

# Impact of Overt Hypothyroidism on Early Outcomes of Coronary Artery Surgery

**Dong Zhao**

Fuwai Hospital State Key Laboratory of Cardiovascular Disease

**Wei Zhao**

Fuwai Hospital State Key Laboratory of Cardiovascular Disease

**Xin Yuan**

Fuwai Hospital State Key Laboratory of Cardiovascular Disease

**Chuangshi Wang**

Fuwai Hospital State Key Laboratory of Cardiovascular Disease

**Wei Feng** (✉ [fengwei@fuwai.com](mailto:fengwei@fuwai.com))

Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

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## Research article

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# Abstract

**Background:** The association between preoperative overt hypothyroidism and early outcomes after coronary artery bypass grafting (CABG) is unclear. This study aimed to evaluate the influence of overt hypothyroidism on the outcomes of CABG.

**Methods:** The series included 189 overt hypothyroid patients who underwent CABG at Fuwai Hospital. These patients were 1:4 matched with 737 euthyroid patients using propensity score matching. The early postoperative outcomes were compared.

**Results:** After propensity score matching, the incidences of impaired wound healing, reintubation, and the total complications were higher in hypothyroid patients than euthyroid patients (11.8% vs. 0.9%,  $p<0.001$ ; 2.1% vs. 0.4%,  $p=0.03$ ; 39.6% vs. 30.3%,  $p=0.015$ , respectively). Multivariate analysis showed overt hypothyroidism was significantly associated with the occurrence of impaired wound healing (odds ratio [OR]=12.29,  $p<0.001$ ), reintubation (OR=5.71,  $p=0.047$ ), and the total complications (OR=1.31,  $p=0.049$ ). The OR of the total complications was 1.43 ( $p=0.03$ ) in hypothyroid patients with abnormal thyroid-stimulating hormone compared with euthyroid patients. The proportions of the use of dopamine, adrenaline, milrinone, and dobutamine in hypothyroid patients were higher than euthyroid patients (75.4% vs. 67.6%,  $p=0.038$ ; 10.7% vs. 6.1%,  $p=0.028$ ; 3.2% vs. 0.3%,  $p=0.001$ ; 4.8% vs. 1.2%,  $p=0.004$ , respectively). The total duration of inotropic support and mechanical ventilation time in hypothyroid patients were longer than euthyroid patients (median duration: 4 days vs. 3 days,  $p=0.003$ ; 17 hours vs. 15 hours,  $p<0.001$ , respectively).

**Conclusions:** CABG in overt hypothyroid patients is associated with a higher incidence of postoperative complications, stronger postoperative inotropic support, and longer mechanical ventilation time.

## Background

The thyroid function influences every structure of our body. Thyroid hormones have direct effects on cardiovascular function and indirect effects mediated through the autonomic nervous system, vascular compliance, vasoreactivity, and renal function[1]. The prevalence of hypothyroidism is between 1% and 17% [2, 3]. Overt hypothyroidism is a more severe stage than subclinical hypothyroidism and is accompanied by increased serum thyroid-stimulating hormone (TSH), decreased thyroxine, and symptoms. Overt hypothyroidism is associated with impaired cardiac contractility, decreased cardiac output, increased systemic vascular resistance, accelerated atherosclerosis, and increased risk of coronary artery disease[1, 4–6]. Patients with severe coronary diseases who underwent coronary artery bypass grafting (CABG) are at high risk of adverse cardiovascular events. The postoperative recovery of these patients may be complicated by preoperative overt hypothyroidism. However, limited data are available on the relationship between preoperative overt hypothyroidism and early outcomes after CABG, most of which were limited by small sample sizes. This study aimed to evaluate the influence of overt hypothyroidism on the recovery of patients after CABG by using a propensity score matching method.

## Methods

From December 2014 to December 2018, 189 patients with overt hypothyroidism who underwent CABG at Fuwai Hospital (Beijing, China) were identified. The exclusion criteria of the hypothyroid group included (1) no thyroid function tests within two weeks before surgery, (2) patients with subclinical hypothyroidism, (3) concurrent with other cardiac surgery, and (4) previous sternotomy (Fig. 1). The exclusion criteria of the euthyroid group were (1) no thyroid function tests within two weeks before surgery, (2) abnormal thyroid function results, (3) history of thyroid or pituitary disease, (4) concurrent with other cardiac surgery, and (5) previous sternotomy. Finally, 6759 euthyroid patients were identified. The hypothyroid patients were then 1:4 matched with euthyroid patients. Medical history and perioperative records were collected. Echocardiography was used to measure left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF). Because this was a retrospective analysis of data collected for routine clinical care, individual informed consent was waived by the ethics committee. The study design was approved by the local ethics committee of Fuwai Hospital, Beijing, China (Approval NO. 2019 – 1151; Date of review: June 26, 2019).

Median sternotomy is the preferred approach in all patients. The decision to use cardiopulmonary bypass (CPB) was left to the operating surgeon and was mostly based on the severity and extent of disease of the target vessels. CPB was conducted on moderate hypothermia, and myocardial protection was achieved by using intermittent antegrade hyperkalemic cold blood cardioplegia. The final goal of CABG was to obtain complete myocardial revascularization.

