Nonthyroidal illness syndrome in off-pump coronary artery bypass surgery

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Abstract

Objective: It is well known that coronary artery bypass grafting (CABG) is often the cause of non-thyroidal illness syndrome (NTIS). Non-thyroidal illness syndrome (NTIS) is a state characterized by low levels of tri-iodo-thyronine (T3) and high levels of reverse T3 (rT3), with normal or low levels of thyroxin (T4) and normal, low-normal, or low levels of thyroid-stimulating hormone (TSH). Today, there are two main techniques of CABG: CABG with the use of cardiopulmonary bypass (on-pump coronary artery bypass - ONCAB) and CABG without the use of cardiopulmonary bypass (off-pump coronary artery bypass OPCAB), or 'beating-heart surgery.' The OPCAB technique is considered to be less invasive. We prospectively investigated the influence of these surgical techniques on the occurrence of NTIS.

Methods: Serum levels of free fractions of thyroid hormones (FT3 and FT4) and TSH were analyzed in 70 consecutive patients subjected to CABG surgery, using the ONCAB technique in 36 patients and OPCAB technique in 34 patients. The measurements of hormone levels were performed prior to surgery and 12 hours and 14 days after surgery.

Results: The basic, the early, and the late postoperative serum levels of FT3 ($p=0.458$, $p=0.632$, $p=0.869$, respectively), FT4 ($p=0.664$, $p=0.301$, $p=0.417$, respectively), and TSH ($p=0.249$, $p=0.058$, $p=0.324$, respectively) were similar in both groups. The levels of FT3 and TSH were significantly lower 12 hours after surgery ($p<0.0001$, $p<0.0001$, respectively), and the FT4 levels rose at the same time ($p<0.0001$). The third measurement showed the return of all investigated parameters back to physiological levels, although they were still not precisely within the initial values.

Conclusion: NTIS occurs significantly in patients subjected to CABG. Although the OPCAB technique is considered to be less invasive, its impact on the occurrence of NTIS does not differ significantly from the ONCAB technique. *(Anatol J Cardiol 2015; 15: 836-42)*

Keywords: off-pump coronary artery bypass, non-thyroidal illness syndrome, coronary artery bypass grafting, cardiac surgery, thyroid

Introduction

Non-thyroidal illness syndrome (NTIS) is a state characterized by low levels of tri-iodo-thyronine (T3) and high levels of reverse T3 (rT3), with normal or low levels of thyroxin (T4) and normal, low-normal, or low levels of thyroid-stimulating hormone (TSH) (1-4). NTIS is seen in prolonged starving, sepsis, myocardial infarction, cardiac and non-cardiac surgery, acute respiratory distress syndrome, bone marrow transplantation, trauma, severe burns, shock of various origins, and other serious diseases. The most information regarding NTIS in cardiac surgery is obtained during the research of NTIS in coronary artery bypass grafting (CABG). CABG is a considerable stress for the patient and can cause the occurrence of NTIS in a significant number of patients subjected to this kind of surgery (5, 6). It is performed using two basic techniques: CABG with the use of cardiopulmonary bypass (on-pump coronary artery bypass-ONCAB) and CABG without the use of cardiopulmonary bypass (off-pump coronary artery bypass- OPCAB). OPCAB has some advantages, because it reduces the need for blood transfusions, it is associated with shorter mechanical ventilation time, a smaller amount of cardiac enzymes is released (7, 8), and for older patients, the risk of postoperative complications is smaller (9, 10). The use of cardiopulmonary bypass was considered for a long time to be the cause of NTIS, because of hemodilution, non-pulsatile blood flow, systemic heparinization, and hypothermia (11, 12). In order to find the frequency of occurrence of NTIS in patients subjected to CABG and investigate whether the use of cardiopulmonary bypass (CPB) increases the occurrence of NTIS in cardiac surgery, we analyzed 70 patients subjected to CABG, with or without the use of CPB.

