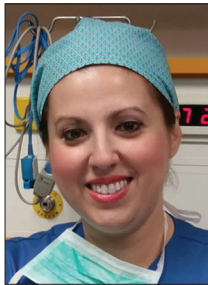# Factors Affecting Stress Levels in Hospitalized Patients after Implementation of Fast-Track Protocol in Hepatopancreatobiliary Surgery

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ABSTRACT

Objective: The objective was to explore factors affecting stress levels in hospitalized patients after implementation of fast-track (FT) protocol in hepatopancreatobiliary surgery. **Methods:** This was a prospective cross-sectional study, where 90 patients were included. Exploration of environmental postoperative stress levels was conducted by serum adrenocorticotropic hormone and cortisol levels, the Intensive Care Unit Environmental Stressor Scale, and three self-reported Numeric Analog Scale questions, with regard to emotional/stress level, specifically "How sad do you feel right now?" "How stressed do you feel right now?" and "How optimistic do you feel right now, about the future?" at 3 time points: (T_1) Before surgery, (T_2) the day of surgery, and (T_3) the 3rd postoperative day. The trial profile is conformed according to the CONSORT guidelines. Statistical analysis was carried out by SPSS software version 22 (IBM SPSS software, Chicago, Illinois, USA) at a significance level of 0.05. **Results:** Serum cortisol T_2 levels were positively correlated with the day of removal the drainage tube (rho = 0.235, P = 0.027). Furthermore, serum cortisol T_3 levels were positively correlated with age and body mass index and negatively with the day of drainage tube removal (rho = 0.231, P = 0.028, rho = 0.235, P = 0.026, and rho = −0.279, P = 0.008, respectively). **Conclusions:** The findings of this study highlight that after evaluation of stress levels; nurses could interfere and reduce stress levels, knowing the factors which cause the increased stress levels, after the implementation of FT protocols.

Key words: Enhanced recovery after surgery program, fast-track surgery and hepatopancreatobiliary surgery, stress levels and surgery

Introduction

Fast-track (FT) protocols are widespread in several types of surgeries. In 1990, Kehlet and Wilmore introduced the FT surgery approach in patients' postoperative care. First, FT programs were developed to enhance postoperative recovery, such as early mobilization and resumption of diet, in patients undergoing knee-and-hip surgery, as well as gynecology surgery. The main aim of FT was to reduce complications.[1] FT protocols are shown to have positive results in clinical trials for patients with regional analgesia and those with early resumption of diet and ambulation, but in practice, the evaluation of stress levels is not described.[2]

Aim

The physiological and endocrine stress systems activate acute stress, especially after trauma and surgery.[3] Various studies have been conducted to associate the triggering of biological stress systems with changes in the subjective emotional experience of stress.[4] Furthermore, a constant exposure to stressors can activate a biological system such as the hypothalamic–pituitary–adrenal axis (HPA axis). The HPA axis can not only be triggered by different stressors which can release various biomarkers, but also be activated by adaptive abilities which are inherited by individual's experience.[5]

It is well established that corticotropin-releasing hormone is excreted by the hypothalamus which stimulates the excretion of adrenocorticotropic hormone (ACTH), which, in turn, stimulates the adrenal cortex to produce cortisol[6] which is the primary hormonal end product of the HPA axis, and is characterized as stress biomarker.[3]

The aim of this study was to explore the factors affecting stress levels in hospitalized patients after implementation of FT protocol in hepatopancreatobiliary surgery. Exploration was conducted with the values of serum ACTH and cortisol levels, Intensive Care Unit Environmental Stressor Scale (ICUESS), and the three self-reported Numeric Analog Scale ([NAS]: 0–10) questions, with regard to stress level.[7,8]

Methods

This prospective cross-sectional study was carried out at a large oncological hospital in Athens, Greece, between May 2012 and March 2015. The surgical operations of this study were performed by the same surgical team.

The study was approved by the scientific committee of the oncological hospital (ID: 4051/448) and the Ethical Committee of the Faculty of Nursing of the National and Kapodistrian University of Athens, Greece (ID: 87). In addition, the trial was registered in the clinicaltrials.gov (registration number NCT02524925). The study patients received a written informed consent, ensuring full respect of data confidentiality throughout the research.

