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# Emotional Processes in Patients Undergoing Coronary Artery Bypass Graft Surgeries with Extracorporeal Circulation in View of Selected Indicators of the Inflammatory Condition

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**Background:** The aim of this study was to describe positive and negative emotions in patients undergoing coronary artery bypass graft (CABG) surgeries with extracorporeal circulation and the correlations between emotions and basic indicators of the inflammatory condition: C-reactive protein (CRP) concentration, body temperature, and leukocyte count.





**Material/Methods:** Standardized tools were used to select 52 patients (aged 47–63 years, 6 women – 11.5% and 46 men – 88.5%) without dementia or depression. The Positive and Negative Affect Schedule (PANAS) was used to examine positive affect (PA) and negative affect (NA) and the State-Trait Anxiety Inventory (STAI X1 and X2) was used to examine the anxiety level. The patients underwent CABG surgery according to a common anesthesia protocol and for 5 consecutive days they were observed in the ward, where selected indicators of the inflammatory condition were monitored.

**Results:** A detailed description of the results of examinations of emotions was presented. The patients with low PA-trait level, high NA-trait level, and high anxiety-trait level (STAI X2) exhibited statistically significantly higher body temperatures than the other patients in the postoperative period. The patients with high NA-trait and anxiety-state levels (STAI X1) had statistically significantly lower CRP levels in the postoperative period than the patients with low NA-trait and anxiety-state levels (STAI X1).

**Conclusions:** Patients undergoing CABG operations express both positive and negative affects. The changes in the inflammatory markers are expressed mostly by CRP concentration. There exist relationships between the result of tests assessing emotions and the markers of the inflammatory condition.

**MeSH Keywords:** **Anxiety • Body Temperature • C-Reactive Protein • Coronary Artery Bypass • Emotions • Leukocytes**

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## Background

The necessity to undergo surgeries affects patients' emotional states [1]. Two approaches to a surgery can be observed among patients. By expressing agreement to the surgery the first group of patients perceives the operation as an inevitable need to continue treatment rather than as a therapeutic procedure and the patients see themselves only as passive participants of a complicated medical procedure. The patients do not associate the coronary artery bypass graft (CABG) surgery with a chance to improve their quality of life. Before the cardiac surgery, those patients' emotions are concentrated on fear of the surgery itself [2]. The other group of patients who make a decision to undergo operative treatment of coronary heart disease are the people who see the surgery as a great chance to improve the quality of their lives. For them the surgery is a stage on the way to better life, so they concentrate their attention and emotions on the future and returning to everyday life when they leave hospital [3]. The surgery may evoke strong emotions in a patient. It is widely known that these are various negative emotions (Negative Affect NA; trait: NA-T, state: NA-S), ranging from states of anxiety and fear to anxiety disorders and depression. By contrast, positive emotions (Positive Affect PA; trait: PA-T, state: PA-S) are often ignored in the literature [4]. In everyday practice the basic methods of assessment of the inflammation intensity are measurements of the C-reactive protein (CRP) concentration, leukocyte count, and body temperature.

The synthesis of CRP in the liver is caused by IL-1 and 6 and CRP is a major acute-phase proteins. It also takes part in the development of nonspecific immunity [5]. CRP is described as one of the factors contributing to the development of atherosclerotic lesions in the walls of blood vessels. Fichtlscherer called it an independent, transient factor of endothelial dysfunction and, simultaneously, he proved the presence of dependence between the high CRP level and impaired reactivity of coronary vessels in patients with ischemic heart disease. The effect disappears when the CRP level decreases [6]. Similarly to other surgical specializations, in cardiac surgery, postoperative changes in the CRP level are used to determine the dynamics of the inflammatory process and the occurrence of possible infectious complications [7].

During the initial period of extracorporeal circulation (ECC) the leukocyte count decreases due to hemodilution. However, the leukocyte count and activity gradually increase during and after the end of extracorporeal circulation. Three types of leukocytes are activated during ECC: neutrophils, monocytes, and lymphocytes. The activity of neutrophils increases the most and fastest. Initially, the level of monocytes begins to increase unnoticeably to reach the highest level several hours after ECC. On the other hand, the level of all lines of lymphocytes decreases during and after ECC [8].

The normal body temperature measured in the oral cavity of adult patients under age 40 years is  $36.8 \pm 0.4^\circ\text{C}$ . The peripheral body temperature is about  $0.5^\circ\text{C}$  lower and it depends on the patient's age, sex, phase of the menstrual cycle, circadian rhythm, physical effort, temperament, personality factors, and even the method of measurement [9]. It is also assumed that body temperature is the highest between 4:00 and 6:00 p.m. and it is the lowest around 6:00 p.m. [10]. In the classic theory, in response to the damaging agent, endogenous pyrogens – IL-1, IL-6, TNF- $\alpha$ , and interferons – stimulate the development of prostaglandins in the organum vasculosum of the lamina terminalis, which act as agents in the development of fever. However, a multi-factor development of fever in response to the inflammatory stimulus has recently been postulated [11].

For decades, the interrelations of the disordered function of the central nervous system and immune system have been the subject of research, and the role of pro-inflammatory cytokines (IL-1, IL-6 and TNF- $\alpha$ ) in the initiation of sleep disorders and fatigue syndrome has already been discussed [12].

To date, research on perioperative emotions has been concentrated on anxiety, which intensifies the stress reaction of the organism. The sympathetic part of the autonomous system is activated and the concentrations of adrenaline, noradrenaline, and cortisol increase in the circulatory system with the consequent intensification of the inflammatory reaction [13]. In some patients, the high level of preoperative anxiety involves higher intensity of postoperative pain and the occurrence of cognitive function disorders, which may prolong hospital treatment [14].