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Table 1. Characteristics of patients in relation to the operative technique

		Operative technique		
		ONCAB	OPCAB	*P*
Age, years	$\bar{x}$±SD	59.9±4.92	57.8±5.79	0.116[a]
Gender (n, %)	M	24 (70.6%)	33 (91.7%)	0.050[b]
	F	10 (29.49%)	3 (8.3%)	
Smoking (n, %)	No	20 (58.8%)	22 (61.1%)	1.000[b]
	Yes	14 (41.2%)	14 (38.9%)	
Arterial hypertension (n, %)	No	7 (20.6%)	6 (16.7%)	0.909[b]
	Yes	27 (79.4%)	30 (83.3%)	
Dyslipidemia (n, %)	No	16 (47.1%)	15 (41.7%)	0.831[b]
	Yes	18 (52.9%)	21 (58.3%)	
Diabetes mellitus (n, %)	No	18 (52.9%)	24 (66.7%)	0.354[b]
	Yes	16 (47.1%)	12 (33.3%)	
Coronary disease type (n, %)	Single-vessel	2 (2.9%)	9 (12.9%)	<0.0001[b]
	Double-vessel	3 (4.3%)	10 (14.3%)	
	Triple-vessel	31 (44.3%)	15 (21.4%)	
Number of grafts (n, %)	One	2 (2.9%)	6 (8.6%)	<0.0001[b]
	Two	2 (2.9%)	6 (8.6%)	
	Three	21 (30%)	18 (25.7%)	
	Four	10 (14.3%)	0	
	Five	1 (1.5%)	0	

F - female; M - male; ONCAB - number of patients operated on using on-pump coronary artery bypass technique; OPCAB - number of patients on operated using off-pump coronary artery bypass technique; SD - standard deviation.
Parameters are displayed as mean value and standard deviation and in absolute numbers; [a] - t-test and [b] - chi-square test

Methods

A prospective study was conducted on 70 patients subjected to CABG: 34 patients operated on using OPCAB and 36 patients operated on using the ONCAB technique. The inclusion criteria were: patients subjected to CABG, both sexes, age 50-70, with normal thyroidal hormonal status at the beginning of the study, those who, according to anamnesis and medical documentation, did not suffer from thyroidal disorders or receive replacement hormonal therapy or thyrostatic agents, and those who prior to and during the study did not receive amiodarone or any other drug that might significantly affect the occurrence of NTIS.

The research was approved by the Ethical Committees in the institutions in which the research was conducted.

The blood samples were obtained upon hospital admission, 12 hours after surgery, and 14 days after surgery. Each sample was stored at 4°C up until the centrifugation. Within 6 hours, the centrifugation was performed at 3000 rpm during 15 minutes. The serum was separated by suction and then frozen at -20°C until the time of analysis. The levels of FT3, FT4, and TSH were measured in each sample. All chemical analyses for FT3, FT4, and TSH were performed using radio-immunoassay (RIA) by IMMUNOTECH on a Wizard 1470 Automatic Gamma Counter. Reference values were: FT3 from 3.4 to 8.5 pmol/L, FT4 from 10 to 25 pmol/L, TSH from 0.3 to 4.0 mIU/mL. Besides thyroid hormone levels, the age and gender of the patients were also analyzed, as were smoking, hypertension, dyslipidemia, diabetes mellitus (DM), EuroSCORE values, and the amount of time spent in the intensive care unit (ICU).

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences for Windows (version 20.0 SPSS Inc., Chicago, IL, USA). Within the descriptive statistical analysis, the qualitative variables were displayed as frequencies or percentages. Tests of normality that were used were Kolmogorov-Smirnov and Shapiro-Wilk. Quantitative variables are displayed as mean values with standard deviations or medians with interquartile ranges, depending on data distribution. For testing the hypothesis between the two independent groups (OPCAB and ONCAB), the t-test and Mann-Whitney U test were used, depending on distribution, and for repeated measurements with one factor, repeated-measures ANOVA or an alternative non-parametric Friedman test was applied. For the analysis of categorical variables, the relation between the predictors and the quantitative outcome parameters (dependent variable-NTIS) was shown by chi-square independence test (2x2 or 2xk). For statistical significance of the 'p' value, the usual level of significance of 'p<0.05' was chosen.