For thyroid function tests, serum TSH, free thyroxine (FT4), total thyroxine (TT4), free triiodothyronine, and total triiodothyronine were measured using electrochemiluminescence immunoassays on a Siemens analyzer. Overt hypothyroidism was defined as a documented history of overt hypothyroidism in the patients' clinical record, or a TSH level  $> 4.78$  uIU/mL, FT4  $< 0.8$  ng/dL and TT4  $< 4.29$  ug/mL without a history of thyroid diseases. Euthyroidism was defined as  $0.55$  uIU/mL  $\leq$  TSH level  $\leq 4.78$  uIU/mL,  $0.8$  ng/dL  $\leq$  FT4  $\leq 1.88$  ng/dL and  $4.29$  ug/mL  $\leq$  TT4  $\leq 12.47$  ug/mL at the time of surgery, and no documented history of thyroid disease in the patients' clinical record.

The primary outcome was postoperative complications, which included impaired wound healing, reintubation, tracheotomy, reoperation, thoracentesis or pericardiocentesis, intra-aortic balloon pump (IABP) implantation, dialysis, postoperative stroke, pacemaker implantation, ventricular arrhythmia, atrial fibrillation, and death. The impaired wound healing was defined as hematoma, wound dehiscence, skin necrosis, lymphatic wound drainage, and local signs of infection. Postoperative stroke was defined as a new neurological deficit with imaging of the central nervous system infarction or hemorrhage. Reoperation was defined as the second operation under general anesthesia during the same hospitalization. Patients were routinely monitored postoperatively for the occurrence of arrhythmia by bedside monitors. When needed, 12-lead electrocardiograms were obtained to determine the exact cardiac rhythm.

The secondary outcomes included postoperative inotropic support and mechanical ventilation time. Postoperative inotropic support included the use of dopamine, adrenaline, noradrenaline, milrinone, and

dobutamine. Both the proportion and duration of these drugs were recorded. The total duration of inotropic support was the sum of dopamine duration, adrenaline duration, noradrenaline duration, milrinone duration, and dobutamine duration. When postoperative cardiac output was low and cardiovascular performance was bad, dopamine, dobutamine, or milrinone may be infused initially. When an insufficient response was obtained from these drugs, adrenaline was added or substituted. When hypotension existed in the presence of adequate cardiac output, noradrenaline was used. For patients with overt hypothyroidism, levothyroxine treatment started on the first day after surgery.

Continuous variables are expressed as median (25th, 75th percentile) and were compared in unmatched pairs using the Wilcoxon rank-sum test. Continuous variables in matched pairs were compared using the Wilcoxon signed-rank test. Dichotomous variables are expressed as percentages. The McNemar's test was applied for dichotomous variables in matched pairs data. Risk factors of postoperative complications were analyzed by condition logistic regression, stratified on the matched sets. Factors for which the univariate analysis gave a p value  $\leq 0.1$ , or of known biologic significance, were included in a logistic multivariate regression model. Odds ratio (OR) and 95% confidence interval (CI) were calculated.

To account for the intergroup clinical imbalance caused by the selection bias inherent in the nonrandomized nature of the study, a continuous propensity score matching (PSM) analysis was performed. A logistic regression model was built to calculate the probability of each patient and to determine the propensity score. Variables in the model included age, gender, weight, myocardial infarction, diseased vessels, previous percutaneous coronary intervention, hyperlipemia, hypertension, diabetes mellitus, stroke, smoking, chronic obstructive pulmonary disease (COPD), preoperative LVEDD, preoperative LVEF, preoperative glomerular filtration rate (GFR), use of CPB and number of distal anastomoses. A greedy matching algorithm was used to perform the 1:4 match on the logit of the propensity score with a caliper width of 0.2. Finally, we matched 187 overt hypothyroid patients with 737 euthyroid patients. The balance of the 2 matched groups was evaluated by standardized mean differences in the matching variables. Usually, a maximum standardized mean difference of 0.1 is considered acceptable.

A p value  $< 0.05$  was considered to be statistically significant. The statistical analysis was performed using SPSS version 22.0 for Windows (SPSS Inc., Chicago, IL, USA).

## Results

After PSM, the baseline and intraoperative characteristics were similar in the two groups (Table 1). 168 hypothyroid patients received levothyroxine treatment before surgery. Hypothyroid patients had lower FT4, TT4, free triiodothyronine, total triiodothyronine, and higher TSH levels (all  $p < 0.001$ , Table 2).

