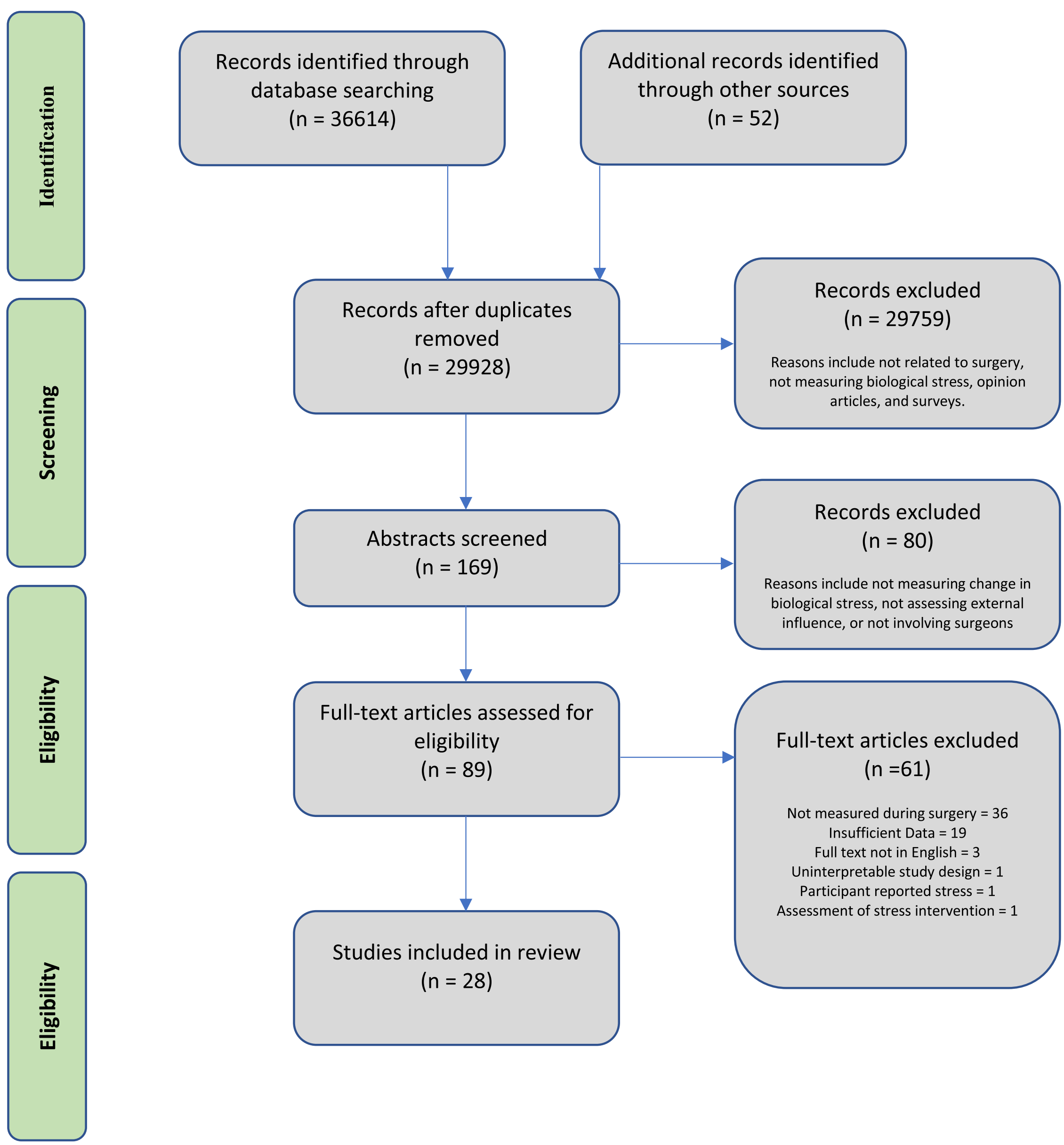

Fig. 1. PRISMA Diagram.

Results

Search results are presented in the PRISMA diagram in Fig. 1. Twenty-eight studies with a total of 433 participants were included. Reported biological measures included salivary cortisol, heart rate (HR) maximum, HR mean, indices of heart rate variability (HRV) (proportion of beat-to-beat measures more than 50ms apart, standard deviation of beat-to-beat variability, root mean square of the standard deviation of beat-to-beat variability, and low-frequency to high-frequency ratio) and electrodermal activity in live and/or simulated surgery. Table 1 summarises the measures included in this review. Tables 2 and 3 summarise the risk of bias for randomised and non-randomised included studies respectively. Tables 4 and 5 summarise the results of the included trials for each of the biological measures identified, separated by whether measures were assessed during live or simulated surgery.

How do surgeons' acute stress levels change during an operation, as measured by biological stress measures?

Fifteen studies involving 263 participants investigated the change in biological measures of stress from baseline to during either live surgery or simulated surgical exercises. Reported measures include salivary cortisol, mean HR, HRV, and skin conductance changes [23–37].

Change in salivary cortisol was reported by four studies (Table 4). The studies were of low quality and there was considerable variation in the frequency and timing of comparative salivary cortisol measurements with respect to surgery or simulation. A single study undertaken during live endoscopic surgery with small sample size [23] reported an increase in salivary cortisol from baseline to 45 min intraoperatively. In three simulation studies [26,28,29], post simulation measure of cortisol ranged from immediately to 30 min after completion of the exercise, with no significant changes in cortisol demonstrated in any study.

Changes in HR were reported in nine studies (Table 4) involving between 6-75 participants conducting general, neurological, orthopaedic, and gynaecological surgical procedures. Mean HR was elevated in all studies by 6 to 22 beats per minute during the procedure relative to baseline, however, one study reported intraoperative mean HR referenced to 30 min postoperatively [24] where all other used preoperative HR as a baseline. None of the identified studies accounted for changes in HR due to specific activities or physical workload. In contrast to their salivary cortisol findings, mean HR was demonstrated to significantly increase during simulated endoscopic exercises in medical students [26] with a reduction in that increase as students progressed their training over the four simulations.

