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ASSESSMENT OF SURGICAL STRESS RESPONSE AND PREDICTING ITS FUNCTIONAL IMPLICATIONS

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ABSTRACT: Surgery alters the homeostatic balance and defence mechanisms in body eliciting certain responses called as stress response. In addition certain peri-operative factors may also influence the degree of stress response reflecting surgical recovery. The present study is an attempt to assess surgical stress response and to determine the influence of peri-operative factors on it. This study investigates the effects of surgery on early non specific immune and endocrine responses. 100 subjects undergoing minor and major elective surgeries were studied. Blood samples were collected before, immediately after and 72 h after the surgery. Total WBC count, differential neutrophil count, random blood sugar and pulse rate were assessed. Pain (Allina scale) and Depression Anxiety Stress scale (DAS) were used for evaluating the relation to stress response. In addition we used Estimation of Physiological Ability and Surgical Stress (E-PASS) scoring system for predicting the risk of post operative complications by quantifying patients reserve and degree of surgical stress. In minor surgeries, there was no significant drop in total counts after surgery, whereas in major surgery total count was decreased. In both the surgeries, the percentage of neutrophil count increased immediately after surgery but later dropped to less than preoperative count after 72 h and blood sugar levels were also found to be elevated in early post operative period. We observed a great relation between the pain and psychological stress to surgical recovery. Thus we suggest considering peri-operative management as a clinical significance to improve patient safety and care.

INTRODUCTION: Surgical stress is the systemic response to surgical injury and is characterized by the activation of hypothalamo pituitary adrenal axis reflecting a combination of endocrinal, immune and hematological changes. Stress response is protective for survival of the person until the injuries are healed by catabolizing stored body fuels and retaining water and salt.

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The magnitude of injury determines the severity and degree of stress response [1]. High stress state however, can result in harmful outcomes to host such as hyperglycemia, cardiovascular instability (hypertension and tachycardia) and immune suppression.

Trauma due to the surgery follows tissue repair in which neutrophils plays a significant role as they are involved in phagocytosis which is related to repair processes. Surgical stress causes non specific immune response depression in the early post operative period addressing the surgical recovery [2]. Under several conditions, immune suppression could be prolonged leading to post operative complications [3].

Irrespective of patient diabetic status, surgical stress induces post operative hyperglycemia results in worse surgical outcomes. The risk of post operative complications increase by 30 % with every 40 point increase from normoglycemia (110 mg/dl) and often leads to longer hospitalization [4]. Psychological stress is often associated with early surgical recovery addressing speed of wound healing and a significant impact on incidence of post operative supra ventricular tachycardia. Psychological preparation for surgery improves post operative outcomes [5].

Patients who suffer from wound pain can experience worries and frustrations about the wound and reduced self esteem, which can have a negative impact on psychological functioning. The relationship between pain and stress is complex. It is known that pain can contribute to stress and other negative emotional states such as anxiety, fear and depression. It has been suggested that anxiety leading to stress can decrease one's pain threshold, reduce pain tolerance and impact the immune system. Wound healing can be delayed as a consequence of these [6, 7].

The Estimation of Physiologic Ability and Surgical Stress (E- PASS) scoring system evaluate surgical risk after surgery, and it predicts postoperative fatal complications [8]. Moreover, the E-PASS scoring system is useful for predicting and recognizing the risk of post-operative complications and for obtaining a better therapeutic outcome [9].

Aim and Objectives:

Aim: This study aims to assess the surgical stress response and its relation to nociception and psychological stress.

Objectives:

- To assess the surgical stress responses (CVS instability, hyperglycemia, immunological changes).
- To predict preoperative risk and surgical stress thereby concluding comprehensive risk for assessing the incidence of morbidity and mortality.
- To assess pain and to relate its effect on stress response.
- To assess psychological stress and to relate its effect on stress response.

MATERIALS AND METHODS: 100 patients undergoing surgeries at General Surgery Department (male and female), Rajiv Gandhi Institute of Medical Sciences, Kadapa were included in this prospective study done over a period of 6 months after obtaining approval by the Hospital Research Ethics Committee. The required information was collected by both "patient interview and chart review method" which are well suited to access the results.