Table 1  
Variables included for the propensity score matching model

	Before matching			After matching		
	Hypothyroidism (n = 189)	Euthyroidism (n = 6759)	SMD	Hypothyroidism (n = 187)	Euthyroidism (n = 737)	SMD
Age (years), median (Q1, Q3)	63 (57, 69)	62 (55, 67)	0.164	63 (58, 69)	62 (57, 67)	0.065
Female, n(%)	82 (43.4%)	1465 (21.7%)	0.437	80 (42.8%)	307 (41.7%)	0.009
Weight (kg), median (Q1, Q3)	71 (63, 80)	73 (65, 80)	0.117	71 (62, 79)	71 (63, 80)	0.010
Myocardial infarction, n(%)	57 (30.2%)	2077 (30.7%)	0.012	56 (29.9%)	216 (29.3%)	0.013
Diseased vessels, median (Q1, Q3)	3 (3, 3)	3 (3, 3)	0.309	3 (3, 3)	3 (3, 3)	0.039
Previous percutaneous coronary intervention, n(%)	17 (9.0%)	899 (13.3%)	0.150	17 (9.1%)	57 (7.7%)	0.051
Hyperlipemia, n(%)	120 (63.5%)	5155 (76.3%)	0.265	119 (63.6%)	471 (63.9%)	0.006
Hypertension, n(%)	128 (67.7%)	4381 (64.8%)	0.062	127 (67.9%)	491 (66.6%)	0.030
Diabetes mellitus, n(%)	60 (31.7%)	2561 (37.9%)	0.132	59 (31.6%)	237 (32.2%)	0.006
Stroke, n(%)	26 (13.8%)	999 (14.8%)	0.030	26 (13.9%)	126 (17.1%)	0.094
Smoking, n(%)	66 (34.9%)	3940(58.3%)	0.489	66 (35.3%)	278 (37.7%)	0.040
COPD, n(%)	7 (3.7%)	93 (1.4%)	0.123	7 (3.7%)	29 (3.9%)	0.016

COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; SMD, standardized mean differences.

<sup>a</sup>The glomerular filtration rate (GFR) was estimated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

	Before matching			After matching		
Preoperative LVEDD (mm), median (Q1, Q3)	48 (44, 50)	48 (45, 52)	0.263	48 (44, 50)	47 (44, 50)	0.016
Preoperative LVEF (%), median (Q1, Q3)	62 (60, 65)	61 (58, 65)	0.196	62 (60, 65)	62 (59, 65)	0.005
Use of CPB, n(%)	80 (42.3%)	3266 (48.3%)	0.121	80 (42.8%)	335 (45.5%)	0.045
Number of distal anastomoses (n), median (Q1, Q3)	3 (3, 4)	3 (3, 4)	0.012	3 (3, 4)	3 (3, 4)	0.004
Preoperative GFR <sup>a</sup> (ml/min), median (Q1, Q3)	79 (66, 93)	88 (75, 99)	0.395	79 (66, 93)	82 (69, 93)	0.043
COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; SMD, standardized mean differences.						
<sup>a</sup> The glomerular filtration rate (GFR) was estimated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.						

Table 2  
Preoperative thyroid function tests and postoperative outcomes

	Hypothyroidism (n = 187)	Euthyroidism (n = 737)	P value
<b>Preoperative thyroid function tests</b>			
FT4 (ng/dL), median (Q1, Q3)	1.0 (0.8, 1.2)	1.1 (1.0, 1.2)	< 0.001
TT4 (ug/mL), median (Q1, Q3)	7.2 (5.3, 8.5)	8.1 (7.0, 9.2)	< 0.001
Free triiodothyronine (pg/mL), median (Q1, Q3)	2.4 (2.1, 2.7)	2.8 (2.6, 3.0)	< 0.001
Total triiodothyronine (ng/mL), median (Q1, Q3)	0.9 (0.8, 1.0)	1.0 (0.9, 1.1)	< 0.001
TSH (uIU/mL), median (Q1, Q3)	6.5 (3.4, 23.1)	1.9 (1.3, 2.7)	< 0.001
<b>Postoperative outcomes</b>			
ICU stay (day), median (Q1, Q3)	2 (1, 4)	2 (1, 4)	0.14
Mechanical ventilation time (h), median (Q1, Q3)	17 (14, 21)	15 (11, 19)	< 0.001
Postoperative stay (day), median (Q1, Q3)	7.0 (7.0, 10.0)	6.7 (6.5, 8.5)	< 0.001
Postoperative LVEDD (mm), median (Q1, Q3)	46 (41, 49)	46 (43, 50)	0.04
Postoperative LVEF (%), median (Q1, Q3)	60 (58, 63)	60 (58, 64)	0.94
<b>Complications</b>			
Impaired wound healing, n(%)	22 (11.8%)	7 (0.9%)	< 0.001
Reintubation, n(%)	4 (2.1%)	3 (0.4%)	0.03
Tracheotomy, n(%)	1 (0.5%)	2 (0.3%)	0.49
Reoperation, n(%)	3 (1.6%)	11 (1.5%)	1.00
Thoracentesis or pericardiocentesis, n(%)	8 (4.3%)	21 (2.8%)	0.32

FT4, free thyroxine; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; ICU, intensive care unit; TSH, thyroid-stimulating hormone; TT4, total thyroxine.

<sup>a</sup>includes impaired wound healing, reintubation, tracheotomy, reoperation during same hospitalization, thoracentesis or pericardiocentesis, IABP implantation, dialysis, postoperative stroke, pacemaker implantation, ventricular arrhythmia, atrial fibrillation, death.

	Hypothyroidism (n = 187)	Euthyroidism (n = 737)	P value
IABP implantation, n(%)	0	8 (1.1%)	0.37
Dialysis, n(%)	0	1 (0.1%)	1.00
Postoperative stroke, n(%)	0	11 (1.5%)	0.13
Pacemaker implantation, n(%)	0	3 (0.4%)	1.00
Ventricular arrhythmia, n(%)	25 (13.4%)	77 (10.4%)	0.26
Atrial fibrillation, n(%)	37 (19.8%)	146 (19.8%)	1.00
Death, n(%)	0	2 (0.3%)	1.00
Total <sup>a</sup> complications, n(%)	74 (39.6%)	223 (30.3%)	0.015
FT4, free thyroxine; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; ICU, intensive care unit; TSH, thyroid-stimulating hormone; TT4, total thyroxine.			
<sup>a</sup> includes impaired wound healing, reintubation, tracheotomy, reoperation during same hospitalization, thoracentesis or pericardiocentesis, IABP implantation, dialysis, postoperative stroke, pacemaker implantation, ventricular arrhythmia, atrial fibrillation, death.			