HRV changes from baseline to during surgery were reported in eight studies (Table 5). While all studies reported the frequency domains of HRV, two studies reported only descriptive results of change in the low-frequency to high-frequency ratio (LF:HF ratio) [34,38]. Only two studies [35,36] reported on measures of HRV in the time domain. The proportion of beat-to-beat measures more than 50ms apart (pNN50) was not reported by any of the studies. The standard deviation of beat-to-beat (SDNN) was reported by two live surgery studies. In the larger study of 20 surgeons [35], there was a significant decrease from baseline to during surgery of SDNN as well as the root mean square of SDNN (rMSSD). A small study of two participants [36] performing a mastoidectomy and facial nerve dissection reported the decrease in SDNN from baseline did not reach significance during mastoidectomy but did continue to decrease during the dissection of the facial nerve to be significantly lower than baseline. The frequency domain of HRV was reported by all studies with no difference in LF:HF ratio from baseline to during surgery or simulation reported in three studies [26,31,36]. In

Table 1
Summary of Biological Markers of Acute Stress.

Marker of Stress	Unit of Measure	Reaction to Stressor	Timing
Cortisol	Nanomole per litre (nmol/L)	Slow response – requires release of adrenocorticotropin to increase secretion of glucocorticoids.	Appears within 15 min of a stressor. Half-life of 30–90 min.
Heart Rate (maximum)	Beats per minute (bpm)	Activation of sympathetic nervous system transmits signals to adrenal medulla to release catecholamines which increases heart rate.	Earliest response to stressors. Measures a single moment in time. Half-life of catecholamines is approximately two minutes in the circulation leading to quick return to baseline.
Heart Rate (mean)	Beats per minute (bpm)	Heart rate changes over time reflecting sympathetic and para-sympathetic balance.	Approximates sympathetic stimulation over time. Higher mean heart rate reflecting increased sympathetic nervous system stimulation.
Heart Rate Variability (HRV):	This is the oscillation in time between interval consecutive heart beats and is an indicator of sympathovagal balance. Reduced HRV is associated with increased sympathetic activity with a number of methods described to report HRV in time and frequency domains.		
Proportion of beat-to-beat variability greater than 50ms (pNN50)	Measured as a percentage, this is the proportion of beat-to-beat intervals greater than 50ms apart divided by total beat to beat intervals.	A lower pNN50 reflects greater sympathetic stimulation and greater reaction to stressors.	Measures interval differences in the beat-to-beat variation of the heart rate over longer periods of time than mean heart rate.
Standard deviation of beat-to-beat variability (SDNN)	Measured in milliseconds (ms), this is the standard deviation of beat-to-beat intervals	A higher SDNN reflects greater parasympathetic activity and less reaction to stressors.	Measurements of short-term variation are used to estimate high-frequency variations.
Root mean square of the standard deviation (rMSSD)	Measured in milliseconds (ms), this reflects the beat-to-beat variance in the heart rate	A lower rMSSD reflects greater sympathetic stimulation and greater reaction to stressors.	
Low-Frequency to High-Frequency Ratio (LF:HF Ratio)	Reported as a ratio of low-frequency (ms^2) to high-frequency (ms^2) variances in heart rate.	Increased low frequency variance and decreased high frequency variance occurs in response to a stressor.	Represents short term recordings of sympathovagal balance. Reflects the persistence of a stressor over time.
Electrodermal Activity	MicroSiemens (μS)	Sympathetic activity increases sweat gland activity which then increases skin conductance.	Early response to a stressor. Requires persistent stimulation to sweat glands to measure stress over time.

Table 2
Risk of Bias in Randomized Studies.

Study	Random sequence generation	Allocation concealment	Blinding participants and personnel	Blinding outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall
Abdelrahman 2016	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Alobid 2011	High risk	High risk	High risk	Low risk	Low risk	Low risk	High risk	High risk
Heemskerk 2014	High risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Moore 2015	High risk	High Risk	High risk	High risk	Low risk	Low risk	Low Risk	High Risk
Theodoraki 2015	Low risk	Unclear risk	Unclear/ Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Table 3
Risk of Bias in Non-Randomized Studies.

Study	Selection Representative of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability Controls for most important factor	Controls for additional factor	Outcome Assessment of outcome	Follow-up long enough for outcomes	Adequacy of follow-up	Overall
Bergovec 2008	Y	N/A	Y	Y	Y	Y	Y	Y	N/A	7/7
Berguer 2001	N	N/A	Y	Y	N	N	Y	N/A	N/A	3/6
Berguer 2006	N	N/A	Y	N	N	N	Y	Y	N/A	3/7
Bohm 2001	N	N	Y	Y	N	Y	Y	Y	Y	6/9
Crewther 2015	N	N/A	Y	Y	Y	Y	N	Y	N/A	5/7
Dedmon 2019	N	N/A	Y	Y	N	Y	Y	Y	N/A	5/7
Ducarme 2015	Y	N/A	Y	Y	Y	Y	Y	Y	N/A	6/6
Hubert 2013	Y	Y	Y	N	N	N	Y	Y	N/A	5/8
Hurley 2015	N	N/A	Y	Y	Y	Y	Y	Y	N/A	6/7
James 2011	N	Y	Y	Y	N	Y	Y	Y	N/A	6/8
Jones 2015	Y	N/A	Y	Y	N	Y	Y	Y	N/A	6/7
Jukes 2017	Y	N/A	Y	Y	N	Y	Y	N/A	N/A	5/6
Klein 2010	Y	N/A	Y	N	N	Y	Y	N/A	N/A	4/6
Kuhn 2013	Y	N/A	Y	Y	N	Y	Y	N/A	N/A	5/6
Lowndes 2019	Y	Y	Y	N	Y	N	Y	Y	Y	7/9
Marrelli 2014	N	Y	Y	Y	N	N	Y	N/A	N/A	4/7
Payne 1985	Y	N/A	Y	Y	Y	N	Y	N/A	N/A	5/6
Prichard 2012	Y	N/A	Y	Y	N	Y	Y	N/A	N/A	5/6
Song 2009	N	N/A	Y	N	N	N	Y	N/A	N/A	2/6
Weenk 2017	Y	N/A	Y	Y	Y	N	Y	N/A	N/A	5/6
Yamanouchi 2015	N	N/A	Y	Y	N	Y	Y	N/A	N/A	4/6

contrast, an increased LF:HF ratio was demonstrated in the other three studies [30,33,35], although, in one of these studies, only one of the two participants had a significant change in LF:HF ratio [33]. Of the two studies that reported SDNN, a corresponding increase in the LF:HF ratio was only reported in the larger study.

