

Evaluation of olfactory memory after coronary artery bypass grafting



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Abstract

Introduction: This study determined whether coronary artery bypass grafting (CABG) surgery has any effect on olfactory function, employing the Brief Smell Identification Test (B-SIT).

Material and methods: All the participants were informed preoperatively about the B-SIT test and the mode of its application. The test was performed by each patient preoperatively (d0) as well as 1 (d1) and 3 (d3) days following the surgery. C-reactive protein (CRP) levels were recorded at the same time as the smell test.

Results: This prospective study included 45 patients. The mean age was 67 ± 7.55 , and the group was 29% male. The mean durations of cross clamping and cardiopulmonary bypass were 54 ± 32 min and 62.5 ± 37.0 min, respectively. Eleven different odors were tested. Significant differences were observed for several odors: leather between d0 and d3, pine between d0 and d3, onion between d0 and d1, onion between d0 and d3, and soap between d0 and d1. The postoperative CRP levels were significantly higher than the preoperative levels. The correlation analysis determined that the postoperative CRP levels were negatively correlated with the B-SIT score ($r = -0.48$, $p = 0.001$).

Conclusions: Our findings suggest that patients after CABG are prone to develop olfactory dysfunction in the early postoperative period and that olfactory dysfunction is associated with postoperative CRP levels.

Key words: CABG, olfactory dysfunction, CRP levels.

Streszczenie

Wstęp: Celem niniejszej pracy było zbadanie za pomocą testu B-SIT (Brief-Smell Identification Test™), czy operacje pomostowania aortalno-wieńcowego (*coronary artery bypass grafting* – CABG) mają wpływ na zmysł węchu.

Materiał i metody: Wszystkim uczestnikom przed operacją przedstawiono informacje o teście B-SIT i sposobie jego wykonania. Test wykonywano u każdego z pacjentów przedoperacyjnie (d0) oraz 1 (d1) i 3 (d3) dni po operacji. Stężenie białka C-reaktywnego (*C-reactive protein* – CRP) badano w tym samym czasie co zmysł węchu.

Wyniki: W prospektywnym badaniu wzięło udział 45 pacjentów. Ich średni wiek wyniósł $67 \pm 7,55$ roku; 29% badanych stanowili mężczyźni. Czas zakleszczenia i czas użycia płucoserca wyniosły odpowiednio 54 ± 32 minuty i $62,5 \pm 37$ min. Przetestowano 11 różnych zapachów. W przypadku kilku z nich wystąpiły znaczące różnice pomiędzy badaniami: skóra (między d1 a d3), sosna (między d0 a d3), cebula (między d0 a d1), cebula (między d0 a d3) oraz mydło (między d0 a d1). Pooperacyjne stężenia CRP były znacznie większe niż stężenia przedoperacyjne. Wykonana analiza korelacji pozwoliła na ustalenie, że pooperacyjne stężenia CRP były negatywnie skorelowane z wynikiem testu B-SIT.

Wnioski. Wyniki wskazują, że pacjenci po operacjach CABG są narażeni na zaburzenia węchu we wczesnym okresie pooperacyjnym, a ponadto, że zaburzenia węchu są powiązane z pooperacyjnym stężeniem CRP.

Słowa kluczowe: CABG, zaburzenia węchu, stężenie CRP.

Introduction

Cardiovascular disease is a leading cause of death, and coronary artery bypass grafting (CABG) is the standard treatment for patients with advanced coronary artery

disease [1]. In addition to the general risks of surgery, on-pump CABG presents the risk of complications specific to this procedure. There are many risks associated with the use of the pump, including bleeding, blood clots, stroke, kidney or lung damage, and death.

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Olfactory disorders occur at the rate of approximately 5% in the general population [2]. The sense of smell may be influenced by many factors, such as upper respiratory infections, head trauma, or nasal and paranasal sinus diseases. Additional factors that can influence olfactory function include age, sex, smoking behavior, and neurodegenerative diseases [3].

It has been suggested that the use of the cardiopulmonary bypass pump can cause neurocognitive dysfunction in some patients [4]. However, no study has researched the effect of CABG on olfactory function. In this study, we evaluated the effect of CABG on olfactory memory, using the Brief Smell Identification Test (B-SIT).

Material and methods

Ethical considerations

This study was conducted at the Department of Cardiovascular Surgery of the Abant İzzet Baysal University Hospital. Ethical approval was granted by the local research ethics committee of the Abant İzzet Baysal University, Bolu, Turkey (No: 2012/115). Written consent was obtained from each patient. This was a prospective clinical study with 45 patients undergoing elective CABG.

Exclusion criteria included structural and infectious diseases of the nose (septum deviation, polyps, and rhinitis) as well as renal, hepatic, neurological, or psychiatric disorders and prolonged intubation (> 8 hours). Prospective evaluations started with an initial baseline evaluation (d0), followed by two evaluations on the first (d1) and third (d3) postoperative day.