In 189 hypothyroid patients, the causes of overt hypothyroidism included chronic autoimmune disease (70/189, 37.0%), thyroidectomy (43/189, 22.8%), benign nodular thyroid disease (22/189, 11.6%), treatment for hyperthyroidism with radioiodine (33/189, 17.5%), hypophysectomy (1/189, 0.5%), and unknown causes (20/189, 10.6%).

The outcomes after CABG are summarized in Table 2. The mechanical ventilation time was longer in hypothyroid patients than euthyroid patients (median time: 17 hours vs. 15 hours,  $p < 0.001$ ). The postoperative stay was also longer in hypothyroid patients than euthyroid patients (median time: 7.0 days vs. 6.7 days,  $p < 0.001$ ). Postoperative LVEDD of hypothyroid patients was smaller than that of euthyroid patients ( $p = 0.04$ ), while postoperative LVEF was similar between the two groups. The incidences of impaired wound healing and reintubation were higher in hypothyroid patients than euthyroid patients (11.8% vs. 0.9%,  $p < 0.001$ ; 2.1% vs. 0.4%,  $p = 0.03$ , respectively). The incidence of the total complications was also higher in hypothyroid patients compared with euthyroid patients (39.6% vs. 30.3%,  $p = 0.015$ ).

Multivariate analysis showed that overt hypothyroidism was significantly associated with the occurrence of impaired wound healing (OR = 12.29,  $p < 0.001$ , Fig. 2), reintubation (OR = 5.71,  $p = 0.047$ , Fig. 3), and the total complications (OR = 1.31,  $p = 0.049$ , Fig. 4). To further evaluate the effect of preoperative thyroid status on postoperative complications, hypothyroid patients were divided into two groups: 58 hypothyroid patients with normal TSH and the other 129 hypothyroid patients with abnormal TSH (Table 3). After adjusting for age and LVEF by multivariate analysis, the OR of the total complications was 1.10 (95% CI, 0.68 to 1.77,  $p = 0.71$ ) in hypothyroid patients with normal TSH and 1.43 (95% CI, 1.04 to 1.98,  $p = 0.03$ ) in hypothyroid patients with abnormal TSH compared with euthyroid patients.

Table 3  
Risk of the total complications in hypothyroid patients compared with euthyroid patients after adjusting for age and left ventricular ejection fraction.

Factor	OR (95% CI)	P value
hypothyroid patients with normal TSH	1.10 (0.68–1.77)	0.71
hypothyroid patients with abnormal TSH	1.43 (1.04–1.98)	0.03
CI, confidence interval; OR, odds ratio; TSH, thyroid-stimulating hormone.		

Postoperative inotropic supports of drugs are summarized in Table 4. The proportions of the use of dopamine, adrenaline, milrinone, and dobutamine in the hypothyroid group were higher than those in the euthyroid group (75.4% vs. 67.6%,  $p = 0.038$ ; 10.7% vs. 6.1%,  $p = 0.028$ ; 3.2% vs. 0.3%,  $p = 0.001$ ; 4.8% vs. 1.2%,  $p = 0.004$ , respectively). The total duration of inotropic support in hypothyroid patients was longer than euthyroid patients (median duration: 4 days vs. 3 days,  $p = 0.003$ ).

Table 4  
Postoperative inotropic support

	Hypothyroidism (n = 187)	Euthyroidism (n = 737)	P value
Use of dopamine, n(%)	141 (75.4%)	498 (67.6%)	0.038
Dopamine duration (day), median (Q1, Q3)	3 (2, 5)	3 (2, 4)	0.24
Use of adrenaline, n(%)	20 (10.7%)	45 (6.1%)	0.028
Adrenaline duration (day), median (Q1, Q3)	2 (2, 5)	2 (1, 4)	0.69
Use of noradrenaline, n(%)	93 (49.7%)	350 (47.5%)	0.58
Noradrenaline duration (day), median (Q1, Q3)	3 (2, 4)	3 (2, 4)	0.05
Use of milrinone, n(%)	6 (3.2%)	2 (0.3%)	0.001
Milrinone duration (day), median (Q1, Q3)	1 (1, 2)	1	1.00
Use of dobutamine, n(%)	9 (4.8%)	9 (1.2%)	0.004
Dobutamine duration (day), median (Q1, Q3)	2 (1, 3)	1 (1, 2)	0.34
Total <sup>a</sup> duration of inotropic support (day), median (Q1, Q3)	4 (2, 7)	3 (1, 6)	0.003
<sup>a</sup> includes dopamine duration, adrenaline duration, noradrenaline duration, milrinone duration, and dobutamine duration.			

## Discussion

This study summarizes our surgical experience of overt hypothyroid patients who underwent CABG surgery. To our knowledge, our study is the largest cohort comparing early postoperative clinical results of overt hypothyroid patients with euthyroid patients. The major finding of this study is that overt hypothyroidism is associated with a higher incidence of impaired wound healing, reintubation, and total postoperative complications, stronger postoperative inotropic support, longer mechanical ventilation time and hospital stay. Postoperative complications could be reduced by controlling preoperative TSH within the normal range.

