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ORIGINAL ARTICLE

Influence of subclinical hypothyroidism on early outcome of patients undergoing CABG surgery

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ABSTRACT

Background: Subclinical hypothyroidism is associated with elevated TSH with normal T3 and T4 levels. Its effect on cardiac surgery outcome is controversial. Some authors revealed adverse outcome in form of arrythmia and congestive heart failure. This study aimed to investigate the effect of subclinical hypothyroidism on early outcome of patients undergoing coronary artery bypass graft (CABG) surgery.

Methods: This study included 27 patients with subclinical hypothyroidism subjected to elective CABG surgery (Group A) and group B that contained 27 patients with normal thyroid function. Both groups were followed up for one month postoperative regarding operative mortality and postoperative outcomes.

Results:
Cases required prolonged mechanical ventilation and postoperative inotropic support were significantly higher among the SCH group compared to the euthyroid group (p=0.024, 0.018 respectively). The occurrence of postoperative AF and the respiratory complications was significantly higher in SCH group in comparison to the euthyroid group (p=0.039, 0.022 respectively). Mortality was recorded in only one case of SCH group and in 2 cases of the euthyroid group (p=0.998).

Conclusion: SCH is associated with increased postoperative AF, need for inotropic support and prolonged mechanical ventilation. Preoperative assessment of thyroid functions is recommended to be performed routinely before surgery.

Keywords: Coronary artery bypass graft (CABG); Subclinical hypothyroidism (SCH); Atrial fibrillation (AF)

INTRODUCTION

Altered thyroid function including hypothyroidism or hyperthyroidism is known to be associated with adverse postoperative outcome after cardiac surgery and preoperative control of thyroid function is necessary [1]. Subclinical hypothyroidism (SCH) is a frequent disorder that is associated with elevated serum thyroid-stimulating hormone (TSH) level with normal T3 and T4 [2]. SCH is considered as a risk factor for congestive heart failure, atrial arrythmia and coronary artery disease [3,4].

However, the effect of subclinical hypothyroidism on outcome of patients underwent coronary artery bypass graft (CABG) surgery is still controversial. Park et al. found that it might increase transient atrial fibrillation (AF) post CABG patients [3]**.** Other reports did not find significant difference in the effect of SCH on postoperative CABG patients [5]. In addition, controversies are still present about ideal management of patients having subclinical hypothyroidism and prepared for CABG surgery [6]. In this study, we aimed to investigate the effect of subclinical hypothyroidism on early outcome of patients undergoing CABG surgery.

PATIENTS AND METHODS

Study design and patient selection:

This is a prospective case-control study that was carried out during the period from June 2018 to May 2021. It included 27 patients with SCH (TSH level above 4mIU/l with normal FT4 and FT3 levels) subjected to elective CABG surgery (Group A) that was matched 1:1 with group B that contained 27 patients with normal thyroid function Fig 1. Exclusion criteria included: (1) patients with preoperative AF, (2) patients undergoing off-pump CABG surgery, (3) emergency CABG, (4) combined valve and CABG surgery. All participants signed an informed consent before enrolling in the study. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Tanta University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Medical history and preoperative evaluation:

All patients enrolled in this study underwent complete history taking including age, gender, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), history of myocardial infarction (MI), history of renal dysfunction and history of cerebrovascular accident. BMI (body mass index) was calculated for all cases. Echocardiography was carried out for assessment of ejection fraction and the presence of wall motion abnormalities. Free thyroxin (T3), free triiodothyronine (T4), and TSH were assessed preoperatively using the enzyme-linked immunosorbent assay (ELISA) technique.

Operative procedure:

All patients in our study were subjected to on pump CABG surgery through median sternotomy under cardiopulmonary bypass. Left internal mammary artery (LIMA) was harvested and anastomosed to left anterior descending (LAD) and saphenous vein grafts were anastomosed to the remaining vessels. Cardiopulmonary bypass time and cross clamp time were recorded in all patients.

Postoperative outcomes:

All patients, in this study, were followed up for operative mortality that is considered during hospitalization or within 30 days of operation due to cause related to operation. Postoperative mechanical ventilation more than 24 hours was recorded. Postoperative inotropic support, that is defined as a need for adrenaline, noradrenaline, dobutamine or dopamine ≥5 μg/kg/min, was considered. Occurrence of postoperative atrial fibrillation, postoperative acute renal failure, needed postoperative renal dialysis, re-exploration for bleeding, neurological insults, postoperative respiratory complications and wound infection were observed and recorded.