A single study of surgical simulation measured changes of electrodermal activity (Table 4) from baseline to during a simulated knot tying task for 28 surgeons [25]. A significant increase in skin conductance during the simulated task was reported but not skin conductance times with the study at moderate risk of bias.

What factors influence surgeons' acute stress levels during surgery?

A summary of findings of acute stress differences under different external influences is presented in Fig. 2. This includes difference in acute stress based on the type of surgery, environment stressors, role in surgery, and surgical experience.

Type of surgery

The difference in biological measures of stress between two surgical techniques was the most common potential influencing factor studied. We identified 10 studies [23,25,28,37–44] including 121 participants measuring salivary cortisol, mean HR, HRV, and skin conductance in live and simulated surgical environments.

Measures of salivary cortisol were reported in three studies (Table 4). In two trials comparing single-port to conventional four-port laparoscopic cholecystectomy [39,42], higher intraoperative cortisol in the single-port group was reported. Cortisol values, tests of significance and pre-surgery confounders were not reported. The third study in this group reported no differences when performing a 4.5 min task via robotic assisted laparoscopic surgery versus standard four-port laparoscopic surgery [28].

HR was measured in eight studies (Table 4) comparing one surgical technique to another.

Maximum HR was significantly higher during single incision laparoscopic cholecystectomy compared to conventional four-port laparoscopy [39]. Two trials comparing robotic versus conventional laparoscopic cholecystectomy both demonstrated higher mean HR during laparoscopic surgery but neither assessed changed from baseline. In addition, one study involved just two participants [41]. In the second study, the authors reported an increase in physical activity of the trapezius and dorso-lumbar muscles during conventional laparoscopy [43] but did not draw direct conclusions to HR. Three simulation studies compared robotic and conventional laparoscopy with conflicting results. In a randomised trial of 32 surgeons [44], mean HR from baseline to during the task was higher in the robotic approach compared with the conventional approach. Conversely, a cross-over study of 16 medical students [28] reported higher mean HR in the conventional group and a smaller cross-over study of 10 participants [40] found no difference between groups. In the remaining two studies [23,37], no difference in mean HR change was reported when assessing the impact of computer aids in ENT surgery.

Three studies assessed changes of HRV based on surgical technique [37,38,41]. Two small randomised trials assessed the difference between conventional and laparoscopic [38] or laparoscopic and robotic-assisted surgery [41] with only two surgeons participating in each. They both reported an increased LF:HF ratio however one involved surgeons of different seniority and experience and the second used an uneven distribution of surgical techniques between surgeons [41]. The third study randomised 10 surgeons allocated to computer aided navigation or no navigation during ENT surgery [37] with reported no difference in LF:HF ratio.

Three studies of simulated surgical tasks assessed electrodermal activity differences between two types of surgical approach (Table 4). Two studies measured palmar skin conductance with one study showing no difference during simulated tasks between conventional and robotic-assisted laparoscopy [40]. In the second study, skin conductance significantly increased from rest to simulated task but no difference identified when comparing open versus endoscopic knot tying [25]. The third trial measured skin conductance of the foot with significantly higher conductance during conventional laparoscopic simulated exercises compared to robotic-assisted laparoscopy [28].

Environmental factors

Three studies were identified that assessed environmental stress including ergonomics, time pressure, and types of vascular injury. In a study of 10 surgeons performing laparoscopic cholecystectomy [45] with a single monitor in poor position versus dual monitors in ideal line

Table 4
Studies measuring Salivary Cortisol, Heart Rate, and Skin Conductance.

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
SALIVARY CORTISOL *Live Surgical Environment*						
Lowndes 2019	Randomized trial	1 senior surgeon 9 trainee surgeons 48 Laparoscopic cholecystectomies	*Surgical Approach* Single port laparoscopy versus conventional 4 port laparoscopy	Pre-operatively Intra-operative (cystic duct and artery clipping) Post-operative (final suture)	Intra-op cortisol significantly higher in single port versus 4 port for senior surgeon ($p < 0.01$). No difference in trainees	No absolute cortisol data provided No record of change from baseline to intra-operative
Abdelrahman 2016	Randomized Trial	1 surgeon 48 procedures	*Surgical Approach* Single-incision laparoscopic cholecystectomy (SILC) vs. conventional lap chole (CLC)	Pre-operatively Intra-operative (cystic duct and artery clipping) Post-operative (final suture)	*Pre-operative:* No difference Intra-operative: 41.25% higher in SILC vs. CLC ($p < 0.05$) Post-operative: Higher in SILC vs. CLC ($p = 0.02$), cortisol values not reported	No comparison of baseline to intra- or post-operative period Absolute values of cortisol not provided Intra-operative time point of measure unlikely to reflect source of stress.
Alobid 2011	Randomized Trial	15 novice surgeons	*Determine Change* Performance of endoscopic nasal surgery with vs. without computer aid vs. a "control" day	30 min prior to surgery Beginning of surgery Intra-operatively (15 min) Intra-operatively (45 min) 30 min after.	increase from baseline to 45 min intra-operative period (9.7 vs 12.6, no p value) Increased 45 min during surgery versus control day (no data or p values)	Cortisol peaked at intra-operative 45 min time point No data values or statistics given "Control" day = no surgery

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Table 4 (*continued*)