Results

Basal characteristics

The basic characteristics of the patients in the study are displayed in Table 1. Patients with single- or double-vessel coronary disease were treated much more often by OPCAB, and those with triple-vessel coronary disease were more often treated by ONCAB (p=0.001). Patients who received four or five grafts were operated on exclusively using the ONCAB technique, which is also the case in the majority of the patients who received three grafts. On the other hand, patients who were operated on using OPCAB significantly more often received one or two grafts (p=0.0001). In both groups (OPCAB and ONCAB), male patients were the majority. There were no other significant differences between the groups. Regarding the ejection fraction, although there was a numerical tendency that the OPCAB group had a better left ventricular ejection fraction and that ONCAB patients were more diverse in this parameter, there was no significant difference between the groups: the OPCAB group had an LVEF of 46.23%±10.14, and the ONCAB group had an LVEF of 42.37%±12.02 (p=0.47). Functional capacity was also similar

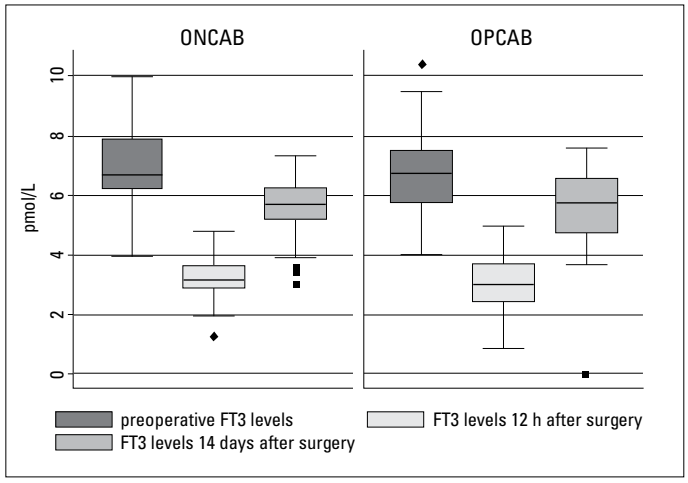

Figure 1. FT3 levels measured before surgery, 12 hours after surgery, and 14 days after surgery among patients operated using ONCAB and the patients operated using OPCAB technique

FT3 - free fraction of tri-iodothyronine; ONCAB - patients operated on using on-pump coronary artery bypass technique; OPCAB - patients operated on using off-pump coronary artery bypass technique

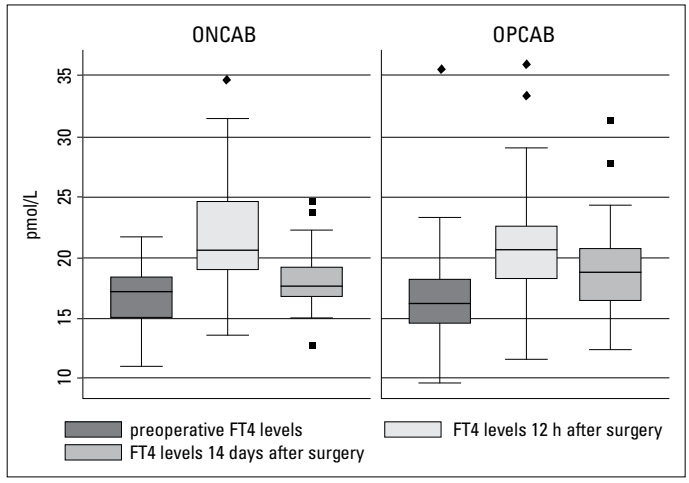

Figure 2. FT4 levels measured before surgery, 12 hours after surgery, and 14 days after surgery among patients operated using ONCAB and the patients operated using OPCAB technique

FT4 - free fraction of thyroxine; ONCAB - patients operated on using on-pump coronary artery bypass technique; OPCAB - patients operated on using off-pump coronary artery bypass technique

between the groups: NYHA I was the functional capacity of both patient groups.