During the study the patient's case records were received and the required data like demography, admitting diagnosis, past medical history, type of surgery *etc*. were collected in a well-structured data collection form (Annexure-I) and then by patient interview psychological status and pain were assessed.

Preoperative:

- The details of the patient were collected after obtaining the informed consent from the patient. Patient's consent was taken after explaining our study clearly to those patients who are willing to participate in our study.
- Data including demographic details, associated risk factors (Cardiovascular, Pulmonary, DM *etc*.), and all other necessary details were recorded on a data sheet. After collecting the data E-PASS scoring system was used to estimate preoperative risk score.
- Psychological stress (Depression, Anxiety and Stress scale) scale was used to assess the extent of stress level.
- All the laboratory data including (WBC, DC and RBS) were recorded.
- Preoperative vitals were recorded on a data sheet.

Post-operative: Vitals were recorded in the data sheet.

- Necessary details like blood loss, type, duration of surgery *etc*., were recorded.
- EPASS was used to asses surgical stress score.
- Pre-operative risk score obtained initially was added to the surgical stress score to obtain Comprehensive Risk Score (CRS).

- CRS thus obtained used to assess the incidence of morbidity and mortality.
- Pain scale (Allina health pain assessment scale) was used to assess the intensity of pain.
- 2 ml of patient's blood was taken for assessing parameters like WBC, differential count and random blood sugar.
- The results obtained were recorded.
- The process of blood collection was repeated after 72 h for assessing same laboratory data.
- Subjects were followed and monitored closely up to their discharge to assess the pain and to find whether any complications developed
- Results were assessed using the above data.

Statistical Analysis: Chi square test was used to determine the association between the surgery and various peri-operative factors. Statistical analysis was done using the Statistical Package for Social Scientists (SPSS) software version 16. Student's t test was used for comparing the initial values. P value < 0.05 was considered as statistically significant.

RESULTS: In this study, 100 subjects were included during the study period as per inclusion criteria of which, 38 were male while 62 were female. Out of 100 patients, 32 developed post-operative complications among them females (59.37 %) were reported to develop more in comparison to males. Majority of the patients (46%) experienced complications belonged to age group of 40-50 years **Table 1**. Recently as said in various studies, E-PASS has been used as a means of predicting post-operative complications in the present study. A CRS of 1.0 is a verge for increasing fatal post operative complications. It was clearly evident from our observation that with an increase in CRS; there is an increase in post-operative complications incidence suggesting proportionality. Different parameters that are used for calculating E-PASS in order to assess the relation to post operative complications are shown in **Table 1**.When related to the peri-operative hospital stay, patients with high comprehensive risk score has mean peri-operative hospital stay of 18.2 days which was shown in detail in **Fig. 1**.

TABLE 1: RELATIONSHIP BETWEEN THE DIFFERENT PARAMETERS AND THE NO. OF PATIENTS THAT EXPERIENCED POST-OPERATIVE COMPLICATIONS

Parameter	No. of patients (100)	No. of Patients who experienced post operative complications
Age (years)		
20-30	18	0
30-40	36	12
40-50	46	20
Blood loss (ml)		
10-20	26	0
20-30	24	4
30-40	24	8
40-50	6	6
>50	20	14
Duration of surgery (min)		
10-30	14	2
30-60	44	12
>60	42	18
Pre-operative risk score		
0.1-0.5	42	6
0.5-1.0	44	16
>1.0	14	10
Surgical stress score		
<0.05	62	14
0.05- >0.1	38	18
Comprehensive risk score		
<0.1	38	6
0.1-0.5	44	12
0.5-1.0	18	14
>1.0	0	0