Descriptions of PA and its potential relations with the inflammatory condition have been ignored in the perioperative evaluation of patients. This study attempts to describe these issues.

We assumed the hypothesis that selected emotional states (PA, NA, anxiety) may modify the inflammatory reaction in the postoperative period.

We analyzed the following elements in the patients undergoing scheduled coronary artery bypass graft surgeries with extracorporeal circulation:

1. the PA, NA, and anxiety levels on the day before the surgery;
2. the intensity of the inflammatory reaction measured with changes in the CRP concentration, leukocyte count, and variations in the body temperature after CABG for 5 consecutive postoperative days;
3. the correlations between high or low intensity of emotions and anxiety and selected indicators of the inflammatory reaction.

## Material and Methods

### Group of patients

Having received the approval of the Bioethics Committee at Poznan University of Medical Sciences (Resolution No. 265/12), the research was carried out at the Department of Cardiac Surgery, Józef Struś General Hospital, Poznań, Poland. Patients qualified and prepared for scheduled CABG surgeries with extracorporeal circulation were asked to take part in the research.

Patients were included into the research group according to the following criteria:

1. participation in scheduled CABG surgeries with ECC under general anesthesia;
2. ejection fraction (EF)  $\geq 40\%$ ;
3. age: 45–65 years;
4. Polish as the native language;
5. completion of at least 8 years of primary school education;
6. the patient's informed consent to participation in the research.

Patients were excluded from the research group according to the following criteria:

1. emergency surgeries;
2. cerebrovascular accident (stroke, TIA) in the 3 months before the surgery;
3. diagnosis and treatment of mental disorders;
4. Mini-Mental State Examination (MMSE)  $< 24$ , Clock-Drawing Test (CDT) above the first level of errors according to the Shulman scoring method, The Sense of Coherence Subscale Meaningfulness according to the Antonovsky scoring method  $< 34$  pts;
5. permanent pacemaker;
6. chronic liver failure (AIAT and AspAT 2 times higher than normal values in starting tests);
7. chronic kidney disease (creatinine level  $> 2$  mg/dl in starting tests);
8. chronic psychotropic drug therapy (everyday intake of psychotropic drugs for at least 3 months before the surgery);
9. alcohol addiction (everyday consumption of at least 25 g of pure alcohol or weekly consumption of 500 g of pure alcohol);
10. unregulated diabetes (postprandial glucose concentration over 11.1 mmol/l and HbA1c  $> 9\%$ );
11. preoperative anemia (Hb  $< 7.0$  mmol/l, HCT  $< 34\%$ );
12. hyperthyroidism or hypothyroidism (TSH beyond the norm of the laboratory testing the blood sample);
13. no consent to research;
14. postoperative complications:
  - a. respiratory failure requiring mechanical ventilation for over 48 h;
  - b. pneumonia;

- c. septic state;
- d. low cardiac output syndrome;
- e. perioperative acute renal failure requiring renal replacement therapy.

Seventy-eight patients were offered participation in the research. Eighteen patients refused to take part in the research and gave the following reasons for their refusal: too high pre-operative anxiety (5 patients), unwillingness to take part in scientific research (7 patients), no reading glasses (2 patients), reading inability (1 patient), no reason for refusal given (2 patients). One patient was not qualified for the research because of abnormal results in screening tests (MMSE  $< 24$  pts; CDT: error level IV). Fifty-nine patients who expressed their written consent after initial information were qualified for the research and 52 of them completed the research. Seven patients did not complete the research because 1 of them made a decision not to have a surgery, and in 5 cases there were intraoperative decisions to change the extensiveness of treatment [2 patients had off-pump CABGs without ECC and 3 patients underwent not only a CABG surgery but also an aortic valve replacement surgery (1 patient) or mitral valve replacement surgery (2 patients)]. One patient developed ARDS in the postoperative period and required mechanical ventilation for more than 48 h.

### Research tools

The following tools were used in the research:

#### Initial assessment

Initial assessment was carried out on the day of the patients' admission to hospital, 24 h before the scheduled surgery. In the initial assessment the patients were diagnosed by means of a Mini-Mental State Examination (MMSE) and Clock-Drawing Test (CDT) to exclude the concomitant dementia and by means of the SOC-29 (Subscale Meaningfulness) according to the Antonovsky scoring method to exclude depression [15–17].

#### Psychological tests

The patients who passed the initial qualification were examined by means of the Positive and Negative Affect Schedule (PANAS) and State-Trait Anxiety Inventory (STAI). There are 2 versions of PANAS – the shorter one with 20 points and the longer one with 30 points. The shorter schedule is used for population-based studies and the longer schedule is used for clinical studies. The longer schedule was used in this research. It included 15 statements concerning positive affect and 15 statements concerning negative affect. The Polish version of the PANAS, which was developed by Brzozowski, was used in this research. It enables assessment of the current emotional state (State; -15-S) and the constant predisposal to react with

emotions, i.e. traits (Trait; -15-T). The model internal consistency (Cronbach's alpha) is 0.86–0.9 [18]. Anxiety was assessed by means of the State-Trait Anxiety Inventory (STAI; state: STAI X1, trait: STAI X2) with the internal consistency (Cronbach's alpha) ranging from 0.87 to 0.9 [19]. The test was conducted on the day preceding the cardiac surgery.

### Assessment of inflammatory condition parameters

#### CRP measurement

The first measurement of the CRP concentration was carried out on venous blood, which was routinely collected from each patient on the day of their admission to hospital. The second measurement was carried out on the blood which was collected immediately after insertion of an arterial catheter in the operating theatre. The next test was made 6 hours after incising the sternum and then tests were carried out every morning for 5 consecutive days following the surgery.