Hormone profile

There were statistically significant changes of FT3, FT4, and TSH levels during the study ($p<0.0001$) but without significant differences in average serum levels of these hormones between the patient groups (ONCAB and OPCAB) (Fig. 1, Fig. 2, Fig. 3).

Basal values of FT3 were in the physiological range of 6.68±1.43 pmol/L in ONCAB and 6.92±1.26 pmol/L in the OPCAB group (p=0.458). FT3 levels significantly decreased at 12 hours after surgery: 3.02±1.02 pmol/L in ONCAB and 3.12±0.68 pmol/L in the OPCAB group (p=0.632). On the 14th day after surgery, they were again in the physiological range, with 5.74 (4.70-6.55) pmol/L in ONCAB and 5.70 (5.00-6.20) pmol/L in the OPCAB group (p=0.869), but still did not strictly reach preoperative values (Fig. 1).

Basal values of FT4 were in the physiological range of 16.12 (14.34-18.23) pmol/L in ONCAB and 17.11 (14.92-18.47) pmol/L in the OPCAB group (p=0.664). FT4 levels rose significantly at 12 hours after surgery: 20.68 (18.18-22.70) pmol/L in ONCAB, and 20.58 (18.80-24.70) pmol/L in the OPCAB group (p=0.301), although in fact only a small number of patients had an increase of these values above the physiological range. On the 14th day after surgery, they were in the physiological range, with 18.75 (16.13-20.61) pmol/L in ONCAB and 17.70 (16.65-19.26) pmol/L in the OPCAB group (p=0.417), but these, too, still did not strictly reach preoperative values (Fig. 2).

Serum levels of TSH remained within the physiological range but significantly varied during the study. Basal values of TSH were 2.27 (1.40-3.92) mIU/L in ONCAB and 2.00 (1.30-2.85) mIU/L in the OPCAB group (p=0.249). TSH levels decreased at 12 hours

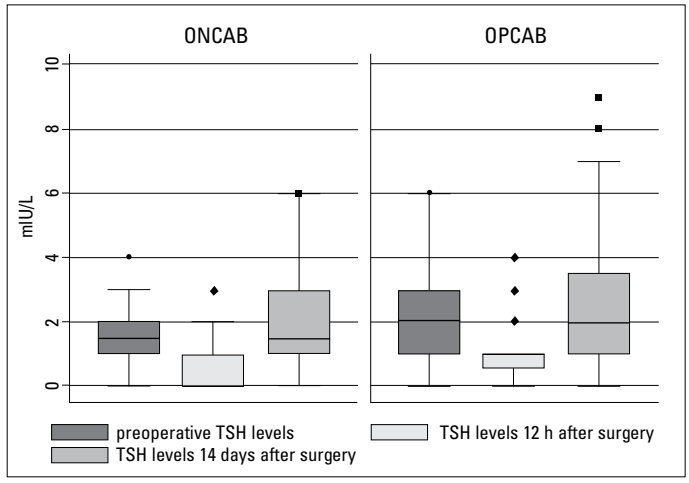

Figure 3. TSH levels measured before surgery, 12 hours after surgery, and 14 days after surgery among patients operated using ONCAB and the patients operated using OPCAB technique

ONCAB - patients operated on using on-pump coronary artery bypass technique; OPCAB - patients operated on using off-pump coronary artery bypass technique; TSH - thyroid-stimulating hormone

after surgery to 1.60 (0.92-1.98) mIU/L in ONCAB and 0.93 (0.65-1.66) mIU/L in the OPCAB group (p=0.058). On the 14th day after surgery, they were at 2.26 (1.63-4.27) mIU/L in ONCAB and 2.02 (1.47-3.51) mIU/L in the OPCAB group (p=0.324), which is insignificantly higher than prior to surgery (Fig. 3).