In our study, overt hypothyroidism leads to an increased risk of postoperative complications. Many conditions related to overt hypothyroidism may contribute to this result. First, hypothyroidism is associated with increased systemic capillary permeability and disturbances in electrolyte metabolism[7]. This could cause fluid retention in interstitial spaces and serous cavities, leading to impaired wound healing and reoperation. Several studies have been published on pericardial effusions and cardiac tamponade secondary to hypothyroidism[7–9]. In our study, three hypothyroid patients underwent reoperations because of impaired wound healing and massive pericardial effusions, while 11 euthyroid patients underwent reoperation for controlling bleeding. Second, hypothyroidism could change the structure of connective tissue[10]. Hypothyroid patients had abnormal tissue integrity[11], which could impair wound healing. Third, hypothyroidism may induce a wide spectrum of alterations in neuromuscular function and lead to muscle dysfunction[12]. Reduced diaphragmatic muscle strength and lower forced vital capacity were found in hypothyroid patients[13]. In our study, the incidence of reintubation was 2.1% in overt hypothyroid patients and 0.4% in euthyroid patients. Forth, electrocardiographic changes can be seen in hypothyroidism, including sinus bradycardia, a prolonged QTc with increased risk of torsade de pointes ventricular tachycardia, low voltage, and the rare instance of atrioventricular block[1, 14]. All these factors may lead to an increased risk of postoperative complications in overt hypothyroid patients.

Hypothyroid patients also needed stronger and longer postoperative inotropic support than euthyroid patients after CABG, although they had similar preoperative and postoperative LVEFs. The cardiovascular system is a major target of thyroid hormone action. Overt hypothyroidism is associated with impaired cardiac contractility, decreased cardiac output, increased systemic vascular resistance, accelerated atherosclerosis, and coronary artery disease[1, 4, 5]. In our study, hypothyroid patients had smaller LVEDDs than euthyroid patients after surgery, although they sheared similar preoperative LVEDDs. This may indicate the association between hypothyroidism and impairment of left ventricular diastolic function. Hypothyroidism could lead to a dramatic loss of cardiac arterioles, resulting in severe, progressive systolic dysfunction[15]. Thyroid hormone deficiency is responsible for an increased risk of heart failure events[16]. In our study, the free triiodothyronine level was lower in hypothyroid patients, which was found to be a strong predictor of death and low cardiac output in CABG patients[17]. All these impairments may lead to stronger and longer postoperative inotropic support in hypothyroid patients.

Hypothyroid patients with normal preoperative TSH levels have a similar risk of postoperative complications compared with euthyroid patients. Our study was a retrospective exploratory study, and 58 hypothyroid patients obtained a normal TSH level before surgery. Among patients with coronary heart disease, preoperative use of levothyroxine will increase oxygen consumption of myocardium and provoke

anginal symptoms, which may limit the attainment of euthyroidism. The starting dose is usually low and the adjustment is slow[18]. CABG in hypothyroid patients before restoration of euthyroidism was due to severe anginal symptoms or left main coronary artery occlusion. Surgery in these patients is associated with an increased risk of several postoperative complications, which should be anticipated and preemptively managed in the course of their perioperative care.

The incidence of postoperative atrial fibrillation did not differ between hypothyroid patients and euthyroid patients. Our incidence of atrial fibrillation was approximate 20%, which was in agreement with previous reports[19, 20]. Jaimes and his colleagues[21] reported that hypothyroidism was a risk factor for the onset of postoperative atrial fibrillation in patients undergoing CABG. But the exposed patients in their study included ones only with TSH elevation, and preoperative baseline characteristics were not evenly distributed among the two groups. The perioperative thyroid hormone levels were also not analyzed. Park and his colleagues[22] reported that subclinical hypothyroidism appeared to increase the development of postoperative atrial fibrillation, but the number of their cohort was small.

Despite the use of various statistical measures (such as PSM and logistic regression) to help control selection bias and confounding factors, the findings should be interpreted cautiously given the relatively small sample size. Also, postoperative thyroid hormone levels were not measured, so that we could not verify the relationship between postoperative hormone levels and the development of complications. Further large prospective studies with long-term follow-up are needed on this issue.

## Conclusions

CABG in overt hypothyroid patients is associated with a higher incidence of impaired wound healing, reintubation, and total postoperative complications, stronger postoperative inotropic support, longer mechanical ventilation time and hospital stay. Postoperative complications could be reduced by controlling preoperative TSH within the normal range.

## List Of Abbreviations

CABG = coronary artery bypass grafting

OR = odds ratio

TSH = thyroid-stimulating hormone

FT4 = free thyroxine

TT4 = total thyroxine

LVEDD = left ventricular end-diastolic diameter

LVEF = left ventricular ejection fraction

IABP = intra-aortic balloon pump

CI = confidence interval

PSM = propensity score matching

COPD = chronic obstructive pulmonary disease

CPB = cardiopulmonary bypass

GFR = glomerular filtration rate

ICU = intensive care unit

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration

SMD = standardized mean differences

## Declarations

**Ethics approval and consent to participate:** The study design was approved by the local ethics committee of Fuwai Hospital, Beijing, China (Approval NO. 2019-1151; Date of review: June 26, 2019). Because this was a retrospective analysis of data collected for routine clinical care, individual informed consent was waived by the ethics committee.