#### Leukocyte count measurement

The leukocyte count was measured once a day in the morning for 5 consecutive days of the observation, from a blood sample collected after fasting.

#### Body temperature measurement

The body temperature was measured every day at 4-hour intervals between 10 a.m. and 10 p.m. The choice of the time of body temperature measurement resulted from the need to maintain the normal night-day/sleep-wakefulness cycle. The temperature was measured with electronic Rycom RC003T thermometers.

### General anesthesia protocol

#### Preparation for anesthesia

On the evening before the surgery, the patients were orally administered 1 tablet of 2 mg estazolam (Estazolam, Polfarmex, Poland). On the surgery day, 30–60 minutes before the surgery, they were orally administered midazolam (Dormicum, Roche, Switzerland) at a dose of 0.05–0.15 mg/kg of body weight.

#### Anesthesia before CABG surgery

The patients qualified for the research were anaesthetized according to the guidelines of Fast Track Cardiac Anesthesia [20]. The patients were brought into anesthesia with propofol (Propofol 1% MCT/LCT Fresenius, Austria) administered at a dose of 1–1.5 mg/kg of body weight and fentanyl (Fentanyl WZF, Polfa SA, Poland) at a dose of 3–10 µg/kg of body weight.

When sedation reached the depth of BIS 40–45, rocuronium bromide (Rokuronium Kabi, Fresenius Poland), a muscle relaxant, was administered at a dose of 0.6–0.8 mg/kg of body weight. The patients were ventilated mechanically in the IPPV mode with the tidal volume of 6 ml/kg of ideal body weight, PEEP 3–5 cm Hg. Anesthesia was sustained through the combination of continuous infusion of propofol at a dose of 2–3 mg/kg of body weight per hour and inhalation of sevoflurane (Sevorane Abbott, United Kingdom), with MAC values ranging from 0.4 to 0.6 and determined on the basis of its concentration at the end-expiratory phase. During extracorporeal circulation, general anesthesia was sustained only through the continuous infusion of propofol at a dose of 3 mg/kg of body weight per h, whereas fentanyl was infused at a dose of 0.01–0.02 µg/kg of body weight per min. The patients were in slight hypothermia (35°C) during the surgery. During extracorporeal circulation (Stöckert S5, Stöckert GmbH; Germany), the mean arterial pressure (MAP) was maintained at 60–75 mmHg.

### Admission to Postoperative Ward

After the surgery the patients were transferred to the Postoperative Ward in the Department of Cardiac Surgery. The infusion of propofol and fentanyl was maintained until the patients were admitted to the Postoperative Ward. The monitoring of the patients started in the operating theatre and continued in the postoperative ward, where hourly postoperative drainage and hourly diuresis were additionally controlled.

### Statistical analysis

The descriptive statistics of the results of the research with psychological tools, intraoperative parameters and inflammation parameter values include the range and means with standard deviation values.

The results of the research with psychological tools were presented in the form of high and low scores, including the median. In the identification of important differences in averages of 2 subgroups we used Student's t-test, where  $p < 0.05$  was assumed as a statistically significant value. A chi-squared test was used to analyze differences in the sex, education, and occupational activity between the subgroups with high and low scores in psychological questionnaires. The analysis also included cardiac surgery data in the subgroups (ejection fraction, BSA, BMI, extracorporeal circulation time, aortic clamping time, and reperfusion time).

## Results

Fifty-two patients aged 47–63 years completed the research, including 6 women (11.5%) and 46 men (88.5%). Six patients

**Table 1.** Descriptive statistics of the results of the psychological tests in the whole group of patients under study.

Psychological tests	N	Minimum	Maximum	Mean	Standard deviation
PANAS PA-15-T	52	27.00	74.00	53.25	9.50
PANAS NA-15-T	52	15.00	54.00	29.23	9.37
PANAS PA-15-S	52	15.00	62.00	40.83	9.56
PANAS NA-15-S	52	15.00	56.00	33.77	12.90
STAI X-1	52	25.00	70.00	44.86	11.01
STAI X-2	52	25.00	60.00	40.86	7.94

PANAS PA-15-T – positive affects-trait; PANAS NA-15-T – negative affects-trait; PANAS PA-15-S – positive affects-state; PANAS NA-15-S – negative affects state; STAI X-1 – anxiety-state; STAI X-2 : anxiety-trait.

**Table 2.** The distribution of sten values in the PANAS and STAI. The number of patients and percentage.

Stens/ Number of patients (%)	1	2	3	4	5	6	7	8	9	10
PANAS PA-15-T	0	1 (1.9%)	1 (1.9%)	2 (3.8%)	4 (7.7%)	5 (9.6%)	8 (15.4%)	9 (17.3%)	8 (17.3%)	13 (25%)
PANAS NA-15-T	0	4 (7.7%)	3 (5.7%)	8 (15.4%)	12 (23.1%)	14 (26.9%)	6 (11.5%)	4 (7.7%)	1 (1.9%)	0
PANAS PA-15-S	1 (1.9%)	2 (3.8%)	3 (5.7%)	8 (15.4%)	13 (25%)	9 (17.3%)	7 (13.5%)	3 (5.7%)	2 (3.8%)	4 (7.7%)
PANAS NA-15-S	2 (3.8%)	0	2 (3.8%)	1 (1.9%)	3 (5.7%)	12 (23.1%)	12 (23.1%)	12 (23.1%)	6 (11.5%)	2 (3.8%)
STAI X-1	0	0	3 (5.7%)	6 (11.5%)	9 (17.3%)	7 (13.5%)	9 (17.3%)	6 (11.5%)	7 (13.5%)	5 (9.6%)
STAI X-2	4 (7.7%)	5 (9.6%)	5 (9.6%)	9 (17.3%)	16 (30.8%)	6 (11.5%)	3 (5.7%)	4 (7.7%)	0	0

PANAS PA-15-T – positive affects-trait; PANAS NA-15-T – negative affects-trait; PANAS PA-15-S – positive affects-state; PANAS NA-15-S – negative affects state; STAI X-1 – anxiety-state; STAI X-2 – anxiety-trait.