NTIS occurred after surgery in two-thirds of patients (Fig. 4). There was no significant difference in the occurrence of NTIS between the patients operated on with the use of CPB in comparison to those operated on the beating heart (Fig. 5).

Only the complexity of coronary disease had a significant impact on the occurrence of NTIS (p=0.016, Table 2), while an increased number of bypass grafts, higher EuroSCORE values, and longer periods of time spent in the ICU showed only a numerical tendency towards the occurrence of NTIS, but statis-

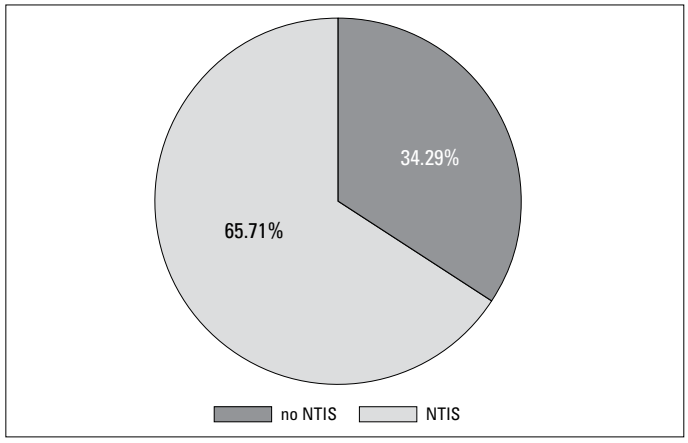

Figure 4. Occurrence of NTIS among operated patients
NTIS - non-thyroidal illness syndrome

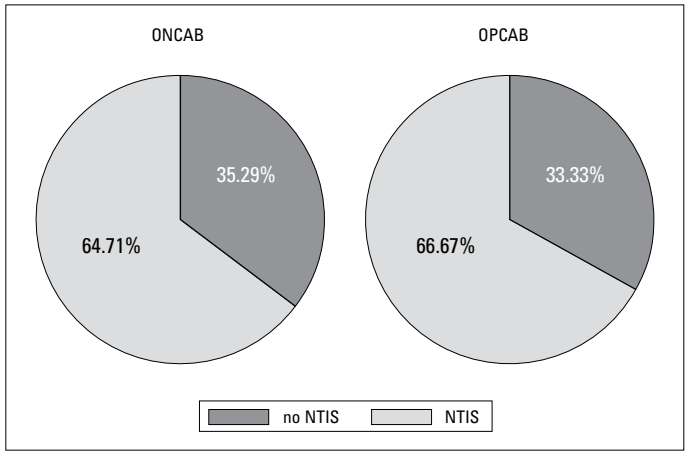

Figure 5. Occurrence of NTIS among patients operated using ONCAB and among patients operated using OPCAB technique
NTIS - non-thyroidal illness syndrome; OPCAB - patients operated on using off-pump coronary artery bypass technique

tical significance was not reached on a sample of this size. The investigated coronary disease risk factors had no influence on the occurrence of NTIS.

Discussion

Our results show that NTIS occurs in a significant number of patients subjected to CABG and that there is no difference in the incidence of NTIS between patients operated on using the OPCAB and ONCAB techniques. This is in concordance with the results of Cerillo et al. (6) and their study of 20 patients subjected to CABG with or without the use of CPB and following the levels of FT3, FT4, rT3, and TSH. Still, we emphasize that in our study, NTIS occurred in some two-thirds of patients, which is less than in the studies of other authors. A possible reason for this might be that we precisely determined the age group of 50-70-year-old patients, while patients in the other studies were up to 80 years of age and even older. Age is considered to be a well-known statistical confounder and can potentially be associated with adverse outcomes. We wanted to select the patients in whom age would have minimal or no impact on outcome and to try to isolate the factors outside of age that might affect the occurrence of NTIS. This is why we have chosen a relatively compact and uniform (regarding age) group of patients. We also had a sample of 70 patients, while the earlier studies of this subject were performed on smaller samples (5, 6, 13). The most common form of NTIS after CABG in our study was the one with a significant decrease of FT3, a mild (but statistically significant) decrease of TSH, which remained within the physiological range, and an increase of FT4 levels.