The trial profile is conformed according to the CONSORT guidelines and is reported in Figure 1. Statistical analysis was carried out using SPSS software version 22 (IBM SPSS Software, Chicago, Illinois, USA) which compared the aforementioned parameters between the two groups of patients after conducting Kolmogorov–Smirnov test of normality. Comparisons were made using the Chi-square and Mann–Whitney tests. The data were expressed as mean (standard deviation), at a significance level of 0.05, while correlations were expressed using Spearman's test (rho).

Demographic data such as gender and age, as well as body height, body weight, and body mass index (BMI), were recorded. Stress levels were assessed at the same time point with the blood samples.

Patients who participated in the FT protocol were started on oral fluid intake (0.5 L) for 6 h and mobilized for 4 h on the day of surgery, progressively. Nasogastric tube was removed as early as possible after the surgery. On the 1st postoperative day (PD), patients started hydric diet (tea-soup-gel), while on the 2nd–3rd PDs, they started normal diet. Patients were discharged on the 4th–6th PDs.

The environmental stress levels were assessed by the ICUESS[9], with values ranging from 1 (not stressful) to 4 (very stressful); the minimum score was 40 and maximum was 160. This specific scale is the only published environmental scale for patients admitted to the intensive care unit (ICU). It is a self-reported questionnaire including forty stressful factors, for which patients are called to refer how stressful there are during their hospitalization to ICU; it was validated for use in Greek through a translation and back-translation process.[10] Its Cronbach's α estimation was $\alpha = 0.84$.

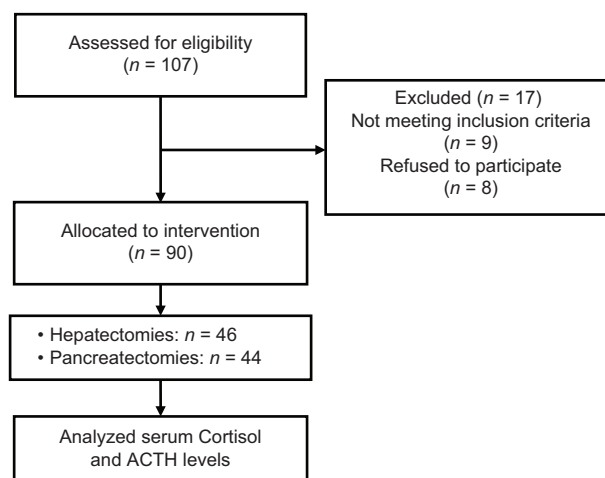Patients were asked three self-reported NAS (NAS: 0–10) questions (0 = not at all to 10 = very much): "How sad

Figure 1: Flow diagram of the progress through the phases of the trial

do you feel right now?" "How stressed do you feel right now?" and "How optimistic do you feel right now, about the future?" in order to determine their emotional/stress state, at 3 time points: (T_1) Before surgery, (T_2) the day of surgery, and (T_3) the 3rd PD. The NAS questions have been used in patients admitted to ICUs and myocardial infarction patients and are credible, having high correlations with established patient stress scales.[7,8]

Furthermore, the peripheral blood samples were collected consistently at the same time point of the day (6 pm), the same time points as mentioned above; were centrifuged at 3000 rpm for 20 min; and the sera were stored at −80°C. Serum cortisol (ng/mL) and ACTH (pg/mL) levels were quantified by an electrochemiluminescence immunoassay. Serum ACTH and cortisol levels were evaluated in a private laboratory with ISO 9001, in which they have developed and used their own antibodies for analyses. The researcher collected all data regarding stress tools, prior to acquiring the blood samples for the assessment of ACTH and cortisol levels.

Results

Demographic and clinical data

Of a total of 107 patients assessed against the eligibility criteria, 90 patients who underwent pancreatectomy or hepatectomy were finally included in the study [Figure 1]. The demographic data of the two groups are shown in Table 1, and the psychological response rates and clinical data are summarized in Tables 2 and 3.