(11.5%) had primary education, 24 patients (46.2%) had vocational education, 14 patients (26.9%) had secondary education, and 8 patients (15.4%) had higher education. Thirty-one patients (59.6%) were occupationally active and 21 patients (40.4%) did not have jobs. None of the jobless patients was a disability pensioner due to cardiac diseases.

The arithmetic means of biometric parameters were as follows: height 172.13 cm (SD 7.51), weight 86.28 kg (SD 17.76), BMI 28.91 kg/m<sup>2</sup> (SD 4.67).

Concomitant diseases:

1. arterial hypertension (24 patients, 46.2%),
2. myocardial infarction in the patient's past medical history (11 patients, 21.2%),
3. diabetes with stabilized glycemia (5 patients, 9.6%),
4. gout (5 patients, 9.6%),
5. bronchial asthma (2 patients, 3.8%),
6. chronic obstructive pulmonary disease (2 patients, 3.8%),
7. gastric ulcers (2 patients, 3.8%),

8. hypothyroidism during euthyroid (2 patients, 3.8%),
9. obliterating endarteritis (2 patients, 3.8%),
10. individual cases of the following diseases: the condition after hormonal therapy due to prostate cancer in remission, rheumatoid arthritis, systemic lupus erythematosus without the need of treatment, psoriasis without the need of treatment, nasal polyps (1.9%),
11. other burdens included smoking (14 patients, 26.9%) and alcohol addiction (2 patients, 3.8%) – 1 patient had abstained from alcohol for 20 years, the other for 3 years.

### Results of research with psychological tools

Self-report tools were used in the research. The patients filled in PANAS and STAI forms on the day of their admission to hospital, usually 1 day before the surgery, between 9 a.m. and 9 p.m.

The raw scores of the PANAS PA-15-T and PANAS PA-15-S schedules were higher than the scores of the PANAS NA-15-T and PANAS NA-15-S schedules. The scores in the STAI X1 schedule



**Table 3.** Descriptive statistics of the perioperative cardiac surgery data.

	N	Minimum	Maximum	Mean	Standard deviation
Ejection fraction EF (%)	52	40.00	61.00	51.19	5.88
Body surface area BSA (m <sup>2</sup> )	52	1.59	2.51	1.20	0.21
Extracorporeal circulation time (min)	52	25.00	98.00	66.96	15.67
Aortal clamping time (min)	52	12.00	48.00	32.08	7.24
Reperfusion time (min)	52	8.00	49.00	25.94	9.39
Number of coronary bypass grafts	52	1.00	4.00	2.82	0.71
Postoperative drainage (ml)	52	200.00	2100.00	536.35	350.87

**Table 4.** The C-reactive protein (CRP) concentration during hospitalization in the group under study.

CRP concentration/ time of measurement	N	Minimum (mg/L)	Maximum (mg/L)	Mean (mg/L)	Standard deviation
Admission to hospital	52	0.10	17.80	2.46	2.94
Measurement before surgery	52	0.60	10.00	2.97	2.14
6 hours after cutting sternum	52	0.90	10.30	3.10	1.81
Day 1 after surgery	52	20.60	136.70	69.70	23.45
Day 2 after surgery	52	65.50	318.60	152.67	56.70
Day 3 after surgery	52	40.30	279.50	122.70	56.84
Day 4 after surgery	52	26.40	234.00	86.79	47.66
Day 5 after surgery	52	16.30	148.80	58.56	31.35

were higher than the scores in the STAI X2 schedule. Table 1 shows the scores in detail (Table 1).

When the raw scores in the PANAS and STAI were obtained, they were referred to Polish population norms, expressed with sten values. The converted scores expressed in the sten scale – stens 1 to 4 refer to low scores and poor intensity of the emotion under study, stens 5 and 6 classify the emotions as moderately intense, and the converted scores from sten 7 to sten 10 refer to high intensity of the emotion under study. Most of the patients had high PANAS PA-15-T and PANAS NA-15-S scores. The largest percentage of the patients had medium PANAS NA-15-T and PANAS PA-15-S scores. The majority of the patients had high STAI X-1 scores and low STAI X-2 scores. Table 2 shows detailed scores in the sten scale for the PANAS and STAI (Table 2).

**Cardiac surgery data**

There were no complications in the intraoperative course of the surgery. Table 3 shows perioperative data in detail (Table 3).

**Indicators of inflammatory condition**

*CRP concentration*

The analysis of variation in the CRP concentration revealed a 30-fold postoperative increase in the protein concentration on the second day after the surgery, but the concentration tended to decrease gradually. In spite of reduction in the CRP concentration, it still exceeded the upper reference limit 12 times on the fifth day after the surgery. Table 4 shows the details of variation in the CRP concentration during the research (Table 4).