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
Marrelli 2014	Case-control	15 surgeons: 5 senior (> 10yr experience) 5 expert (5-10yrs) 5 junior (<5yrs)	*Surgical Experience*	T1 Morning: (7:30-8am) T2 Intra-op T3 2 h Post-op	No data provided. Descriptive results Easy procedure: T1 Significantly higher in expert than senior and junior T2 Non-significant rise in expert surgeons T3 Significant increase in junior surgeons Difficult procedure: Junior surgeon high cortisol at all time points	Surgery all between 10am and 1pm Insufficient data provided
Arora 2010	Cohort	11 surgeons, mixed specialties	*Surgeon reported stress* Surgeon stress (defined by increased in STAI) vs. non-stress	Immediately Pre-operatively Immediately post-operatively	Pre-operative "stressed" = 4.83 mmol/L vs. "non-stressed" 6.00 nmol/L ($p > 0.05$) Post-operative "stressed" = 6.53 mmol/L vs. "non-stressed" 4.26 nmol/L ($p > 0.05$)	No analysis of change from baseline to post-operative STAI* determine "stressful" surgeries Post-operative cortisol correlated with mean and maximum heart rate changes
Simulated Surgical Environment						
Wetzel 2011	Randomized Trial	16 surgeons	*Stress reduction intervention* 2 simulated carotid endarterectomy, having received stress training or not	5 min prior to simulation immediately after 10 min after	Cortisol difference from baseline to simulation not reported. No difference between 1st and 2nd simulation	Unclear if simulations performed on same day.
Crewther 2015	Cohort	12 medical students	*Determine Change Surgical Experience* Simulated intra-corporeal suturing and knot tying over 4 sessions: BASE, MID, POST, & RETEST	5 min prior to exercise 10 min after	Pre- to post-exercise: Increased at BASE but decrease in MID, POST, and RETEST (nil significant change) BASE to other session: No effect seen (X^2 (3) = 4.19, p = 0.241)	Small number of participants Time of day exercises 3-7pm

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Table 4 (*continued*)

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
Hurley 2015	Cross-over	16 medical students completing 4 tasks	*Determine Change* *Surgical Approach* Robotic assisted laparoscopy surgery (RALS) vs. standard laparoscopy surgery (SLS)	Start of task End of task (30 min) 15 min post task 30 min post task	Mean change in cortisol from baseline to post-surgery: No difference between SLS and RALS (17.1 vs 8.19, $p = 0.73$)	All session performed in the afternoon between 2 and 7pm No discussion of length of time of tasks
James 2011	Cohort	29 male surgeons and trainees	*Determine Change* Performance of a simulated colonoscopy to reach pre-defined targets: Novice vs. surgeon	Immediately after consent to exercise Immediately after completion	Mean change in cortisol from baseline to post-exercise: No difference in either novices or surgeons	No absolute numbers provided Correlation with heart rate and STAI below
HEART RATE *Live Surgery*						
Abdelrahman 2016	RCT	1 specialist surgeon 48 procedures	*Surgical Approach* Single-incision laparoscopic cholecystectomy vs. conventional laparoscopic cholecystectomy	Maximum heart rate (HR): Pre-operatively Intra-operative (cystic duct and artery clipping), Post-operative (final suture)	Maximum HR in all procedures 5.74% lower post-op vs. intra-op (p=0.02) Maximum HR intra-op 13.74% higher in SILC vs. CLC (p=0.038)	No reports of change from baseline No absolute data presented
Theodoraki 2015	RCT	10 surgeons (2 specialists, 8 trainees)	*Determine Change* *Surgical Approach* Use of computer navigation in ENT surgery vs. no navigation	Continuous heart rate monitoring during surgery	Mean HR during surgery vs. baseline 98 vs. 92, p not reported Mean HR computer aid vs. not aided 98 vs. 97, $p = 0.569$	
Heemskerk 2014	RCT	2 surgeons	*Surgical Approach* Laparoscopic Cholecystectomy (CC) vs. robot-assisted laparoscopic cholecystectomy (RC)	Bipolar ECG, sampled in 5 min segments 7 defined stages during surgery: 1. Baseline 2. Insertion of trocar 3. Calot's triangle 4. Cystic duct and artery 5. Dissection of gallbladder 6. Removal of gallbladder 7. Closure	Lower mean HR in CC vs. RC at each defined stage except baseline (all p<0.001): 2- 82.7 vs 89.2, 3- 78.7 vs. 92.8, 4 - 75.7 vs. 97.2, 5 - 75.3 vs. 96.2. 6 - 76.6 vs. 95.6, 7- 79.3 vs. 91.3	Small number of surgeons
Alobid 2011	RCT	15 novice surgeons	*Determine Change* *Surgical Approach* Performance of endoscopic nasal surgery (ESS) with vs. without computer aid vs. "control" day	Mean heart rate 30 min prior to surgery Beginning of surgery Intra-operatively (15 min)	Significantly higher Intra-operative (15 min) in ESS vs. control: 73 vs. 64 ($p <$	Study controlled for sleep, alcohol, coffee, and intercourse from might prior to morning of study.

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Table 4 (*continued*)