At T_1 time point, the results of NAS questions were as follows: "How sad do you feel right now?" – 6.06 (3.01), "How stressed do you feel right now?" – 6.24 (8.09), and "How optimistic do you feel right now, about the future?" – 7.36 (2.43). At T_2 time point, the results of NAS questions were as follows: "How sad do you feel right now?" – 4.52 (2.85), "How stressed do you feel right now?" – 4.24 (3.09), and "How optimistic do you feel right now, about the future?" – 7.9 (2.13). At T_3 time point, the results of NAS questions were as follows: "How sad do you feel right now?" – 4.12 (2.89), "How stressed do you feel right now?" – 3.85 (3.19), and "How optimistic do you feel right now, about the future?" – 7.77 (2.29).

The complications noted were nausea/vomiting in 13 patients, fever in 5, and pancreatic fistula in 1 patient, while 71 patients appeared to have no complications.

Bivariate correlations among Intensive Care Unit Environmental Stressor Scale, Numerical Analog Scale self-reported questions, adrenocorticotropic hormone, and serum cortisol levels

Factors affecting the stress levels were evaluated with ACTH and serum cortisol levels, the three NAS self-reported

Table 1: Demographic data of participants

Item	Data	
Age (years) [mean (SD)]	60.53 (11.76)	
Gender, *n* (%)	Male: 52 (57.8)	Female: 38 (42.2)
BMI [mean (SD)] (kg/m²)	27.28 (4.3)	
Body height (cm)	169.53 (9.48)	
Body weight (kg)	78.58 (14.55)	
Operation, *n* (%)		
Hepatectomy	46 (51.1)	
Pancreatectomy	44 (48.9)	

BMI: Body mass index

Table 2: Patients Psychological Response Rate [Mean (SD)]

Item	Data
ACTH T_1 (pg/mL)	15.24 (18.33)
ACTH T_2 (pg/mL)	42.58 (81.7)
ACTH T_3 (pg/mL)	11.83 (23.09)
Cortisol T_1 (ng/mL)	16.74 (29.09)
Cortisol T_2 (ng/mL)	41.74 (25.52)
Cortisol T_3 (ng/mL)	20.77 (17.94)
ICUES Scale	46.51 (6.11)
NAS questions	
How sad do you feel right now? T_1	6.06 (3.01)
How sad do you feel right now? T_2	4.52 (2.85)
How sad do you feel right now? T_3	4.12 (2.89)
How stressed do you feel right now? T_1	6.24 (8.09)
How stressed do you feel right now? T_2	4.24 (3.09)
How stressed do you feel right now? T_3	3.85 (3.190)
How optimistic do you feel right now, about the future? T_1	7.36 (2.43)
How optimistic do you feel right now, about the future? T_2	7.9 (2.13)
How optimistic do you feel right now, about the future? T_3	7.77 (2.29)

Table 3: Patients clinical data [Mean (SD)]

Item	Data
Day of soup-cream-gel resumption	3.46 (1.66)
Day of normal diet resumption	5.18 (1.62)
Total days of postoperative intravenous fluid administration	3.77 (1.93)
Day of removal nasogastric tube	1.38 (1.06)
Day of removal drainage tube	5.31 (1.47)
Day of removal urine catheter	3.44 (1.55)
Postoperative hospitalization (days)	6.85 (2.63)

questions, as well the ICUESS. It was revealed that the stress levels were affected by age, BMI, day of diet resumption, the day of drainage tube, and urine catheter removal. Specifically, serum cortisol T_2 levels were positively correlated with the day of drainage tube removal (rho = 0.235, $P = 0.027$). In addition, serum cortisol T_3 levels were positively correlated with age and BMI and negatively with the day of drainage tube removal (rho = 0.231, $P = 0.028$, rho = 0.235, $P = 0.026$, and rho = −0.279, $P = 0.008$, respectively).