**Table 5.** The leukocyte count during hospitalization in the group under study.

Leukocyte count/ time of measurement	N	Minimum (1000/ $\mu$ L)	Maximum (1000/ $\mu$ L)	Mean	Standard deviation
Admission to hospital	52	3.90	13.70	7.67	2.19
Day 1	52	4.90	21.20	9.83	3.24
Day 2	52	3.40	18.10	9.61	3.08
Day 3	52	3.80	18.50	8.59	3.07
Day 4	52	3.20	14.40	7.48	2.30
Day 5	52	2.70	13.70	7.58	2.22

**Table 6.** Body temperature in the group under study.

Body temperature/ Time of measurement	N	Minimum $^{\circ}$ C	Maximum $^{\circ}$ C	Mean $^{\circ}$ C	Standard deviation
Day 1 measurement 1 (D1 M1)	52	34.80	37.60	36.42	0.55
Day 1 measurement 2 (D1 M2)	52	35.70	37.00	36.37	0.31
Day 1 measurement 3 (D1 M3)	52	35.40	38.00	36.51	0.48
Day 1 measurement 4 (D1 M4)	52	35.30	37.40	36.42	0.43
Day 2 measurement 1 (D2 M1)	52	35.40	37.30	36.33	0.34
Day 2 measurement 2 (D2 M2)	52	35.10	37.60	36.39	0.41
Day 2 measurement 3 (D2 M3)	52	35.40	38.00	36.55	0.53
Day 2 measurement 4 (D2 M4)	52	34.60	37.20	36.41	0.40
Day 3 measurement 1 (D3 M1)	52	35.80	37.30	36.37	0.32
Day 3 measurement 2 (D3 M2)	52	35.80	38.00	36.52	0.49
Day 3 measurement 3 (D3 M3)	52	35.90	37.60	36.60	0.42
Day 3 measurement 4 (D3 M4)	52	36.00	37.70	35.52	0.35
Day 4 measurement 1 (D4 M1)	52	35.80	37.10	36.36	0.29
Day 4 measurement 2 (D4 M2)	52	35.70	37.60	36.42	0.36
Day 4 measurement 3 (D4 M3)	52	35.80	37.60	36.43	0.36
Day 4 measurement 4 (D4 M4)	52	35.80	38.30	36.43	0.37
Day 5 measurement 1 (D5 M1)	52	35.00	37.60	36.30	0.35
Day 5 measurement 2 (D5 M2)	52	35.70	37.40	36.42	0.30
Day 5 measurement 3 (D5 M3)	52	35.90	37.30	36.42	0.33
Day 5 measurement 4 (D5 M4)	52	35.70	37.30	36.43	0.34

The highest mean leukocyte count was observed on the first day after the surgery. On the second day, the leukocyte count began to decrease. There was a considerable decrease in the leukocyte count on the fourth day after the surgery. On the last (fifth) day the mean leukocyte count was lower than on

the day of admission to hospital. During the whole period of the research, the leukocyte count remained within normal limits, which range from 4 to 11 $\times$ 1000/ $\mu$ L. Table 5 shows the details of variation in the leukocyte count (Table 5).

**Table 7.** The medians of the scores in psychological tests.

Psychological tests	PANAS PA-15-T	PANAS NA-15-T	PANAS PA-15-S	PANAS NA-15-S	STAI X-1	STAI X-2
N	52.00	52.00	52.00	52.00	52.00	52.00
Median	53.50	28.50	41.00	35.50	44.50	41.00

PANAS PA-15-T – positive affects-trait; PANAS NA-15-T – negative affects-trait; PANAS PA-15-S – positive affects-state; PANAS NA-15-S – negative affects state; STAI X-1 – anxiety-state; STAI X-2 – anxiety-trait.

### Body temperature measurement

The mean body temperature ranged within the normal limits, but in individual patients there were postoperative increases in the body temperature up to 38°C. Table 6 shows variation in the body temperature in the postoperative period (Table 6).

Having calculated the median, which was a caesura in the psychological part of the research, the patients were divided into 2 subgroups (with high or low scores). Table 7 shows the medians (Table 7).

Sex, education and occupational activity did not differentiate the patients in both subgroups significantly. There were no statistically significant perioperative differences in the cardiac surgery data in both subgroups (chi-squared test,  $p > 0.05$ ).

The results of the tests conducted with psychological tools in the 2 subgroups were correlated with the indicators of the inflammatory condition: CRP concentration, leukocyte count and body temperature. The following correlations were found:

1. On the third postoperative day, in the second measurement, in the subgroup with the low PANAS PA-15-T score the mean body temperature was 36.69°C (SD 0.55) and it was higher than in the subgroup with the high PANAS PA-15-T score, where it was 36.3°C (SD 0.35);  $p = 0.01$  ( $t = 2.71$ ).
2. In the subgroup with the low PANAS PA-15-T score, the mean body temperature was lower on the first day, in the first measurement, i.e. 36.24°C (SD 0.58), whereas in the subgroup with the high PANAS PA-15-T score it was 36.61°C (SD 0.46). On the third day, in the second measurement the mean body temperature was lower in the subgroup with the low PANAS PA-15-T score and it reached 36.37°C (SD 0.40), whereas in the subgroup with the high PANAS PA-15-T score it reached 36.67°C (SD 0.53);  $p = 0.01$  ( $t = -2.57$ ) and 0.02 ( $t = -2.30$ ), respectively.
3. On the first day after the surgery, the mean CRP concentration in the patients with the low PANAS PA-15-S score was 79.25 mg/L (SD 23.16) and it was greater than in the subgroup with the high PANAS PA-15-S score, where it reached 60.16 mg/L (SD 19.90);  $p = 0.002$  ( $t = 3.17$ ).
4. On the first day after the surgery in the subgroup with the low STAI X-1 score, the CRP concentration was higher, i.e.

it reached 78.22 mg/L (SD 24.23), whereas in the subgroup with the high anxiety-state score it reached only 61.18 mg/L (19.59);  $p = 0.007$  ( $t = 2.79$ ).

5. On the third day after the surgery in the third measurement, the mean body temperature in the subgroup of patients with the low anxiety- trait score (STAI X-2) was 36.49°C (SD 0.36) and it was lower than the mean body temperature in the patient subgroup with the high anxiety-trait score, where it reached 36.73°C (SD 0.45);  $p = 0.037$  ( $t = -2.15$ ).