Most of the other studies followed NTIS through the intraoperative and a very early postoperative period, up to the 6th postoperative day (6, 13-15). In our study, we prolonged the time period of observation of our patients to 14 days, with the thyroid disorder found at 12 hours after surgery. As we can see from the research of Cerillo et al. (6), the levels of thyroid hormones did not reach the preoperative values. Therefore, there was no need to repeat such measurements, as we know that within 1 week, there will be no reversal of the thyroid hormone levels to preoperative values. We therefore wanted to observe if the patients would recover their thyroid function completely after a period of twice as long as that. As the patients in our hospital come to

Table 2. Occurrence of NTIS in relation to perioperative risk, the complexity of postoperative recovery, and coronary disease risk factors

		Operative technique		
		No NTIS	NTIS	*P*
ICU, days	M±IQ	1 (1-2)	1 (1-2)	0.753[a]
EuroSCORE	M±IQ	1 (0-3)	1 (0-6)	0.985[a]
Smoking (n, %)	No	17 (70.8%)	25 (54.3%)	0.280[b]
	Yes	7 (29.2%)	21 (45.7%)	
Arterial hypertension (n, %)	No	2 (8.3%)	11 (23.9%)	0.205[b]
	Yes	22 (91.7%)	35 (76.1%)	
Dyslipidemia (n, %)	No	10 (41.7%)	21 (45.7%)	0.948[b]
	Yes	14 (58.3%)	25 (54.3%)	
Diabetes mellitus (n, %)	No	15 (62.5%)	27 (58.7%)	0.959[b]
	Yes	9 (37.5%)	19 (41.3%)	
Coronary disease type (n, %)	Single-vessel	7 (29.1%)	4 (8.7%)	0.016[b]
	Double-vessel	1 (4.2%)	12 (26.1%)	
	Triple-vessel	16 (66.7%)	30 (65.2%)	
Number of grafts (n, %)	One	4 (16.7%)	4 (8.7%)	0.211[b]
	Two	6 (25%)	14 (30.4%)	
	Three	12 (50%)	19 (41.3%)	
	Four	1 (4.2%)	9 (19.6%)	
	Five	1 (4.2%)	0 (0%)	

EuroSCORE - European System for Cardiac Operative Risk Evaluation; ICU - intensive care unit; M±IQ - median±interquartile range; NTIS - non-thyroidal illness syndrome
Parameters are displayed as n - absolute number and as percentage; [a]- Mann-Whitney U test; [b]- chi-square test

postoperative control examinations on the 14th day (2 weeks) after surgery (a practice established by our surgeons who copied it from the USA and Norway, where most of them were educated in cardiac surgery), we decided to take samples on that day. Since, in our country, we have very limited resources for this kind of research, we could not analyze the samples on each day in particular, but this one point in time seemed to be a logical option. Taking samples on a specific day after this did not seem to be very practical, because control examination schedules after this first postoperative control vary a lot according to the patient's individual condition. Although the levels of thyroid hormones (TH) on the 14th day postoperatively were back to physiological values, they still did not reach preoperative values, which illustrated the severity of the psycho-physical stress that this operation poses for our patients. Still, our results show that NTIS after CABG is a spontaneously reversible phenomenon. These findings are consistent with the earlier observations of NTIS in acute diseases (16) and have to be taken into account when considering the possibility of hormone replacement therapy.

Up until the 1990s, CABG was performed with the use of CPB; so, the earlier studies of NTIS in CABG were focused on CPB as the cause of NTIS during and after CABG. The earlier studies also investigated the effects of different ONCAB techniques on thyroid metabolism. A prospective study by Trush et al. (12) found similar differences of T3, T4, FT3, rT3, and TSH levels in two groups of patients subjected to normothermic and hypothermic ONCAB surgery, which showed that the normothermic technique does not prevent the occurrence of NTIS. Silitreli et al. (11) reported that pulsatile perfusion does not prevent the occurrence of NTIS in comparison to non-pulsatile blood-flow. Somewhat different results were published by Akçevin et al. (17) in the study of pediatric patients subjected to cardiac surgery of congenital heart disease with the use of CPB, where pulsatile perfusion during the operation had a certain protective effect on TH homeostasis in comparison to the non-pulsatile technique.