Evaluation of olfactory capacity

Olfactory function was evaluated using the B-SIT. Twelve odorants were presented to blinded patients at a distance of 2 cm from the nostrils for 2-3 s. The odors were presented at intervals of at least 1 min to prevent olfactory desensitization. The test was designed as a triple forced/multiple-choice test, and the answers were recorded on a computer.

The test consists of a small book with 12 different odorants that are released when scratched with the tip of a pencil. For each odor, the patient is given four different choices with only one correct answer. If the odorant is not identified among the choices, one of the answers must still be selected [5]. The smell diskette odors that we used included mint, honey, banana, lemon, garlic, clove, lilac, leather, strawberry, coffee, chocolate, pine, vanilla, peach, fume (smoggy), cinnamon, soot, grass, peaches, rose, grapes, black pepper, melon, watermelon, peanut, soap, baby powder, chewing gum, and pineapple.

All the participants were informed preoperatively about the B-SIT and the method of its performance. Each patient underwent the test preoperatively, and the scores were recorded. Evaluations included routine clinical and laboratory tests, including tests for C-reactive protein (CRP) levels, a subjective olfactory function test, the B-SIT, and a nasal examination by an otolaryngologist.

Surgical method

The same anesthetic, surgical, and cardiopulmonary bypass (CPB) protocols were used for all patients. Between August 2012 and March 2013, 45 patients underwent on-pump CABG. Anesthesia was induced with 0.50 µg/kg remifentanyl, 0.10 mg/kg midazolam, 3.00 mg/kg thiopental, and 0.90 mg/kg rocuronium. The patients were maintained with 0.25-0.50 µg/kg/h remifentanyl and a 3.00-6.00 mg/kg/h propofol infusion via median sternotomy. Then, aortic cannulation was introduced, and a single right atrial cannula was inserted and connected to a membrane oxygenator (Dideco Avant 903). A single cross-clamp was placed on the aorta, and retrograde blood cardioplegia was performed every 15 min via the coronary sinus. A roller pump was used, and mild systemic hypothermia was maintained (32-34°C). After CPB, heparin sodium was antagonized with protamine sulfate at the ratio of 1 mg protamine sulfate/1 mg heparin. The preferred inotropic agents included dopamine, adrenaline, noradrenaline, and an intra-aortic balloon pump. The preferred vasodilator was nitroglycerin; when necessary, it was followed by sodium nitroprusside. Oxygen was continuously delivered to all patients in the intensive care unit at the rate of 3 l/min via a nasal cannula and was administered intermittently when oxygen saturation decreased below 95%. Cross-clamp time, CPB time, and the use of blood and blood products were also considered.

Statistical analysis

Data analysis was performed using Windows SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive variables with continuous measurements (e.g., age, OAB) are expressed as mean ± standard deviation, while case number (%) is used for categorical variables (e.g., B-SIT scores). A paired-samples *t*-test was used to compare the averages of repetitive continuous variables. The significance of the difference between categorical variables was analyzed using a χ^2 test. Pearson's correlation test was used for normally distributed variables. A *p* value < 0.05 was considered statistically significant.

Results

Forty-five patients were prospectively included in this study. Their mean age was 67 ± 7.55 years, and 29% were male. The mean cross-clamp and CPB times were 54 ± 32 min and 62.5 ± 37.0 min, respectively. Other patient demographics and clinical characteristics are presented in Table I. No patient features were lower compared to the preoperative baseline characteristics. One patient who was unwilling to participate in the study, four patients with previous surgical treatment for nasal polyposis, three patients who developed postoperative septicemia, and one patient with prolonged intubation were excluded from the study. Evaluation of olfactory memory was established using the B-SIT test on d1 and d3, using the preoperative test results as the baseline. Significant differences were observed for several odors: leather between d0 and d3, pine between d0 and d3,

onion between d0 and d1, onion between d0 and d3, and soap between d0 and d1. The postoperative CRP levels were significantly higher than the preoperative levels. The Pearson correlation analysis demonstrated that the CRP levels were negatively correlated with the B-SIT score ($r = -0.48$, $p = 0.001$) (Fig. 1).

Discussion

Olfactory dysfunction after CABG may result in decreased appetite leading to weight loss, malnutrition, and impaired immunity [6, 7]. In older patients, poor nutrition is a common problem [8]. A decreased appetite can worsen co-morbidities in these patients. Nutrition is becoming more significant because of the increased number of older patients undergoing CABG.