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
				Intra-operatively (45 min) 30 min after.	0.05) Nil other significant difference between groups or at other time points	
Dedmon 2019	Cohort	2 neurology fellows	*Determine Change*	Continuous ECG during: Rest Pre-operative Intra-operative	Increased mean HR during surgery vs. baseline (88.8 vs. 66.1m $P < 0.01$)	
Weenk 2017	Cohort	5 specialists 7 fellows 8 trainee surgeons	*Determine Change*	Continuous HR recording through wearable sensor (HealthPatch, Vital Connect) with HRV calculated in 5 min segments. Stress percentage (HR + α * SDNN)	Increased mean HR during surgery vs. baseline (87 vs. 70, $P < 0.001$)	Role in surgery not reported Incomplete recordings in 6/20 participants
Ducarme 2015	Cohort	75 obstetrics & gynecology trainees 124 procedures	*Determine Change* Laparoscopic surgery for infertility	Continuous HR recording with analysis at 9 pre-selected operative steps: 1. Baseline 2. Hand washing 3. Operative fielding 4. Palmer Veress entry 5. Umbilical port insertion 6. Diagnostic exploration 7. Second port insertion 8. Dye test 9. Skin suture	Mean HR increased at all steps compared to baseline (83.2) 2 - 88.6, $p = 0.02$ 3 – 87.4, $p = 0.04$ 4 – 91.6, $p = 0.01$ 5 – 104.8, $p = 0.001$ 6 – 93.7, $p = 0.001$ 7 – 95.3, $p = 0.001$ 8 – 90.7, $p = 0.01$ 9 – 88.2, $p = 0.04$	Study controlled to exclude participants after a night shift or performing other surgery prior to laparoscopy
Jones 2015	Cohort	6 colorectal surgeons 18 surgeries	*Determine Change* Routine anterior resections	Heart Rate sampled in 5 min patches at baseline and 6 well—defined stages during surgery	Mean HR elevated from baseline to operation (67 vs. 88, $P = 0.0007$)	Surgery recorded at 8am Consultant surgeon was always the primary operator
Hubert 2013	Cross-over	11 surgeons	*Surgical Approach* Robotic assisted laparoscopy (RAL) vs. standard laparoscopy (SL)	Continuous HR measured: 5 min prior (at rest) During the procedure, 5min after (at rest)	Mean HR higher during the procedure in SL vs. RAL (92.1 vs. 83.7, $p<0.01$)	Small number of participants Increased physical strain of standard laparoscopy noted
Kuhn 2013	Cohort	7 specialist and 3 trainee surgeons 109 elective coronary bypass grafts	*Surgical Experience* Consultant vs. trainee *Role in Surgery* Primary surgeon vs. assistant	HR recorded at 16 specific time points: Pre-operative Entering operating theatre, Skin incision Sternotomy Internal mammary artery divided	Consultant vs. trainee: No difference (85.6 vs. 82.2, $p = 0.089$) Change from baseline: Primary surgeon - Increased	Small surgical numbers overall Unclear about number of surgeries performed by each surgeon or total procedures performed in the study. Unclear statistical methods to allow for the influence of a certain participant based on the number of times they participated.

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Table 4 (*continued*)

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
				Cannulation Cardiopulmonary bypass Aortic cross-clamping Distal anastomosis Aortic cross-clamp release Proximal anastomosis, Bypass weaning, Haemostasis Sternal closure Skin closure Leaving operating theatre	mean HR during surgery vs. baseline (83.7 vs. 62.3, p=0.024) Assistant Surgeon: Increased mean HR during surgery vs. baseline (p<0.001, HR data not reported)	
Prichard 2012	Cross-over	2 surgeons 3 trainees	*Role in Surgery* Primary surgeon vs. assistant	Continuous HR recording during surgery (Polar RS 800 HR monitor)	Trainees: No difference in HR between assistant and primary operator (73 vs 76, $p = 0.08$) Surgeons: No difference in HR between assistant/ teaching and primary operator (79 vs. 77, $p = 0.56$)	No change in baseline for any participant recorded No comparison between surgeons and trainee
Klein 2010	Case-Control	10 surgeons performing Cholecystectomies	*Ergonomic Stress* Standard operating room (Single laparoscopic monitor in poor position) vs. "modern" operating rooms (dual monitors at line of sight)	3 channel continuous HR recording (Medilog)	No difference in mean HR between standard and modern operating room (90.1 vs. 76.3, $p = 0.575$)	No recording of differences from baseline No comments regarding possible differences in case complexity
Bergovec 2008	Cohort	29 male orthopaedic surgeons	*Determine Change* Hip arthroplasty	Holter monitor with key points described: 1. 30 min pre-op, 2. Skin incision, 3. Exposure of hip, 4. Preparing acetabulum, 5. Preparing femur, 6. Suturing, 7. 30 min post-op	Mean HR higher in points 2-6 (85, 94, 100, 106, 97) vs. point 7 (84) $p \leq 0.003$ Mean HR higher in point 5 (106) vs. point 3 and 6 (94, 97) $p < 0.001$)	Comparison to pre-operative heart rate measures not reported
Payne 1986	Cohort	8 cardiothoracic surgeons and 8 cardiothoracic anaesthetists	*Determine Change*	24 h HR monitoring with specific sampling during surgery	Higher mean HR in surgeons during surgery vs. non-surgical work hours (100 vs. 78bpm, p value not reported)	No baseline at rest reported No statistics provided
Simulated Surgery						
Moore 2015	RCT	32 consultant and trainee surgeons	*Surgical Approach* Robotic vs conventional laparoscopy	Continuous HR measurements with 6 lead monitor	Increase mean HR from baseline to during task:	Well controlled for exercise, caffeine, food, and alcohol use. Single, dominant hand test

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Table 4 (*continued*)

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
					1..91 ($p =$ 0.014) under time pressure 2.73 ($p =$ 0.002) under multi-tasking 3.54 ($p <$ 0.001) under evaluation pressure Mean HR change from baseline to task greater in robot group vs. conventional group ($p =$ 0.006)	
Jukes 2017	Cohort	40 otolaryngology surgeons	*Environmental stress* Jugular vein and Carotid artery injury in sheep	Continuous HR monitoring	Increased maximum HR from baseline to after vascular injury (p<0.001) Higher maximum HR after arterial injury vs. venous injury (p=0.0023)	Controlled for medication effect on HR Level of experience not discussed
Crewther 2015	Cohort	12 medical students	*Determine Change* *Surgical Experience* Simulated intra-corporeal suturing and knot tying over 4 sessions: BASE, MID, POST, & RETEST	Continuous monitoring during simulation. No description of time prior to exercise for baseline	Mean HR increased in simulation vs. baseline at each exercise (40.1, 35.0, 30.2, 31.3bpm; all $P < 0.05$) Significant decrease in mean HR change with each session (p =0.037)	Small number of participants
Hurley 2015	Cross-over	16 medical students completing 4 tasks	*Surgical Approach* Robotic assisted laparoscopy surgery (RALS) vs. standard laparoscopy surgery (SLS)	Continuous HR monitoring	Mean HR higher during SLS vs. RALS (84.4 vs. 76.4, $p =$ 0.004)	Stable environment temperature
Berguer 2006	Cross-over	10 surgeons performing 2 task types	*Surgical Approach* Laparoscopic task vs. robotic trainer task	Continuous HR monitoring	No difference between robotic and laparoscopic in either task	Small numbers No subjective or other physiological data
SKIN CONDUCTANCE *Simulated Surgery*						
Berguer 2001	Cohort	28 surgeons undertaking a knot tying task	*Determine Change* *Surgical Approach* Open technique vs. video-endoscopic surgery (VES)	Skin conductance on right palm	Skin conductance increased: Rest to open task ($p <$ 0.01) Open task to VES ($p <$ 0.01) Skin conductance values not reported	Increased self-reported measure corresponded to change in skin conductance