*Formulas for calculating the Estimation of Physiologic Ability and Surgical Stress (E-PASS) scores: Preoperative Risk Score (PRS), Surgical Stress Score (SSS), and Comprehensive Risk Score (CRS): 1) PRS = −0.0686 + 0.00345X1 + 0.323X2 + 0.205X3 + 0.153X4 + 0.148X5 + 0.0666X6. X1, age (yr); X2, presence (1) or absence (0) of severe heart disease; X3, presence (1) or absence (0) of severe pulmonary disease; X4, presence (1) or absence (0) of diabetes mellitus; X5, performance status index (0 - 4); X6, American Society of Anesthesiologists physiological status classification (1 - 5). Severe heart disease was defined as heart failure that was New York Heart Association Class III or IV, or severe arrhythmia requiring mechanical support. Severe pulmonary disease was defined as any condition with a %VC below 60% and/or an FEV 1.0% below 50%. Performance status index was based on the definition by the Japanese Society for Cancer Therapy. 2) SSS = −0.342 + 0.0139X1 + 0.0392X2 + 0.352X3. X1, blood loss/body weight (g/kg); X2, operation time (h); X3, extent of skin incision (0: minor incisions for laparoscopic or thoracoscopy surgery (including scope-assisted surgery); a) laparotomy or thoracotomy alone; b) both laparotomy and thoracotomy). 3) CRS = −0.328 + 0.936 (PRS) + 0.976 (SSS). VC, vital capacity; FEV, forced expiratory volume.

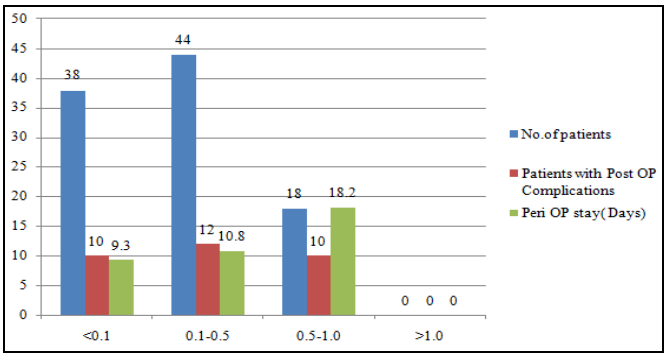

FIG. 1: COMPREHENSIVE RISK SCORE, POST-OPERATIVE COMPLICATIONS AND PERI-OPERATIVE HOSPITAL STAY

In major surgery, there was a significant drop of total count after surgery, from a mean of 8,900 cells/cumm at S1 to 7,600 cells/cumm and 7,054 cells/cumm at S3 while the same response was noted in minor surgeries. In both surgeries mean percentage of neutrophil and RBS increased immediately at S2 later fell to normal at S3 which was depicted in the **Table 2** while incidence of tachycardia was observed only in 8 patients.

TABLE 2: EFFECT OF SURGICAL STRESS RESPONSE ON % NEUTROPHIL AND MEAN RBS COUNT

Total no. of patients screened	Values
Mean neutrophil count (%)	
Before surgery (S_1)	65.98
Immediately after surgery (S_2)	74.88
Within 72 h (S_3)	56.36
Mean RBS count	
Before surgery (S_1)	112.48
Immediately after surgery (S_2)	157.24
Within 72 hours (S3)	130.21

Co-morbidities like HTN, DM, BA were noted in the recruited subjects and those who have co-morbid conditions, incidence of stress response was found to be high than those who doesn't have any co morbid diseases shown detail in **Table 3**.

TABLE 3: EFFECT OF CO MORBIDITIES ON STRESS RESPONSE AND PERIOPERATIVE STAY

Total Patients (n=100)	Incidence of stress response	Peri-operative stay
Patients with Co Morbidities (40)	40	19.7 days
Patients without co Morbidities (60)	58	14.3 days

All the 100 subjects undergoing surgery were asked few questions using DAS scale in order to assess their psychological status as it is related to surgical recovery and hospital stay. We found that most of the patients were under stress and anxiety. Patients whose psychological status was altered had majority of complications **Table 4**. It was also observed that the individuals with great stress and anxiety experienced more post operative pain when compared to others and their stay was also found to be increased due to the burden of developing complications which was indicated in **Table 5**.