Statistical analysis:

Statistical analysis was carried out using Statistical Package for Social Science (SPSS version 26). Data were expressed in terms of frequencies and percentages for categorical variables and mean ± standard deviation (±SD) for continuous variables. Chi-square (X2) and Fischer exact tests were applied for

comparing categorical variables, whereas student's t-test was used for comparing means of continuous variables. A logistic regression model was performed to calculate the probability of each patient and determine the propensity matching score. P values of <0.05 were considered statistically significant.

RESULTS

According to the preoperative TSH and T4 levels, cases were categorized into 2 groups. SCH patients (Group A; 27 cases) and euthyroid patients (Group B; 27 cases) as the control group. The preoperative and operative data are illustrated in table 1. T3, T4 and TSH levels of both groups are represented in Fig 2. Cases required prolonged mechanical ventilation were higher among the SCH group compared to the euthyroid group (29.6% versus 3.7%; p=0.024).

Asignificant relation was detected between the need for postoperative inotropic support and SCH, as 48.1% of SCH group needed postoperative inotropic support compared to only 4.8% of the euthyroid group (p=0.018). The incidence of postoperative AF was also significantly higher in SCH group (33.3%) compared to the euthyroid group (7.4%) [p=0.039]. Also, the incidence of respiratory complications was significantly higher in SCH group (25.9%) in comparison to the euthyroid group (3.7%) [p=0.022].

However, there were no significant differences in the incidence of postoperative neurologic insult, re-exploration for bleeding, postoperative acute renal failure and postoperative wound infection between both groups (p=0.998, 1, 0.669, 0.997 respectively). As regards mortality, it was detected in only one case (3.7%) of SCH group and in 2 cases (7.4 %) of the euthyroid group (p=0.998). The postoperative patients' outcomes in both groups are summarized in table 2.

Table 1: Preoperative and operative patients' characters in both groups.

	Total N=54	Subclinical hypothyroidism Group A N=27 (%)	Normal thyroid Group B N=27 (%)	P value
Age (years) mean± SD		56.37± 5.93	55.48±6.37	0.598
Gender				
Male	34	16 (60)	18 (54)	0.622
Female	20	11 (40)	9 (46)	
BMI mean± SD		28.72±2.89	28.96±2.51	0.712
Medical history				
Hypertension				
Yes	40	22 (81.5)	18 (66.7)	0.214
No	14	5 (18.5)	9 (33.3)	
Diabetes mellitus				
Yes	35	16 (59.3)	19 (70.4)	0.393
No	19	11 (40.7)	8 (29.6)	
History of cerebrovascular accident				
Yes	4	2 (7.4)	2 (7.4)	1
No	50	25 (92.6)	25 (92.6)	
History of renal dysfunction				

Yes	3	2 (7.4)	1 (3.7)	0.522
No	51	25 (92.6)	26 (96.3)	
History of myocardial infarction				
Yes	27	12 (44.4)	15 (55.6)	0.414
No	27	15 (55.6)	12 (44.4)	
History of COPD				
Yes	13	6 (22.2)	7 (26.9)	0.101
No	41	21 (77.7)	20 (73.1)	
Hyperlipidaemia				
Yes	28	15 (55.6)	13 (48.1)	0.586
No	26	12 (44.4)	14 (51.9)	
Previous PCI				
Yes	11	6 (22.2)	5 (18.5)	0.114
No	43	21 (77.8)	22 (81.5)	
Ejection fraction (%) mean± SD		56.67±5.13	56.30±5.07	0.791
Intraoperative characteristics				
Cardiopulmonary bypass time (min) mean± SD		74.26±6.00	70.96±10.40	0.232
Aortic cross clamp time (min) mean± SD		49.30±6.77	50.48±7.49	0.542
Number of anastomoses mean± SD		2.89±0.70	2.96±0.71	0.700

BMI: body mass index, COPD: chronic obstructive pulmonary disease, PCI: percutaneous coronary intervention.

Table2: Postoperative patients' outcome in both groups.