### Discussion

The emotional and mental aspects are important components of patients' well-being, which doctors often tend to ignore, unfortunately. This research analyzed the emotional states and affective traits of patients undergoing scheduled CABG surgeries.

The research participants were a relatively homogenous group. All the patients participating in the research underwent scheduled CABG surgeries. The date of the surgery was always agreed in advance, so there was no element of surprise, which is an additional stress-inducing factor. Unfortunately, the approach to the criteria of patients' inclusion or exclusion from the research was very restrictive, so only 59 patients were qualified for the research and only 52 patients completed it. The same protocol was applied in preparation for the surgery, anesthesia, and postoperative procedures. The course of all the surgeries was typical. There was no case of intraoperative complications, which would significantly influence the time and course of the surgery.

Screening tests were used to exclude the potential influence of concomitant cognitive function disorders and depression on the emotional state. The tests are short and easy to make and it takes only a dozen minutes or so to complete them. The MMS and CDT are commonly recommended tools as initial instruments diagnosing cognitive function disorders [21,22]. The Sense of Coherence Subscale Meaningfulness is the strongest predictor of depression of all the 3 SOC-29 subscales and it is sufficient for initial diagnosis of depression disorders [23].

This study attempted to evaluate preoperative emotions in patients undergoing CABG surgeries. Watson & Tellegen assumed



that there are 2 dimensions, i.e. PA and NA, which are independent of each other [24]. The scientists decided that PA and NA could not be treated as the 2 poles of 1 dimension. According to their concept, people experience positive and negative emotions. Both in the dimension of negative affect and that of positive affect, it is possible to sense these emotions with different intensity, ranging from zero to a specific maximum, but they can be experienced only simultaneously [25]. According to Watson and Tellegen's emotion theory, PA reflects the level of pleasant interaction between the individual and surrounding environment [26]. PA can be described as happiness, pleasure, enthusiasm, satisfaction, joy or even euphoria [27]. NA reflects the individual's unpleasant experiences of withdrawal, distress, misery, or even unhappiness in contacts with the surrounding environment. The experiences can be described as sorrow, anger, hostility, apprehension, helplessness, or sense of guilt [28]. Depending on the duration, we can distinguish between short-lasting emotions induced by a specific stimulus, which are described as states, and permanent predisposal to experience specific emotions, which are described as traits [29].

The research assessed the emotions of 52 patients who were scheduled to undergo a CABG surgery on the day of their admission to hospital, i.e. 1 day before the surgery. Among a large number of tests used to assess emotions and mood, Watson and Clark's self-report PANAS (*The Positive and Negative Affect Schedule*) is relatively often applied in scientific studies. The schedule is described in the literature on the subject [30]. The Polish version of the PANAS, i.e. SUPIN (*Skala Uczuć Pozytywnych i Negatywnych*), which was developed by Brzozowski, was used in this research [18].

Anxiety is a primary emotional state, classified as NA. It is observed as a reaction to more-or-less real danger in everyday life [31]. As indicated by results from long-term observations and studies, individual people experience anxiety in different ways. It is commonly thought that susceptibility to anxiety is determined by individual factors from the group of personality and temperament-related traits. People with temperamental susceptibility to anxiety usually exhibit high levels of introversion and neuroticism [32]. Spielberger was one of the first scientists who suggested considering anxiety in the categories of state and trait. STAI X1 is a transient reaction to a stimulus. It is manifested with subjective, consciously perceived feelings of apprehension and tension. According to Spielberger, high variability caused by factors exerting influence is a characteristic of STAI X1. STAI X2 is a permanent trait of personality and it describes how a particular individual reacts to stressful situations and what their susceptibility to experiencing anxiety is [33]. The Polish version of STAI, edited by Wrześniewski [18], was used to measure the anxiety level. As Rossi and Porois stated in their analysis published in 2012, STAI is a 'gold standard' in the assessment of anxiety [34].

There is a wide range of publications discussing the issue of the influence of emotions on health [35,36]. Most of them concern populations of healthy people, residents of nursing homes, or people suffering from chronic diseases, i.e. bronchial asthma, chronic kidney disease, or ischemic heart disease [37–39]. Most studies discussing emotions in patients in the perioperative period concentrate only on the assessment of preoperative anxiety level [40]. Thus, it was the first analysis attempting to find if emotions could influence the intensity of inflammatory reaction in the early postoperative period.

The emotions of patients undergoing scheduled CABG surgeries were assessed with the Fitzgerald test, which was used to test only the NA level by means of the PANAS. Unfortunately, in contrast to our research, the NA level was measured 1 month before the scheduled surgery. The shorter version of the test was applied in the study. In that study, the high NA level in patients aged 38–77 years was 32%. Alas, the authors did not provide the information whether they tested the emotional state or affect trait, so a comparison with the results presented in our study does not seem to be possible [41].

Differences in the intensity of the affect trait and state are not surprising, because they describe similar rather than identical values [28]. Everyday events do not affect the PA-T or NA-T levels, but they influence our ability to cope with challenges [42]. PA-S and NA-S describe the emotions experienced at the present moment, which appear as a direct reaction to external or internal stimuli. They are characterized by high variability in time. As far as the patients participating in the research are concerned, hospitalization and a scheduled surgery were the external stimuli affecting the level of the patients' emotions during the research. As Pressman and Cohen noted, PA-T and NA-T may have influence on the patient's physiology in the long-term perspective, e.g. when making life decisions or coping with a chronic disease, whereas PA-S and NA-S affect human behavior as reactions to sudden events or exacerbations of chronic diseases, e.g. a bronchial asthma attack or an occurrence of stenocardia [26]. The high PA-T level in most of the patients participating in the research proves that they were highly predisposed to induce positive emotions. On the other hand, the low level of PA-S emotions in most of the research participants shows the level of positive emotions the patients experienced on the day preceding the cardiac surgery. In spite of the fact that the patients were characterized by the predisposition to induce positive emotions, when they faced enormous stress, which a cardiac surgery undoubtedly caused, they experienced positive emotions of moderate intensity.