Although our study was a prospective one, the patients were not randomized to OPCAB or ONCAB, because the decision was made by the cardiac surgeon, taking into account the patient's age, severity of coronary disease, and especially the compromise of the circumflex coronary artery. As a result, the number of diseased arteries and the average number of bypass grafts were smaller in the OPCAB group. This was the limitation of our study that we could not have influenced because of the existing guidelines that surgeons had to follow and the potential benefits for the patients. Our study showed that more complex coronary disease, a larger number of bypass grafts, higher EuroSCORE values, and a longer time period spent in the ICU have a numeric tendency to be associated with NTIS, although the statistical significance in this regard was reached only by the complexity of coronary disease ($p<0.01$).

In our study, patients undergoing ONCAB had more extensive coronary artery disease than the OPCAB patients; yet, there was no difference in thyroid hormone levels. Although we did not observe a difference between ONCAB and OPCAB, this may have been influenced by the different extents of coronary artery disease. Therefore, the question arises if we can safely conclude that the two techniques are equivalent. Maybe we can speculate that ONCAB is more protective, given the fact that more complex coronary disease was associated with more NTIS; yet, ONCAB patients did not have an increased NTIS occurrence, although the patients on ONCAB surgery had more extensive coronary disease. However, real-life situations are not randomized studies, and surgeons clearly show their preferences according to patient characteristics regarding the selection of patients for these particular modalities of treatment. In this regard, when a surgeon chooses appropriately, it can be expected regarding the OPCAB or ONCAB technique that there will be no difference in the occurrence of NTIS.

On the other hand, Cerillo et al. (6), in their study report, expected their patients with less severe coronary disease who undergo less invasive surgery to show smaller alterations of their thyroid metabolism in comparison to those with more severe disease, but this did not happen. We assume that the cause of this might be the sample size.

Inotropic agents were used in our study, which is especially important, because dopamine inhibits TSH secretion directly, depresses the already abnormal thyroid hormone production further, and induces significant worsening of the low hormone levels. However, dopamine is relatively rarely given today in our intensive care unit in the role of inotropic support. It is mostly administered in cases of impaired renal function. In our sample, which consisted of patients who were not too old and had relatively favorable renal status, we recorded the administration of dopamine in two cases in the ONCAB group and one case in the OPCAB group. The groups were similar regarding dopamine administration. Dobutamine is the primary inotrope in our hospital and is given more frequently; it was administered in seven patients in the ONCAB group and five patients in the OPCAB group. The groups were not significantly different in this regard, either.

Cardiac surgery exerts its influence on NTIS occurrence as a stressful event, working over the immunological and neuroendocrine response by an increased secretion of catecholamines, glucocorticoids, and cytokines, which have their effects at various levels, causing the occurrence of NTIS (18-23). By inhibiting the peripheral conversion of T4 to T3 (reduced activity of 5'-mono-deiodinase), the levels of serum T3 and FT3 are decreased (24-26). The increased levels of FT4 can not be disregarded, either, and Affandi et al. (27) report from their study that the cause of this is the effects of serum proteases, which split thyroxine-binding globulin (TBG) and lead to a significant increase in FT4 concentrations. The levels of serum TSH within the physiological range, despite the low FT3, must be considered abnormal, because it demonstrates the inability of normal hormonal regulation by the negative feed-back mechanism (2, 28, 29). It is assumed that the mechanisms leading to NTIS exert their effects on several levels at the same time: blocking 5'-monodeiodinase, changing the hypothalamic-hypophyseal axis, sus-

taining the TSH in its physiological range or suppressing it, inhibiting TH synthesis at the thyroid level by inhibiting thyroid peroxidase (TPO) and thyroglobulin (Tg) genes, and possible effects on transport proteins and TH receptors (1, 2, 21, 26, 27, 30).