(*continued on next page*)

Table 4 (*continued*)

Author	Study design	Participants	Stress event measured	Timing of measurement	Results	Comments
Berguer 2006	Cross-over	10 surgeons performing 2 task types	*Surgical Approach* Laparoscopic task vs. robotic trainer task	Skin conductance on right palm	No difference between robotic and laparoscopic in either task	Small numbers No subjective or other physiological data
Hurley 2015	Cross-over	16 medical students completing 4 tasks	*Surgical Approach* Robotic assisted laparoscopy surgery (RALS) vs. standard laparoscopy surgery (SLS)	Skin conductance on the foot	Higher skin conductance levels during SLS vs. RALS (8.03 vs. 6.71, $p = 0.027$)	Stable environment temperature Correlations with cortisol and HR below

† STAI – State Trait Anxiety Inventory

of sight, there were no differences in mean HR during the procedure. During endoscopic simulation, mean HR was increased when participants were under time pressure or needed to perform tasks concurrently compared to undertaking simulation without these factors [46]. Finally, the impact of arterial versus venous injury on surgeon HR was assessed in a separate simulated study with maximum HR significantly higher after a carotid artery injury compared to jugular vein [47].

Surgical experience

The impact of surgical experience was assessed by three studies that

Table 5
Studies measuring Heart Rate Variability.

Author	Study design	Participants	Stress event measured	Measurement	pNN50	SDNN	rMSSD	LF:HF Ratio	Comments
Live Surgery									
Theodoraki 2015	RCT	8 Trainee surgeons 2 consultant supervisors	*Surgical Approach* Navigation system guided surgery vs no navigation system	Continuous recording from prior to operation until the end	Not Reported	Not Reported	Not Reported	No difference between groups	Results poorly presented to determine heart rate variability measures reported
Bohm 2001	RCT	2 surgeons performing 20 sigmoid resections (10 each)	*Surgical Approach* Conventional vs. laparoscopic sigmoid resections	5 min periods analyzed at 10 pre-defined steps of the operation.	Not Reported	Not Reported	Not Reported	Descriptive results only: Increased LF/HF ratio in conventional group ($p<0.05$)	Well controlled data collection. Poorly presented findings
Heemskerk 2014	RCT	2 surgeons	*Surgical Approach* Laparoscopic Cholecystectomy (CC) vs. robot-assisted laparoscopic cholecystectomy (RC)	Bipolar ECG, sampled in 5-minute segments 7 defined stages during surgery: 1. Baseline 2. Insertion of trocar 3. Calot's triangle 4. Cystic duct and artery 5. Dissection of gallbladder 6. Removal of gallbladder 7. Closure	Not Reported	Not Reported	Not Reported	High LF/HF ratio in CC vs. RC at points 4: 2.98 vs 1.10 ($P<0.001$) 5: 3.12 vs. 1.60 ($p=0.01$) 6: 2.71 vs 1.48 ($p=0.01$)	Small number of surgeons Procedures not evenly distributed between participants
Dedmon 2019	Cohort	2 Neurology Fellows	*Determine Change*	Continuous ECG during: Rest Pre-operative Mastoidectomy Fascial nerve dissection	Not Reported	Mastoid 43.9 vs. 29.4 ($p=0.06$) Fascial nerve 22.8 ($p=0.002$)	Not Reported	No Significant difference	
Weenk 2017	Cohort	5 Consultants 7 fellows 8 trainee surgeons	*Determine Change* Baseline versus surgery	Continuous HR recording through wearable sensor (HealthPatch, Vital Connect) with HRV calculated in 5 min segments.	Not Reported	81 vs 51 ($p<0.001$)	38.97 vs 23.50 ($p=0.001$)	3.97 vs. 6.18 ($p = 0.01$)	Role in surgery not reported Incomplete recordings in 6/20 participants

(*continued on next page*)

Table 5 (*continued*)