In our study the difference between the high level of NA-T and NA-S, i.e. 21.15% and 61.9%, respectively, seems to be surprisingly large. However, Fitzgerald does not think that such a difference should be considered surprising. Patients qualified

for CABG surgeries with ECC due to their underlying disease, i.e. ischemic heart disease, often see the doctor, have considerable awareness of dangers resulting from the disease, and they know what to do if the disease becomes exacerbated. Owing to these facts, those patients' STAI X2 level is lower than in the rest of the population. However, Fitzgerald thinks that this does not exclude a high level of situational anxiety before an atypical event. The surgery was an atypical event for the patients from the group under discussion [41]. A low NA-T level indicates a minimal individual predisposition to induce negative emotions influenced by different stimuli. On the other hand, a high NA-S level in those patients is a direct reaction to the stimulus of the upcoming surgery. In view of the upcoming surgery, which is a dramatic challenge to patients, NAs are prevalent, whereas PA-Ss remain at a medium level.

During the research under discussion, the measurement of anxiety intensity was based on Spielberger's concept. Similarly to the assessment of PA and NA, the difference in the levels of anxiety state and trait is not surprising. We observed a high STAI X1 level in 51.9% of the patients in our research, whereas in the study conducted by Szekely, only 42% of the patients had a high STAI X1 level [42]. In the study conducted by Navarro-Garcia on 100 patients undergoing cardiac surgeries, there was an even lower percentage of patients with a high STAI X1 level, i.e. 32% [43]. When analyzing differences it is necessary to note the fact that our study only included patients undergoing CABG surgeries, whereas the other 2 studies assessed patients undergoing surgeries due to coronary heart disease and patients preparing for valve surgeries [42,44]. It is a well-known fact that patients suffering from ischemic heart disease are characterized by greater neuroticism and susceptibility to anxiety reactions, so a higher level of anxiety in a homogenous group of patients with coronary heart disease seems to be justified [44]. Age is another factor affecting the level of preoperative anxiety. Preoperative anxiety decreases with age and the age under 65 is the most important factor influencing the level of preoperative anxiety in patients undergoing cardiac surgeries [43]. In comparison with the patients participating in the studies conducted by Szekely and Navarro-Garcia, the patients in our research were the youngest. Both of these factors seem to be a sufficient reason why the patients in our research were characterized by greater preoperative anxiety [42,43].

As Bruk-Lee claims, the STAI X2 level should be considered as a very important factor of adaptation to changes occurring in one's environment. He also claims that STAI X2 seems to affect a wide range of components of one's psychological well-being, such as a good frame of mind and mental health. The STAI X2 level may influence the way an individual will experience STAI X1, but it does not determine the level of situational anxiety [44]. Reference publications provide some suggestions that in

specific situations, such as that of an upcoming surgery, STAI X2 inadequately affects the psychological reaction and thus its influence on the STAI X1 level is greater than usual [45-47].

On average the patients participating in the research in question scored 40.86 pts in the assessment of STAI X2. The score was higher than the Polish norm for the same age group, i.e. 38.8 pts. Szekely observed a similar difference between the mean score in the study and the national norm. When she examined 180 patients undergoing cardiac surgeries, she found that the STAI X2 level in the group of patients undergoing cardiac surgeries was 44.5 pts, whereas the Hungarian norm amounted to 42.6 pts. The average STAI X1 level in the patients participating in our research was 44.86 pts and it was higher than the mean level measured in the patients tested. Simultaneously, it was only slightly higher than the average level of the Polish norm, which is 44.42 pts. In the study cited the average STAI X1 level was also higher than the STAI X2 level [42].

In the present research, the intensity of the inflammatory reaction after the CABG surgery was assessed by determining the CRP concentration, the leukocyte count, and assessment of the peripheral body temperature. The choice of such simple parameters used in the assessment of the inflammatory reaction resulted from 2 reasons. Firstly, these parameters are routinely used in everyday medical practice in Poland. Secondly, the research was conducted in a biochemical laboratory of a city hospital, where neither the components of the complement system nor the level of proinflammatory cytokines are measured.

CRP is a sensitive marker commonly used in laboratory diagnostics, although it is non-specific. According to Koj's classification of acute-phase proteins, it is included in the group of 'C' proteins, whose concentration increases by 30-60% under the influence of an inflammatory stimulus [48]. Cytokines IL-1, 6, and TNF- $\alpha$  regulate the genes of proinflammatory proteins, including CRP, so the CRP concentration provides indirect information about the level of cytokines which are significant to the development of an inflammatory reaction [49].

The CRP level was measured 8 times on the basis of the study conducted by Fischer in 1976, which is a classic now. He was one of the first scientists to determine the dynamics of variation in the CRP concentration in response to the stimulus of a surgery. Fischer claims that the CRP level begins to increase as soon as 6 hours following the effect of the surgical stimulus and it reaches the maximum value on the second day. On the third day after the surgery the CRP concentration begins to decrease gradually if there are no septic complications [50]. The dynamics of variation in the CRP concentration was similar in the research under discussion. In the study published by Aouifi the variation in the CRP concentration after scheduled CABG surgeries was different than in our study. The CRP

reached the highest level on the third rather than second day after the surgery. It amounted to 158 mg/l, which was similar to the highest result in our observation. On the third day the CRP began to decrease slowly and it did not reach the normal level until the eighth day, when the measurements ended. The scientists also noted that, depending on the procedure, the CRP reached the maximum level on another postoperative day. Thus, if there was a CABG surgery without ECC, the CRP reached the maximum level on the first day after the surgery. After CABG surgeries with ECC, the CRP concentration increased until the second postoperative day, whereas after heart valve surgeries the CRP concentration was the highest on the third day [7].