Considering that we had a relatively homogenous, younger group of patients, that these were elective cases, and that the average EuroSCORE was 1.6, we can say that our study investigated the real impact of this kind of surgery on the occurrence of NTIS, thus avoiding the effects of older age, comorbidities, and drug use, which can all independently lead to changes in thyroid metabolism. We assume that if the study had included older patients and/or those with high EuroSCORE values, the results might show more severe forms of NTIS, with lower levels of TSH and probably also FT4. This kind of study would demand a longer follow-up time and, in cases of prolonged NTIS, might also demand a reconsideration of hormone replacement therapy. Based on the assumption that NTIS associated with CABG can decrease left ventricular function postoperatively, T3 has sometimes been introduced in cardiac surgery patients, but the results of most studies by several authors denounced the benefits of hormone replacement therapy (13, 31-33). Still, the studies up to now were mostly short-term, and to clarify which patients can actually benefit from hormone replacement therapy, long and long-term prospective studies are necessary (2). Perhaps the best advice regarding the replacement treatment options in NTIS was given by De Groot (34): since low T3 alone has not been shown to correlate with bad outcome, one depends on a low free T4 as the test. De Groot suggests (34) that any free T4 level clearly below normal in this setting brings up a possible treatment-more urgently as T4 becomes lower. In our own research, we observed a rise of free T4, which did not necessitate replacement therapy in our patients. In addition to that, a study performed by Velissaris et al. (35), while obtaining results similar to our own (OPCAB associated with thyroid hormone changes similar to ONCAB), suggests further studies on T3 administration during OPCAB.

Study limitations

The study had several limitations. The sample was precisely chosen to be between the ages of 50 to 70. A sample with a wider age spectrum might have been a more diverse one, but in that case, we can not exclude age being one of the contributing factors in the occurrence of NTIS. A larger sample in general would have had a higher accuracy and more precise results. Also, the sample was pretty uniform regarding the EuroSCORE properties. A sample with more patients with unfavorable EuroSCORE values could show the significance of the EuroSCORE value on the occurrence of NTIS. The similar might be said if the sample could have included more patients with severe left ventricular dysfunction. Although we did not observe a difference in the occurrence of NTIS between ONCAB and OPCAB, there was a significant difference in the occurrence of NTIS regarding the complexity of coronary disease. The fact is that more complex coronary disease was associated with more NTIS; yet, ONCAB patients did not have an increased NTIS occurrence, although they had more extensive coronary disease. So, there is still a dilemma if we can safely conclude that the two techniques are equivalent. But, even if we speculate that ONCAB is theoretically more protective regarding NTIS, surgeons will still be guided in the selection of their patients for a particular technique by patient characteristics and appropriate guidelines. In these real-life circumstances, when surgeons choose appropriately, it can be expected that there will be no difference in the occurrence of NTIS between the OPCAB and ONCAB techniques. These remarks might be a guideline for a new future study.

Conclusion

NTIS occurs in a significant number of patients subjected to CABG. The most common form of NTIS after CABG is the one with a significant decrease in FT3, a mild (but statistically significant) decrease of TSH, which remains within the physiological range, and an increase in FT4 levels. There is no difference in the occurrence or in the severity of NTIS between OPCAB and ONCAB patients. The occurrence of NTIS is more common among patients with more complex forms of coronary disease. NTIS after CABG is a reversible phenomenon, from which patients typically recover without the need to administer substitution therapy.

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Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - S.C., J.C.; Design - J.C., E.O.; Supervision - J.C., E.O.; Resource - J.C., S.C.; Materials - S.C.; Data collection &/or processing - S.C.; Analysis &/or interpretation - S.C., E.O.; Literature search - J.C., S.C.; Writing - S.C., J.C.; Critical review - J.C., S.C.

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