**Consent for publication:** Not applicable

**Availability of data and materials:** The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

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### Authors' contributions

**DZ:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft.

**WZ:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft.

**WF:** Conceptualization; Funding acquisition; Project Administration; Resources; Supervision; Validation; Visualization; Roles/Writing - review & editing.

**XY:** Methodology; Resources; Supervision; Validation; Roles/Writing - review & editing.

**CW:** Data curation; Formal analysis; Methodology; Software; Visualization.

All authors read and approved the final manuscript.

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## Figures

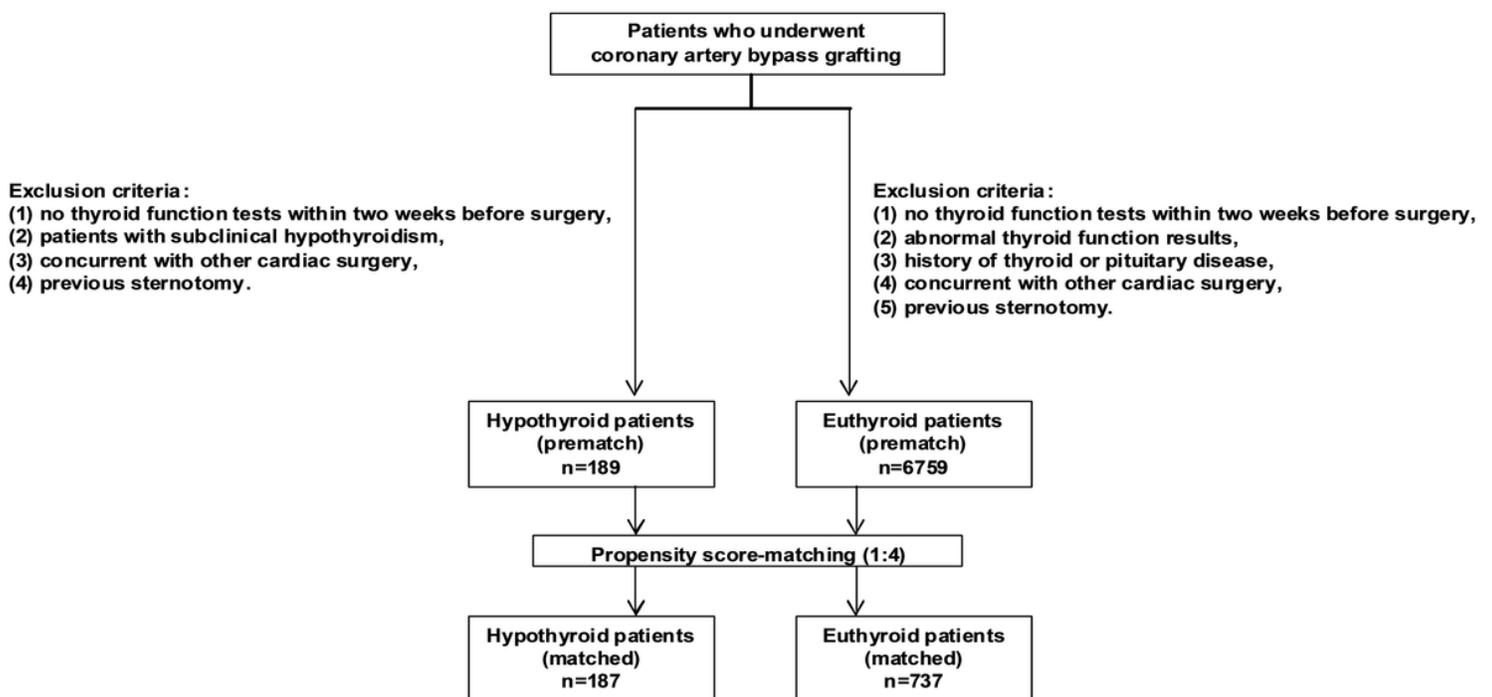


Figure 1

Flow chart of patient selection.