The occurrence of leukocytosis on the first day after the surgery reflects, and results from, changes caused by ECC. There are few studies with observations of the leukocyte count in the postoperative period in patients undergoing CABG surgeries. One of them is the FIFA study (*Fibrinolisi e Infiammazione nella Fase Acuta*). The highest leukocytosis was observed on the second rather than first day after the surgery. However, there was a rapid increase in the leukocyte count on the first postoperative day, whereas the increase between the first and second postoperative days was minimal. On the third postoperative day the leukocyte count began to decrease slowly so that on the day when the patients were discharged from hospital their leukocyte count was still greater than before the surgery [51]. By contrast, the patients from the Italian study were older than those in our research group. Some of the cardiac surgeries were conducted in deep hypothermia (28°C). Unfortunately, neither the extracorporeal circulation time nor the aortic clamping time were given. The patients were brought into anesthesia with thiopental. This drug has anti-inflammatory effect, because it reduces the neutrophil adhesion to endothelial cells [52]. Thus, the factors listed above may have caused different dynamics of variation in the leukocyte count between the research under discussion and the FIFA study.

As we know, it is difficult to specify the normal body temperature, because it is affected by numerous factors, which were discussed in the introduction. Taking all variables affecting the body temperature into consideration, it is possible to assume that during the measurements the mean body temperature of patients participating in the research remained within normal limits. During the first 3 postoperative days there was greater variation in the body temperature between the lowest and highest measurement and the curve showing the body temperature trend was steeper than on the fourth and fifth days after the surgery, when the body temperature remained stable except for the first lowest morning measurement. It is also necessary to note the fact that the greatest amplitude measured within 24 hours was observed on the third day after the surgery (0.27°C), whereas the smallest amplitude was observed on the fourth day of measurements (0.07°C). Even

small amplitudes in the body temperature have prognostic significance. Varela showed that in a group of patients who were treated in an intensive care unit due to multi-organ failure the patients who died had slightly lower body temperatures than the patients who recovered and the amplitude of variation in the body temperature that was statistically significant amounted only to 0.53°C (35.16°C vs. 35.69°C) [53].

It is noteworthy that the greatest leukocyte count was observed on the first day after the surgery, the highest CRP concentration was observed on the second day after the surgery, and the highest body temperature was observed on the third postoperative day.

The research revealed a subtle correlation between the emotions under study and the intensity of inflammatory reaction. PA-T, NA-T and STAI-X2 were discreetly correlated with the body temperature after the surgery. The low PA-T level, high NA-T level and high STAI X2 level were related with a higher body temperature after the surgery. An increased body temperature is related with the influence of endogenous pyrogens. Unfortunately, this cannot be simply related with the results of scientific research. Although a large cohort study by Vogelzangst revealed an increased CRP concentration in men suffering from anxiety disorders in comparison with the control group, there was no correlation between the occurrence of anxiety and IL-6 and TNF- $\alpha$  in the serum. However, it is necessary to stress the fact that those studies included individuals who did not undergo surgeries, so a different profile of inflammatory markers should be expected. Apart from that, the authors suggest that dysregulation of the immune system in the group they studied was particularly marked in people with late onset of anxiety disorders. Thus, they suggest that a specific subtype of anxiety disorders with different etiology should be distinguished. It is noteworthy that in the patients with a high NA-S level and high STAI X1 level, the CRP concentration on the first day after the surgery was lower than in the patients with a low degree of those emotions. The differences were statistically significant and they are different from the body temperature trend, which seems to indicate dysregulation of the immune system in patients from this group [54].

In search of alternative theories, Salim et al. stress the significance of research on the role of inflammatory condition in patients experiencing anxiety and suggest the oxidative stress theory in their review article on the subject [55]. As was reported by Oosthuizen et al. in 2005 [56], among the mediators of the inflammatory condition the potential role of nitrogen oxide in the development of, for example, post-traumatic stress disorder (PTSD), should be taken into consideration. Thus, the supplementation of future studies with correlations between the results of intensity of emotions and the concentration of nitrogen oxide metabolites might be an interesting prospect.

There was no dependence between the emotional states and leukocyte count found. It is necessary to remember that the leukocyte count does not always reflect the intensity of an inflammatory condition in the organism. The absence of this correlation was observed even in patients with a high fever. The analysis of 5628 patients admitted to the Emergency Department of Kaohsiung Medical University Hospital due to fever revealed that 214 patients (3.8%) were characterized by increased CRP concentrations and normal leukocyte counts [57]. According to Peltola et al. [58], the divergences are even more intense in children. As we stressed above, we observed rather discreet changes, so the observation of a larger group of patients might lead to more binding conclusions.

There was no correlation observed between the PA-S and inflammatory response intensity. It may have been related with the fact that most of the patients exhibited a medium PA-S level before the surgery. However, we cannot rule out the likelihood that the analysis of a larger group of patients would have given different results. It is also difficult to compare the results, because, to the best of our knowledge, researchers have been chiefly interested in negative rather than positive emotions represented by anxiety. Thus, at this stage it is premature to conclude that there is no influence of the current positive affect on the inflammatory condition.

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## Conclusions

Emotions in patients undergoing CABG operations are robust, and related to both positive and negative affects. The changes in markers of the inflammatory condition are expressed mostly in CRP concentration. There exist mutual relationships between the result of tests assessing emotions and the markers of the inflammatory condition.



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