TABLE 4: DISTRIBUTION OF PATIENTS BASED ON PSYCHOLOGICAL STATUS

Peri-operative factors	Normal	Mild	Moderate	Severe	Total
Depression	86	14	0	0	100
Anxiety	34	12	36	18	100
Stress	40	36	22	2	100
Complications	00	06	08	18	32

TABLE 5: RELATION BETWEEN PAIN AND PERIOPERATIVE STAY

Total no. of Patients screened n = (100)	Major (42)		Minor (58)	
	With post op Complications (18)	Without post op Complications (24)	With post op Complications (14)	Without post op Complications (44)
No. of days pain exists (Avg)	6.125	4.45	6.83	3.71
Hospital stay	17.25	12.09	14.16	7.61

DISCUSSION: The stress response to surgery comprises a number of hormonal changes initiated by neuronal activation of hypothalamic-pituitary-adrenal axis [10-13]. The present study attempted to assess the effect of surgery on immune and endocrine responses along with the use of E-PASS as a tool to predict post operative complications. In addition to these we also attempted to identify the relation between psychological status and post operative pain to surgical recovery.

In the present study the incidence of complications were more in patients who had undergone major surgery, patients with co-morbidities and in females as they have more psychological stress supporting our results, Hideki Bou *et al*., study also supported same stating the patients with co-morbidities are at high risk. E-PASS is a surgical stress scoring system comprised of a pre operative risk score [20], a surgical stress score and comprehensive risk score. In the present study the incidence of post operative complications increased significantly with rising preoperative risk score and comprehensive risk score and was also significantly related with the length of stay.

In terms of stress responses as a result of surgical trauma, tachycardia was found up to the mark as only in 8 patients among 100 patients but there was a significant increase in neutrophil count at the end of surgery as the mean % neutrophil count S2 was 74.88 when compared to S1 *i.e.* before surgery

where mean count was 65.98, indicating that the neutrophil are in a heightened state of alertness, this study was supported by the results of P. Santosh Prabhu *et al*., later on the neutrophil count was decreased in early post-operative period as the mean count was decrease to 56.36 respectively, which might be resulted for early post-operative complications [14]. As per statistical analysis, there was statistical significance (P > 0.05, by using paired-t test). D. Savitha *et al*., ground work also reflected the same. The study has also revealed the incidence of hyperglycemia in both the surgeries (major & minor).

As per statistical analysis, there was statistical significance between before the surgery (S1) &within 72 h after surgery (S2) (112.48 and 157.24) (P > 0.05, by using paired-t test). This study was supported by Margarita Ramos *et al*., it was evident that post-operative pain influences the surgical recovery [15, 35, 36]. Our results had shown that both in minor and major surgeries the post-operative complications and days of hospital stay were increased in proportion to the pain. By taking hospital stay as an index of recovery, patients with complications had 19.26 days and 14.12 days in major and minor surgeries when compared to patients without complications who had the stay of 12.09 and 7.61 respectively.

In patients whose psychological status altered had an increased risk of developing post-operative complications [19, 37, 38]. In our study, individuals with altered psychological status it was noted that they experience more pain than others leading to complications and increased stay suggesting a relation. Our results were supported by a number of studies [16, 23, 33] done by Marisa Manuela Batista dos Santos *et al*., Jean-Philippe Gouina *et al*., and Broadbent et *al*., Our understanding was still at level of infancy as further studies are required to elicit better results highlighting the relationship between peri-operative factors and stress response

CONCLUSION: In the present study, patients were exposed to an operative procedure which is a form of stress. In the light of present study, it could be concluded that surgical trauma is a form of stress that alters immune, metabolic and neuronal responses. The study has attempted to investigate the effect of surgery on early nonspecific immune response, mainly neutrophilic function which is the body's first line of defense using simple hematological parameters along with the effect on blood sugar (metabolic) and heart rate (neuronal). We observed a decrease in the % neutrophilic count in early postoperative period and increase in heart rate and sugar levels indicating stress response following surgery. In addition to these, we found that pain and psychological state of patients also influence the degree of stress response and can be often related to post-operative complications, and recovery.

To assess the relation of magnitude of surgical stress , further analysis are needed to conclusively determine the potential contribution of post-operative pain and psychological variables as they increase possibility of post-operative complications and interfere with recovery. Hence we suggest considering perioperative management as a clinical significance to improve patient safety and care. Further large scale depth study can be conducted to get more precise result.

Ethical Matter: The study was approved by the Institutional Ethics and Research Committee of PRRMCP, Kadapa. (PRRMCP/IRB/2016/002).

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CONFLICT OF INTEREST: No conflicts of interest.

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