	Total N=54	**Subclinical hypothyroidism Group A N=27 (%)**	**Normal thyroid Group B N=27 (%)**	**P value**
Prolonged mechanical ventilation				
Yes	9	8 (29.6)	1 (3.7)	**0.024***
No	45	19 (70.4)	26 (96.3)	
Need for postoperative inotropic support				
Yes	17	13 (48.1)	4 (14.8)	**0.018***
No	37	14 (51.9)	23 (85.2)	
Postoperative AF				
Yes	11	9 (33.3)	2 (7.4)	**0.039***
No	43	18 (66.7)	25 (92.6)	
Neurologic insult				
Yes	5	2 (7.4)	3 (11.1)	0.998
No	49	25 (92.6)	24 (88.9)	
Re-exploration for bleeding				
Yes	6	3 (11.1)	3 (11.1)	1
No	48	24 (88.9)	24 (88.9)	

Postoperative Acute renal failure				
Yes	8	4 (14.8)	2 (7.4)	0.669
No	46	23 (85.2)	25 (92.6)	
Postoperative wound infection				
Yes	5	2 (7.4)	3 (11.1)	0.997
No	49	25 (92.6)	24 (88.9)	
Respiratory complications				
Yes	8	7 (25.9)	1 (3.7)	**0.022***
No	46	20 (74.1)	26 (96.3)	
Mortality				
Yes	3	1 (3.7)	2 (7.4)	0.998
No	51	26 (96.3)	25 (92.6)	

* Significant (p value <0.05), AF: atrial fibrillation

Figure 1: Flowchart of patient selection

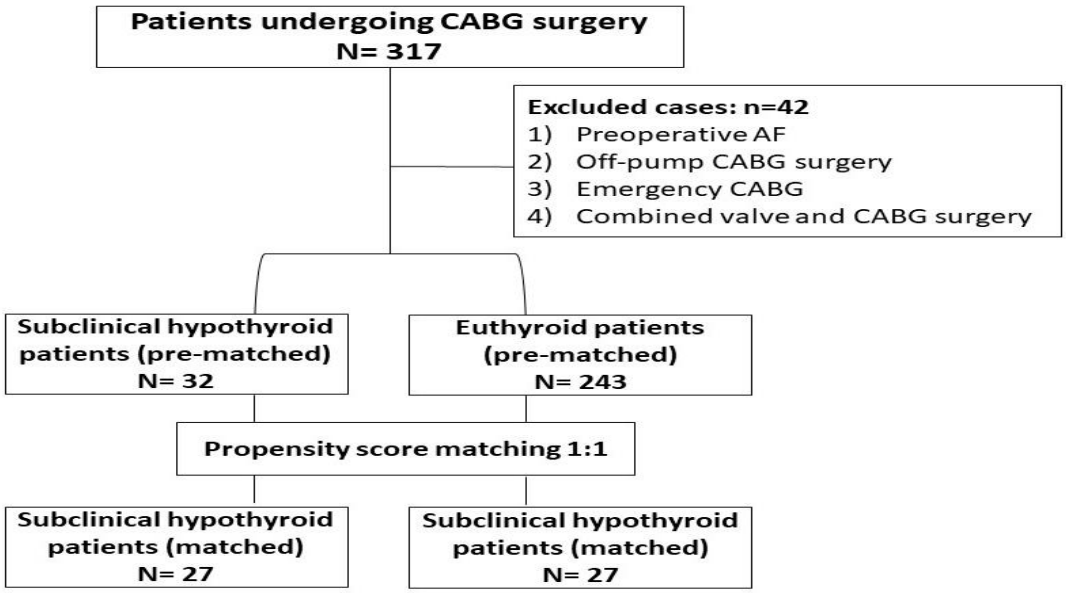
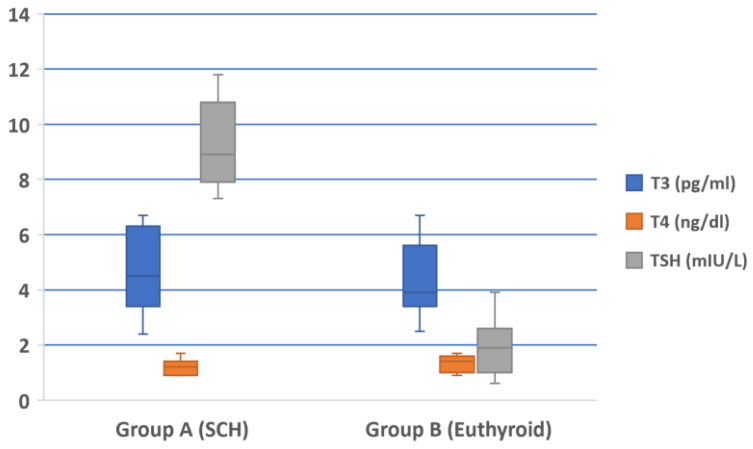


Fig 2: Serum levels of T3, T4 and thyroid stimulating hormone (TSH) levels in both groups. TSH showed significant difference between the studied groups (p<0.001). *SCH; subclinical hypothyroidism*



DISCUSSION

The effect of overt hypothyroidism on outcome of patients after cardiac surgery is well settled, and hypothyroidism is associated with myocardial depression and increased morbidity and mortality in females and old age after CABG surgery [7]. However, the effect of subclinical hypothyroidism is still debatable with many controversies about the best method for preoperative management of those patients.