Author	Study design	Participants	Stress event measured	Measurement	pNN50	SDNN	rMSSD	LF:HF Ratio	Comments
Jones 2015	Cohort	6 colorectal surgeons 18 surgeries	*Determine Change*	Wireless heart rate monitor sampled in 5 min patches	Not Reported	Not Reported	Not Reported	Increased LF/HF from baseline to surgery 4.02 vs. 11.2 ($p<0.001$)	Consultant surgeon always primary surgeon #uses STAI to determine stressful procedure – comment in paper
Yamanouchi 2015	Cohort	2 Surgeons 9 surgeries	*Determine Change*	Continuous monitoring from 1 hr pre-surgery to 1 hr post-surgery	Not Reported	Not Reported	Not Reported	Surgeon 1 (five surgeries): Mean increase 6.03 ($p<0.01$) Surgeon 2: No change	Small sample Different surgeries for the 2 surgeons
Kuhn 2013	Cohort	7 consultant and 3 trainee surgeons performing 109 elective coronary bypass grafts	*Determine Change* *Surgical Experience* Consultant vs. trainee	HR recorded at 16 specific time points: Pre-operative Entering operating theatre, Skin incision Sternotomy Internal mammary artery divided Cannulation Cardiopulmonary bypass Aortic cross-clamping Distal anastomosis Aortic cross-clamp release Proximal anastomosis, Bypass weaning, Hemostasis Sternal closure Skin closure Leaving operating theatre	Not Reported	Not Reported	Not Reported	No difference from baseline to during surgery 8.8 vs. 10.4 ($p=0.185$) Increased in consultants vs. trainee during surgery 11.0 vs. 9.9 ($p=0.009$)	Unclear about number of surgeries performed by each surgeon or total procedures performed in the study.
Prichard 2012	Cross-over	2 Consultants 3 trainees	*Role in Surgery* Primary surgeon vs. Assisting	Continuous HR recording during surgery (Polar RS 800 HR monitor)	14.2 vs 10.2 ($p=0.01$)	355 vs. 270 ($p=0.01$)	406 vs. 304 ($p=0.02$)	140 vs. 87 ($p=0.05$)	No change in baseline for any participant recorded No comparison between consultants and trainee
Song 2009	Cohort	1 Consultant surgeon	*Determine Change* *Environment* 50 Coronary artery Bypass Grafts 30 Primary surgeon 20 Supervisor	Continuous recording from entry to operating room to end of operation	Not Reported	Not Reported	Not Reported	Descriptive changes only: Primary operator – LF/HF reduced from baseline Supervisor – Increased LF:HF during cross-clamp, coronary anastomosis, and unclamp	Single surgeon No other measures of stress No data comparisons between groups
Simulated Surgery									
Crewther 2015	Cohort	12 medical students	*Determine Change* *Surgical Experience* Simulated intra-corporeal suturing and knot tying over 4 sessions: BASE, MID, POST, & RETEST	Continuous monitoring during simulation. No description of time prior to exercise for baseline	Not Reported	Not Reported	Not Reported	Descriptive Only: No difference in LF/HF from baseline Decreased LF/HF ratio with increased training ($p<0.009$)	Small number of participants
Hurley 2015	Cross-over	16 medical students completing 4 tasks	*Surgical Approach* Robotic assisted laparoscopy surgery (RALS) vs. standard laparoscopy surgery (SLS)	Continuous HR monitoring	Not Reported	54.97 vs. 77.82 ($p<0.01$)	33.0 vs. 69.91 ($p<0.01$)	Not Reported	Stable environment

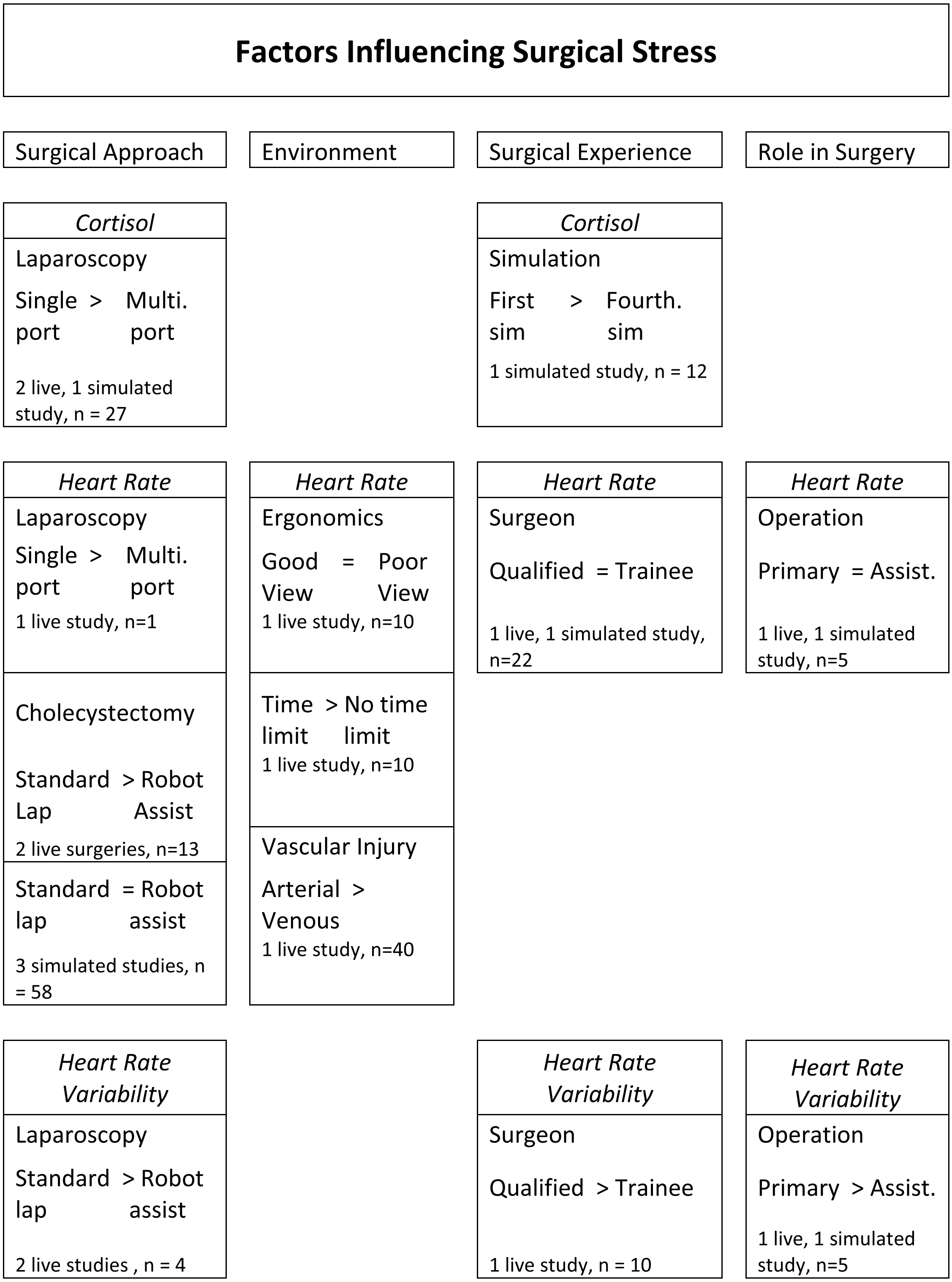

Fig. 2. Summary of acute stress differences under different external influence.
> Denotes which group had greater stress response, = Denotes no difference between groups