Furthermore, serum ACTH T_2 levels were positively correlated with the day of drainage tube removal (rho = 0.254, P = 0.016), the day of resumption soup-cream-gel and normal diet, and the postoperative hospitalization in days (rho = 0.204, P = 0.05, rho = 0.223, P = 0.034, and rho = –0.254, P = 0.016, respectively). Similarly, environmental stress levels, which were evaluated with the ICUES, were negatively correlated with age (rho = –0.218, P = 0.039) and positively with the day of starting oral fluid intake, the total number of days of postoperative intravenous fluid administration, and the day of urine catheter removal (rho = 0.396, P < 0.001, rho = 0.311, P = 0.003, and rho = 0.241, P = 0.022, respectively).

In contrast, the evaluation of ICUESS questions showed the factors which affected patients' environmental stress levels and which did not. The correlations noted are presented in Table 4. The results showed that the presence of relatives or other patients in the room and the interest of nurses decreased the stress levels; on the contrary, the presence of drainage tubes or the catheters and the weakness to sleep increased their stress levels.

Discussion

The current study observes and evaluates stress levels of patients who underwent either hepatectomy or pancreatectomy. It was a prospective study, with cross-sectional correlations. It focused on the assessment of patients' stress levels by nurses, after major abdominal surgery, using specialized tools. The results of this study showed that patients' stress level, which was estimated with ICUESS, three NAS questions, and cortisol and ACTH serum levels, was positively correlated with the presence of drainage tubes or the catheters and the weakness to sleep.

Initially, the positive association between ACTH levels and feeling stressed was worth noting and was in contrast with previous reports on animal models which have shown that HPA axis activation is markedly influenced by the intensity of the triggering stressor. In the same study, in animal models, after shock, there was a lack of significant ACTH sensitization despite a clear corticosterone sensitization. This could originate from

the enhancement of adrenal responsiveness to circulating ACTH or the sensitization of ACTH release could be transient, mainly affecting the initial response to the stressor.[11]

Similarly, age and BMI were positively correlated with cortisol levels on the 3rd PD. The results of our study are in accordance with international studies. In the study of Barth, 2001, the changes in steroid hormones and HPA axis in healthy population were proportional to age.[12] While Rask *et al.*, showed that serum cortisol and ACTH levels were positively correlated with BMI, in overweight women.[13]

Furthermore, in the present study, there was a positive correlation between weakness to sleep and stress levels. These results are in accordance with the results of Otsuka *et al.*[14] In this study, the 16.6% was characterized as stressed individuals and symptoms of insomnia, nightmares, and lack of rest due to sleep deprivation were more likely to occur.[14]

Last but not the least, the nurse could build a relationship with patients, basing on patient communication, which should include eliciting and understanding the patient's perspective, concerns, needs, and feelings. In this way, nurses by understanding the causes of stress in patients could improve their relationship with them.[15]

Limitations

This was a preliminary exploratory study on stress responses in surgical ward, and therefore subject to many limitations. Despite the inherent complexity of postoperative stress responses, we focused on only two types of operations, such as pancreatectomy and hepatectomy. The sample size was kept to a minimum due to the pilot nature of this investigation. Therefore, these results need to be interpreted with caution because both type I and type II errors may have occurred. Moreover, although standard controlled trial procedures were applied, the results cannot be generalized to the entire population of oncological patients because this was a single-center study and therefore prone to biases.

Conclusion

The findings of this study highlight the benefits for evaluating stress levels of surgical oncological patients and

Table 4: Correlations among ICUES scale questions, NAS self-reported questions, and ACTH and cortisol serum levels			
Spearman (rho)	How stressed do you feel right now? T_3	Serum ACTH T_3 levels	Serum Cortisol T_3 levels
Visiting of relatives & friends just for a few hours a day			-0.211, P=0.016
Lack of private space			-0.347, P=0.001
Stay in bed cause of the tubes		0.271, P=0.01	
Sense that nurses constantly do some things around the bed		-0.211, P=0.046	
Taking Blood Pressure several times during the day		-0.28, P=0.007	
Weakness to sleep	0.21, P=0.047		

describe how nurses by knowing the factors which cause increased stress levels can interfere and reduce stress levels, after implementation of FT protocols. As a result, we focus on improving hospitalization conditions, in the form of safer care and fewer complications. Reducing stress levels of patients should be the main target of health professionals, in the modern health-care systems.

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Nil

Conflicts of interest

There are no conflicts of interest.

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