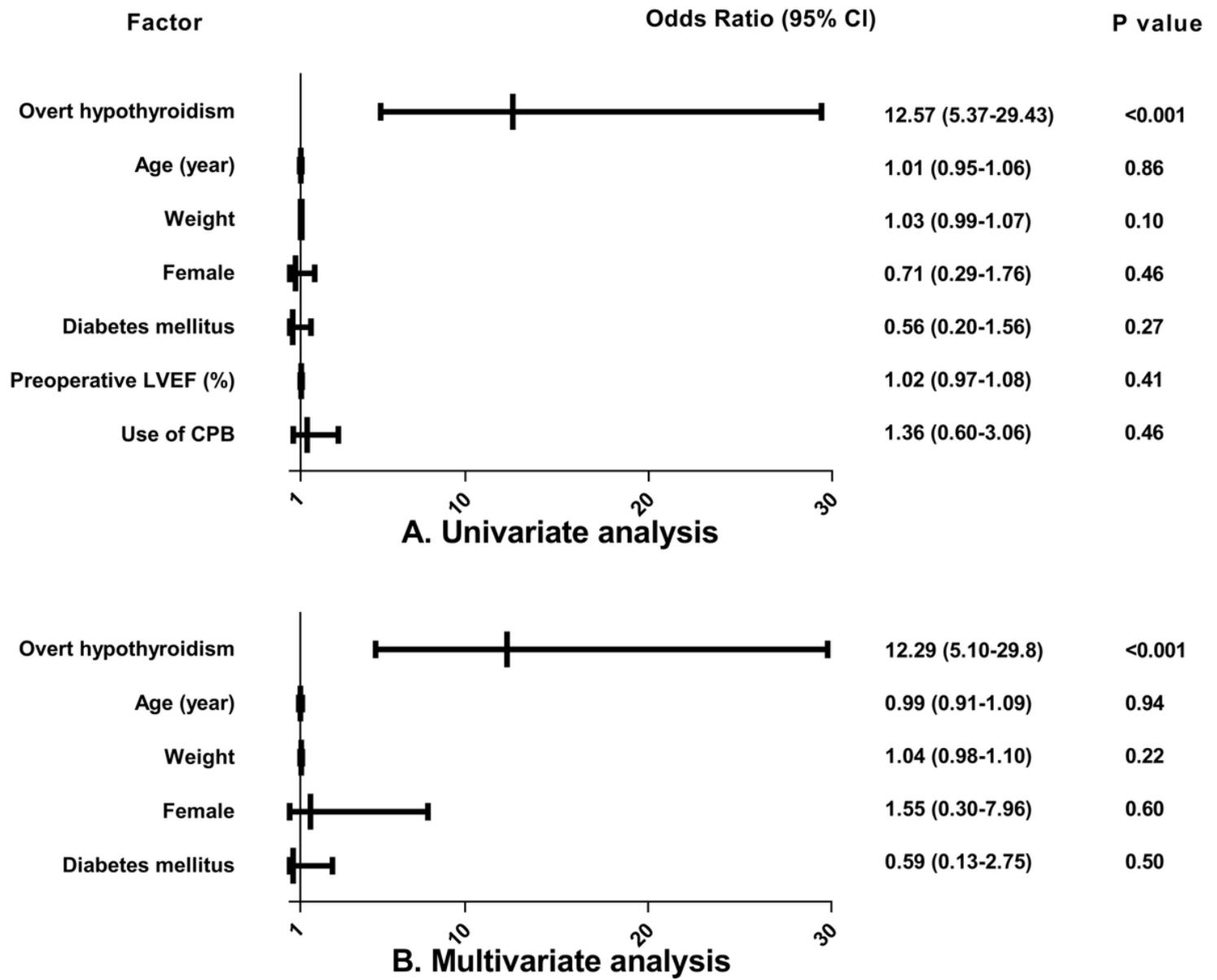
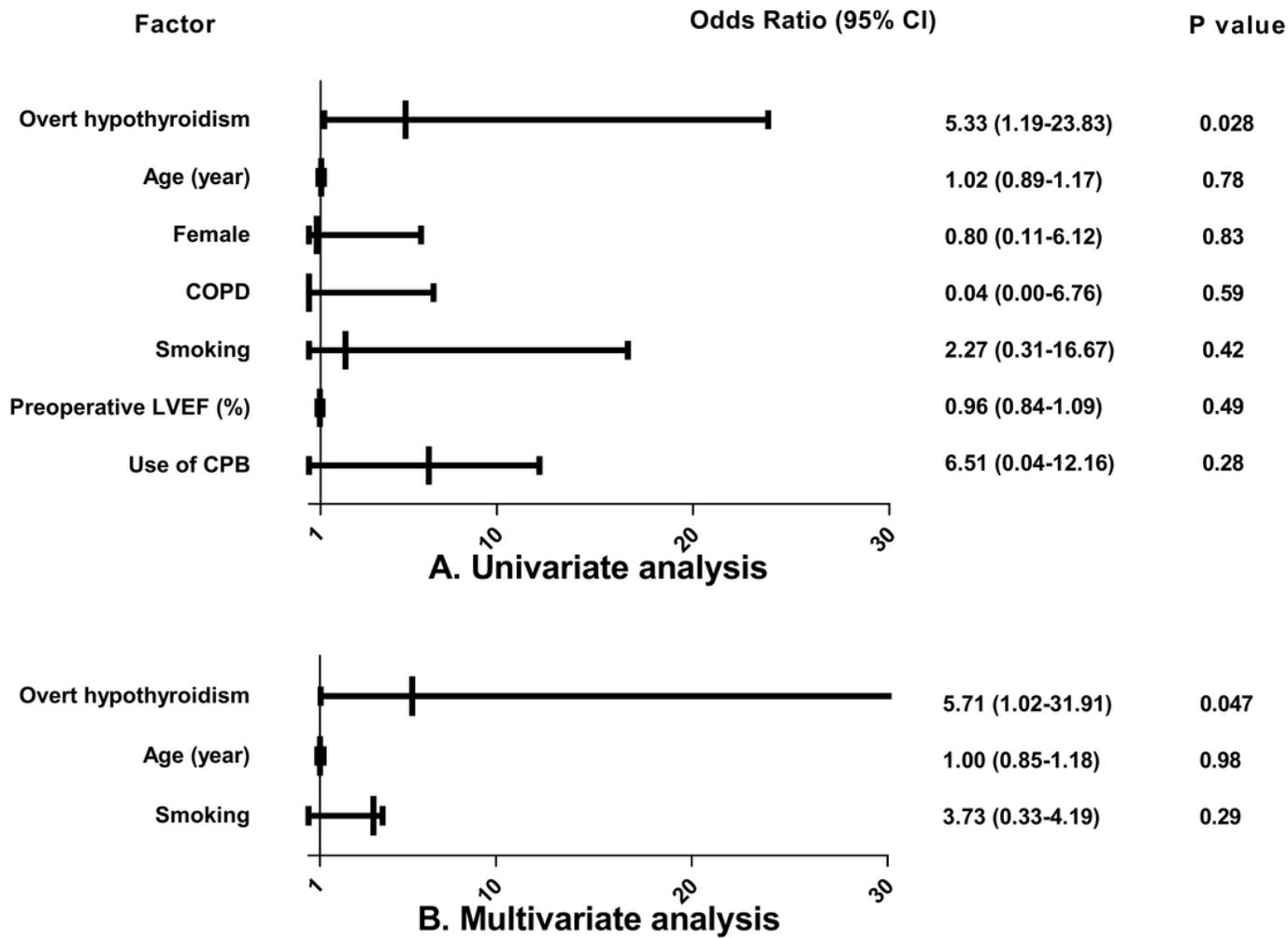