included measures of salivary cortisol, mean HR, and HRV. One study provided descriptive data only of a significantly higher baseline cortisol in surgeons with 5-10 years of experience compared to those with greater than 10 years' experience, however, there were no reported differences in operative cortisol levels [48]. Changes in mean HR were assessed by two studies including 22 participants [26,31]. A cohort study of seven qualified and three trainee surgeons found no difference in mean HR based on experience during 109 coronary bypass grafts [31] however LF:HF ratio increased in consultants compared to trainees (Table 5). In the second study, the mean HR in 12 medical students undertaking simulated intracorporeal suture tasks significantly decreased with each simulated task compared to the baseline [26] although this finding was not reflected in measures of cortisol.

Role in surgery

The impact of role in surgery on stress response was identified in two studies that reported the change of mean HR from baseline in the primary and assistant surgeon (Table 4). A small cohort of 10 participants [31] reported a significant increase in mean HR for both the primary and assistant surgeon but did not report whether there was a difference in the degree of change between primary and assistant surgeons. In another small study of two qualified and three trainee surgeons [49], the authors reported no difference in mean HR of either the qualified or trainee surgeon during the procedure or between them when they were either the primary surgeon or assistant. In contrast, indices of HRV in both the time and frequency domains (Table 5) demonstrated significantly increased HRV when acting as primary surgeon versus assisting, however the study did not stratify this by level of experience.

Discussion

This systematic review has identified very low-quality evidence examining biological markers of acute stress change in surgeons during surgery. Both the quantity of evidence and the quality of evidence is poor and a clear evidence gap has been identified in both a live or simulated surgical setting. Despite identification of studies reporting the biological effects that surgery or simulated surgical tasks cause in a surgeon, the most appropriate biological measures of stress, the timing of their measurement relative to the index surgery, and what constitutes a normal or maladaptive response remain unclear. The underlying causes for such uncertainty are a combination of the innate complexities of measuring biological measures of stress and the limitations of the included studies.

Understanding how to assess stress in surgeons with a view to targeting interventions to decrease that stress is critical to maintain a healthy workforce. The stress response is designed to protect the individual through activation of catecholamines and immunological functions. Prolonged or repetitive stress, even that of less than 2 h may change cognitive [50–52], immune and cardiac function that may lead to hypertension, arrhythmia, oxidation of low-density lipoproteins [53,54], osteoporosis, arthritis, and type 2 diabetes [51]. Excessive levels of acute stress can influence surgeons' fine motor skills, coordination and dexterity, and decision-making ability [55,56] with recurrent events contributing to increased rates of burnout [51].

Assessment of an acute stress response requires evaluation of changes in biological markers over time, however, those markers may be affected by external influences prior to, and during the surgery. Potential biological markers include salivary cortisol, which is minimally affected by physical workload, but is impacted by diurnal variation and has a wide stress initiation to peak salivary cortisol level time as well as a widely reported half-life [57,58]. Currently available evidence suggests that although study conditions could be created to control for internal and external influences, this might affect the external validity of the test when considering it for real world applications.

The review identified mean HR as the most consistent biological marker to change from baseline to during surgery, however, the clinical significance of these changes is unknown. Given the force and rate of contraction of the heart is also controlled by oxygenation and nutritional requirements of the body [39,50], the physical workload of surgery may skew results for both mean and maximum HR. The use of HRV remains promising and as technology improves for both source measurement and interpretation of the HRV raw data, for example by wearable devices [59], there may be greater accuracy in using this to identify stress events in real time and this is a key area for future research in this field [59].

A further avenue for future research is electrodermal increase in conductance times which has only been shown to be possible in a simulated setting [28,40]. In live surgery, limitations may occur with specific locations on the body in areas that need to be surgically cleansed and variation of surface body temperature due to surgical lights. Again, wearable devices may overcome these limitations in the future.

This systematic review found that the majority of included studies had low risk of bias but were limited by small sample sizes, and total number of and variance in procedures. Studies with larger participant numbers and controlled for operative or simulation stressor often used only one reference point for measuring stress, without a baseline measurement [41]. This does not allow for inter or intra-participant variations. While studies have separated out groups by experience in simulation studies, there are no reported comparisons of stress measures between these groups [42,48].

This first systematic review in this area has several limitations. Firstly, it used a deliberately wide inclusion criteria to capture as much information about biological measures of stress as possible. This results in marked heterogeneity between studies and meta-analysis is not possible. Second, many studies used only a single measure of biological stress at one time point and given the marked variability, multiple biological measures of stress reported at a minimum of two time points should be used in future. Third, the timing of stress measures, their measurement relative to the index surgery, and what constitutes a normal or maladaptive stress response remain unclear and needs future research to resolve. Fourth, this review has been limited to biological measures, however, psychological factors are also important. Tools such as the state trait anxiety inventory [60] and visual analogue scale scores of stress [23,61] may be of benefit in conjunction with biological markers for future research and allow a multimodal approach to identifying and intervening in surgical stress.

Conclusion

Research on measures of biological stress in surgeons during surgery is in its infancy. The normal range of change from baseline to during or after surgery is required before considering what is abnormal or maladaptive to allow targeted interventions. Studies in real world settings are crucial to understand biological measures of stress change, with structured repetitive testing in a simulated environment offering additional knowledge in the field.

Author contributions

Concept and design of the review was undertaken by AB, SS, CW, and AH. Literature search was undertaken independently by AB and SS. Analysis of publications for review was undertaken AB, SS, and JA. Manuscript was prepared by AB with all authors contributing to the editing and final manuscript presentation for publication.

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Declaration of Competing Interest

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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