Subclinical hypothyroidism is diagnosed based on normal free T4 level with moderate elevation of TSH level [8]. Elevated TSH is found to be associated with endothelial dysfunction through proliferation of vascular smooth muscles and release of inflammatory cytokines with formation of atheromatous plaques leading to atherosclerosis [9 10]. Ripoli et al. [11] studied the effects of subclinical hypothyroidism on myocardial function and found that subclinical hypothyroidism increased systemic vascular resistance and reduced end diastolic volume, leading to depression of the cardiac pump performance, compared to normal people.

In this study, we tried to investigate the effect of preoperative subclinical hypothyroidism on the early outcome of patients undergoing CABG surgery.

We reported statistically significant relationship between SCH and the incidence of postoperative AF. This is in accordance to the results of Park et al. [3], Worku et al. [12] and Jaimes et al. [13] who demonstrated an association between SCH and postoperative AF, but the sample size in their studies was small. Similar percentages of immediate postoperative AF in patients with SCH were also described in patients subjected to aortic valve replacement surgery [14].

In contrast to our results was the study of Zhao et al. [6] who found that the prevalence of postoperative AF was similar between patients with SCH and euthyroid patients and this was in agreement with Komatsu et al. [5] who demonstrated that hypothyroidism was associated with decreased occurrence of AF compared with euthyroidism taking in consideration that about half of patients in their study underwent valve surgery.

The mechanism of AF in patients with SCH is unclear; however, in vitro studies revealed that reduced intracellular calcium load in SCH is a phenomenon that is observed in arrhythmogenic ionic remodeling and is reported in animal and human models of AF [15]. Moreover, the administration of exogenous T3 was noted to decrease the occurrence of AF after CABG surgery [16].

We did not find, in our study, an effect of subclinical hypothyroidism on postoperative renal function, incidence of perioperative myocardial infarction or stroke. However, Park et al. [3] reported that preoperative SCH might affect CABG outcome if we considered the hemodynamic effects of AF in CABG patients. A study by Tarçın Ö et al. [1] summarized that there was no significant difference between the subclinical hypothyroid or hyperthyroid patients and the control group in terms of the postoperative morbidity and mortality, but they found an association between high EURO score and SCH suggesting the association of SCH with worse postoperative outcome. This finding gives an idea about the importance of preoperative detection of thyroid function before cardiac surgery.

In our study, we found that patients with SCH needed a higher dose of inotropic support than euthyroid patients after CABG. This is in accordance to Zhao et al. [6] who found patients with SCH required more doses and duration of inotropic support than euthyroid subjects. It is well settled that higher TSH level was associated with increased incidence of heart failure. This is because SCH is associated with impaired left ventricular systolic and diastolic function.

Besides, SCH is linked to increased arterial stiffness and altered endothelial function [17-19].

SCH was also found, in our study, to be associated with a longer mechanical ventilation time and increased postoperative respiratory infection but not the extent that could affect postoperative outcome or need for tracheostomy. This could be clarified by the fact that SCH is associated with neuromuscular dysfunction, impaired diaphragmatic muscle force and lowered forced vital capacity [20,21]. Similar results were found by Zheng et al. [22] who reported increased incidence of respiratory tract infection in female patients with SCH post CABG.

This study has some limitations; it was done on relatively a small number of patients. Thyroid function tests were not performed routinely postoperative in all patients. Preoperative control of SCH was not done in our study to avoid delaying patients needed surgery for revascularization.

From our study, we could conclude that SCH is associated with increased postoperative AF, need for inotropic support and prolonged mechanical ventilation. We recommend that preoperative measurement of thyroid function should be done routinely before surgery and patients with SCH should be subjected to strict medical control to avoid postoperative expected atrial fibrillation. Further studies may be needed on large number of patients with possibility of administration of postoperative replacement therapy in SCH patient with poor outcome.

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