The first-order neurons of the olfactory system are located in the nasal mucosa [9]. A clear nasal passage is a prerequisite for normal olfactory function [10]. Inflammation of the olfactory epithelium also affects olfactory function in addition to mechanical obstruction [11]. Nasal inflammation due to allergic, viral, or bacterial etiology is the most common cause of olfactory dysfunction in the general population [12, 13]. Sultan *et al.* [14] used a transgenic mouse model of olfactory inflammation induced by tumor necrosis factor α (TNF- α) to examine the effect of systemic inflammation on olfactory function. They reported that TNF- α caused physiological dysfunction in olfactory neurons. Some studies indicated that not only inflammation but also emotional status may influence olfactory function. For example, Zald *et al.* demonstrated that olfactory function is strongly associated with emotion [15]. The emotional condition of our patients may have affected the test responses in this study.

C-reactive protein is another marker for inflammation and an acute-phase reactant. Ramlawi *et al.* [16] found that the incidence of neurocognitive deficiency after CABG was significantly associated with CRP elevation. They claimed that increased CRP was not the cause of brain injury, but rather was triggered in response to brain injury. Some argue that cognitive dysfunction after CPB is a cerebral inflammatory phenomenon [17, 18]. Similarly, we detected that the postoperative CRP levels were significantly higher than the preoperative levels in all patients. We also found that the postoperative CRP levels were higher in patients with olfactory dysfunction. We believe that these inflammatory markers might have played an important role in the development of olfactory dysfunction in our study population.

The B-SIT test was developed as a useful tool to measure odor identification deficits. The test is a brief, easily administered, and convenient instrument derived from the 40-item University of Pennsylvania Smell Identification Test. Many tests have been used previously for the evaluation of olfactory function. The evaluation of the olfactory function of patients, based on odor recognition, is the most important part of the test. Previous studies have shown that B-SIT has a sensitivity and specificity of 82%. Therefore, the present study employed it to ensure appropriate

Tab. I. Baseline and clinical characteristics of study group

Factor*	n (%)
Number of patients (n)	45
Age (years)	67 \pm 7.55
Male	29 (64.4)
Female	16 (35.6)
Diabetes mellitus	21 (46.7)
Smoking	16 (35)
β -blocker use	20 (44.4)
ACE or ARB use	22 (48.9)
Calcium channel blocker use	11 (24.4)
Antihyperlipidemic therapy	19 (42.2)
Ejection fraction (%)	49 \pm 9.29
Body mass index (kg/m ²)	25.0 \pm 5.5
Cross clamp time (min)	54 \pm 32
CPB time (min)	62.5 \pm 37
Number of vessels	3.5 \pm 1.15
Number of patients requiring inotropic support	10 (22)
Erythrocyte suspension	6.5 \pm 4.9

*Values are expressed as mean \pm SD or n (%).

ACE – angiotensin-converting enzyme inhibitor, ARB – angiotensin receptor blockers, CPB – cardiopulmonary bypass

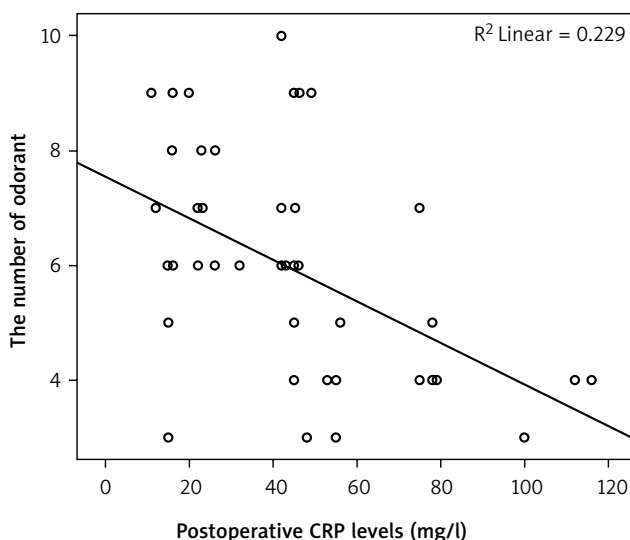


Fig. 1. The Pearson correlation analysis demonstrated that the CRP levels were negatively correlated with the B-SIT score

odor evaluation. The study revealed that the postoperative CRP levels were statistically significantly negatively correlated with the B-SIT score.

Our results suggest that increased postoperative CRP levels are associated with the development of olfactory dysfunction. Additionally, our findings suggest that patients after CABG are prone to develop olfactory dysfunction in the early postoperative period.

The first limitation of this study was the lack of a control group. Secondly, the test protocol involved making a com-

pulsory choice from four options, leaving a 25% chance that the patient chose the correct answer at random. Diabetes mellitus influencing the inflammatory status and the learning effect may also have affected our results. Finally, we evaluated CRP levels as the only parameter of inflammation; we did not use other inflammation markers.

To our knowledge, this is the first study to evaluate the olfactory function in patients undergoing CABG. It revealed that olfactory dysfunction may occur during the early postoperative period after CABG and that this condition is associated with postoperative CRP levels.

Disclosure

Authors report no conflict of interest.

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