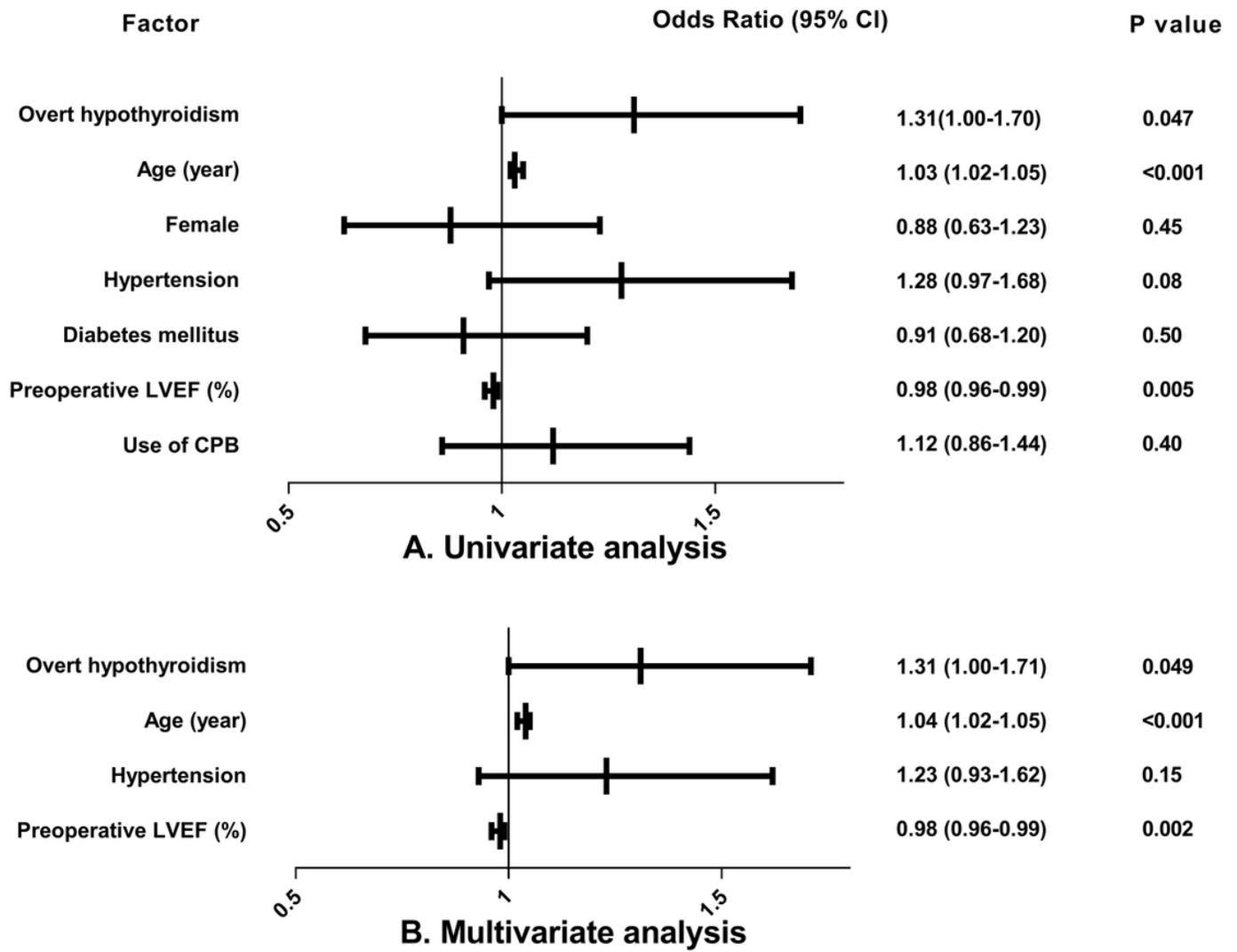
Figure 2

Predictors of impaired wound healing by univariate and multivariate analysis. CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction.



**Figure 3**

Predictors of reintubation by univariate and multivariate analysis. COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction.



**Figure 4**

Predictors of the total complications by univariate and multivariate analysis. CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction.