SAS Journal of Surgery
Abbreviated Key Title: SAS J Surg
ISSN 2454-5104
Journal homepage: https://www.saspublishers.com

OPEN ACCESS

Thoracic Surgery

The Role of Duration in Cardiopulmonary Bypass on Thyroid Function in Cardiac Surgical Patients

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DOI: https://doi.org/10.36347/sasjs.2025.v11i02.009 | **Received:** 04.01.2025 | **Accepted:** 10.02.2025 | **Published:** 13.02.2025

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Abstract **Original Research Article**

Background: Cardiopulmonary bypass (CPB) is an essential technique in cardiac surgery, but it can induce physiological changes, including alterations in thyroid function. Prolonged CPB duration is associated with a stress response, hypothermia, and hemodilution, potentially leading to transient hypothyroidism or euthyroid sick syndrome. This study aimed to assess the role of duration in cardiopulmonary bypass on thyroid function in cardiac surgical patients. ***Methods:*** This comparative study at Bangabandhu Sheikh Mujib Medical University, (BSMMU), Bangladesh from September 2021 to August 2022. A total of 54 cardiopulmonary bypass patients grouped by CPB duration: A (<60 mins), B (60-90 mins), C (>90 mins) were included in this study. Data analysis was done using SPSS 29.0. ***Results:*** TSH and FT3 values decreased significantly across groups (C > B > A). Mean ±SD TSH values in samples I-IV were A: 2.93-2.60, B: 2.51-1.36, C: 2.76-1.06. FT3 values were A: 4.25-4.00, B: 4.29-3.03, C: 4.26-2.46. FT4 values (A: 15.14-14.39, B: 15.30–14.67, C: 15.03-13.94) showed no significant differences. ***Conclusion:*** TSH and FT3 levels show a greater reduction in patients with cardiopulmonary bypass (CPB) durations of 60-90 minutes compared to those with <60 minutes, with the most significant decline observed in patients with CPB durations >90 minutes. Conversely, no notable decrease in FT4 levels was observed across the groups in this study.

Keywords: Cardiopulmonary bypass, Cardiac surgery, FT3, FT4, TSH, Thyroid function.

INTRODUCTION

Cardiopulmonary bypass (CPB) is a vital technique for many cardiac surgeries. It is used to enable an empty heart for intracardiac repair or coronary artery revascularization, ensure cardiac arrest, or support circulation during cardiac manipulation. During CPB, deoxygenated venous blood is routed through an extracorporeal circuit, passing a venous reservoir and pump before undergoing gas exchange in a membrane oxygenator and returning to the arterial circulation [1]. CPB induces unique tissue injury due to surgical trauma, extracorporeal circulation, hypothermia, and non-pulsatile blood flow. These factors can cause complications like low cardiac output syndrome, myocardial dysfunction, prolonged anesthesia effects, and extended mechanical ventilation. Additionally, a catabolic state with increased oxygen consumption may delay recovery [2]. The thyroid gland produces two hormones, T3 and T4, which are synthesized using iodine and play key roles in metabolism and protein biosynthesis. These hormones are regulated by thyroid-stimulating hormone (TSH), secreted by the anterior pituitary, which in turn is controlled by the hypothalamus through thyrotropin-releasing hormone. Thyroid hormones (THs) significantly impact the heart and vascular system, increasing heart rate, contractility, and enhancing systolic and diastolic function while reducing systemic vascular resistance at rest [3]. Hypothyroidism leads to reduced cardiac output due to decreased heart rate, stroke volume, and contractility [4]. This condition is linked to myocardial dysfunction resulting from diminished inotropic and chronotropic effects of THs

and can lead to pericardial effusion and cardiomyopathy in severe cases. A reduced metabolic rate in hypothyroid patients may lead to hypothermia and hinder recovery from the low body temperatures induced during cardiopulmonary bypass. Thyroid hormone depletion can also impair nutritional status, promoting a catabolic state by causing intracellular caloric deprivation [5]. Conversely, hyperthyroidism induces cardiac and hemodynamic symptoms such as palpitations, widened pulse pressure, dyspnea on exertion, tachycardia, exercise intolerance, and atrial fibrillation (AF) [6]. THs increase cardiac contractility and resting heart rate, raising cardiac output by 50–300% in hyperthyroidism due to synergistic effects of elevated heart rate, enhanced contractility, and peripheral vasodilation [7]. There remains ongoing debate about the link between thyroid dysfunction and increased cardiovascular risk [8], including its potential association with sudden cardiac death (SCD) [9]. SCD is predominantly caused by lethal ventricular arrhythmias in patients with underlying coronary heart disease [10]. Over 50% of SCD cases are attributed to coronary heart disease, often occurring within 1 hour [11]. Research has investigated whether patients with heart failure (HF) and reduced ejection fraction (EF) and thyroid dysfunction are at an increased risk of sudden cardiac death (SCD). The study found a strong positive correlation between thyroid dysfunction and increased risk of death in patients with symptomatic HF and EF less than 35%, even after adjusting for known mortality predictors [2]. Thyroid dysfunction has been linked to increased overall mortality and SCD risk, and large-scale randomized controlled trials are needed to determine whether treating mild thyroid insufficiency is beneficial [8]. Cardiopulmonary bypass (CPB) leads to significant changes in endocrine balance. Recent studies suggest that both children and adults undergoing CPB may experience a substantial reduction in circulating thyroid hormones, which can contribute to hypothyroidism and compromised cardiac function. The decline in FT4 and FT3 levels may play a role in the pathophysiology of low cardiac output states post-surgery. This hypothesis is supported by findings that triiodothyronine administration after CPB or ischemic injury in animals and humans has a positive inotropic effect [12].

METHODOLOGY

This comparative cross-sectional study was conducted at the Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from September 2021 to August 2022. A total of 54 patients who underwent cardiopulmonary bypass (CPB) for underlying heart diseases were included, and selected using a convenient sampling method. Patients were divided into three groups: group A (18 patients with CPB time < 60 minutes), group B (18 patients with CPB time between 60 and 90 minutes), and group C (18 patients with CPB time > 90 minutes). Inclusion criteria included patients with normal thyroid hormone levels scheduled for cardiac surgery, who provided informed consent. Exclusion criteria consisted of patients diagnosed with hypothyroidism or hyperthyroidism, those with cardiac failure at the time of preoperative evaluation, bleeding disorders, hepatic impairment, abnormal renal function (new kidney injury), or those requiring urgent cardiac surgery. Blood samples for TSH, FT3, and FT4 were collected preoperatively (Sample-I), at the end of CPB (sample-II), on the 1st postoperative day (POD) (sample-III), and on the 3rd POD (sample-IV). The ethical committee of the hospital approved the study, and data were analyzed using SPSS version 29.0. $p>0.05$ was considered not to be significant.

RESULT

In this study, the demographic and clinical characteristics of three groups based on cardiopulmonary bypass (CPB) time were assessed. The mean ages of group A, group B, and group C were 41.67±12.92, 39.50±12.51, and 41.78±16.07 years, respectively, with no statistically significant age differences ($p=0.859$). Gender distribution was also not significantly different across the groups ($p=0.594$). Similarly, the mean BMI for the groups was 21.86±2.82, 21.27±3.27, and 21.33±3.77 kg/m², showing no significant differences ($p=0.843$). Additionally, the mean left ventricular internal diameter in systole (LVIDs) and diastole (LVIDd) were comparable across the groups, with no statistically significant differences (LVIDs: $p=0.859$, LVIDd: $p=0.426$). The left ventricular ejection fraction (LVEF) was also similar among the groups ($p=0.073$). When examining procedural variables, the mean aortic cross-clamp time differed significantly among the groups, with group A having the shortest time (36.39±3.79 minutes), followed by group B (55.61±9.02 minutes), and group C with the longest time (69.28±5.82 minutes), showing a statistically significant difference ($p<0.001$). However, the mean ventilatory support time (VST) and intensive care unit time (ICUT) did not differ significantly between the groups (VST: $p=0.179$, ICUT: $p=0.274$). Regarding thyroid function, the TSH values were assessed at multiple time points. In sample I (preoperative), TSH values were 2.93±0.73, 2.51±0.59, and 2.76±0.60 mIU/L for group A, group B, and group C, respectively, showing no significant differences ($p=0.161$). However, in sample II (end of CPB), significant differences were observed ($p<0.001$), with group A having the highest TSH value (2.05±0.61 mIU/L), followed by group B (0.76±0.77 mIU/L), and group C having the lowest (0.52±0.57 mIU/L). These differences persisted in sample III (1st post-operative day) and sample IV (3rd post-operative day), with significant reductions in TSH levels in groups B and C compared to preoperative values ($p<0.001$). The FT3 levels followed a similar pattern. In sample I, the FT3 values were 4.25±0.96, 4.29±0.73, and 4.26±0.77 pmol/L for group A, group B, and group C, respectively, with no significant differences ($p=0.988$). By sample II, group A had the highest FT3 levels (3.43±0.94 pmol/L), followed by group B (2.40±0.79 pmol/L) and group C

(1.93±1.00 pmol/L), with statistically significant differences ($p<0.001$). These differences continued into samples III and IV, with group C showing the most significant drop in FT3 levels ($p<0.001$). In contrast, FT4 levels did not show any significant differences across the groups at any sample time point, with values in samples I, II, III, and IV remaining similar across groups ($p>0.05$). Comparing preoperative and postoperative thyroid hormone levels, group B and group C showed significant decreases in TSH and FT3 levels from preoperative to postoperative samples, while group A exhibited no significant changes. This highlights the varying impacts of CPB duration on thyroid function across the groups. Overall, the results suggest that prolonged CPB time significantly affects TSH and FT3 levels, whereas FT4 remains relatively unaffected.

Table 1: Comparison of pre-operative attributes

Variables	Group-A	Group-B	Group-C	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
LVIDs (mm)	32.56±6.03	32.39±6.73	34.39±6.58	0.591^{ns}
LVIDd (mm)	44.39±4.17	44.33±7.02	46.61±6.18	0.426^{ns}
LVEF (%)	57.67±5.41	57.17±4.20	60.78±5.28	0.073^{ns}

Table 2: Comparison of aortic cross-clamp time

Variable	Group-A	Group-B	Group-C	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
XCT (min)	36.39±3.79	55.61±9.02	69.28±5.82	<0.001^{s}

Table 3: Comparison of post-operative attributes

Variables	Group-A	Group-B	Group-C	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
VST (hrs.)	5.67±1.08	7.56±3.63	7.94±5.53	0.179^{ns}
ICUT (days)	3.50±0.45	3.97±1.24	4.11±1.55	0.274^{ns}

Table 4: Comparison of TSH, FT3, and FT4 values in samples I, II, III and IV among

Variables	Group-A	Group- B	Group-C	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
Sample I (pre-operative value)				
TSH (mIU/L)	2.93±0.73	2.51±0.59	2.76±0.60	0.161^{ns}
FT3 (pmol/L)	4.25±0.96	4.29±0.73	4.26±0.77	0.988^{ns}
FT4 (pmol/L)	15.14±1.91	15.30±1.98	15.03±1.61	0.909^{ns}
Sample II (At the end of CPB)				
TSH (mIU/L)	2.05±0.61	0.76±0.77	0.52±0.57	<0.001^{s}
FT3 (pmol/L)	3.43±0.94	2.40±0.79	1.93±1.00	<0.001^{s}
FT4 (pmol/L)	11.91±1.38	11.95±1.38	11.31±0.97	0.239^{ns}
Sample III (1st POD)				
TSH (mIU/L)	2.40±0.62	1.14±0.75	0.72±0.64	<0.001^{s}
FT3 (pmol/L)	3.75±0.93	2.77±0.74	2.18±0.99	<0.001^{s}
FT4 (pmol/L)	13.34±1.63	13.45±1.89	12.90±1.25	0.567^{ns}
Sample IV (3rd POD)				
TSH (mIU/L)	2.60±0.64	1.36±0.76	1.06±0.75	<0.001^{s}
FT3 (pmol/L)	4.00±0.94	3.03±0.82	2.46±1.02	<0.001^{s}
FT4 (pmol/L)	14.39±1.65	14.67±1.49	13.94±1.53	0.379^{ns}

Table 5: Comparison of mean values of sample II, III, IV TSH, FT3 and FT4 with sample I TSH, FT3 and FT4 values

Group	At the end of CPB	1st POD	3rd POD	Preoperative	p-value
	II TSH value	III TSH value	IV TSH value	Test value (I TSH)	
Group A	2.05 (30.03%)	2.40 (18.08%)	2.60 (11.26%)	2.93	0.069^{ns}
Group B	0.76 (69.72%)	1.14 (54.58%)	1.36 (45.81%)	2.51	0.015^{s}
Group C	0.52 (81.15%)	0.72 (73.91%)	1.06 (61.59%)	2.76	0.006^{s}
	II FT3 value	III FT3 value	IV FT3 value	Test value (I FT3)	
Group A	3.43 (14.23%)	3.75 (6.25%)	4.00 (5.88%)	4.25	0.087^{ns}
Group B	2.40 (44.05%)	2.77 (35.43%)	3.03 (29.37%)	4.29	0.014^{s}

Group	At the end of CPB	1st POD	3rd POD	Preoperative	p-value
	II TSH value	III TSH value	IV TSH value	Test value (I TSH)	
Group C	1.93 (54.26%)	2.18 (48.82%)	2.46 (42.25%)	4.26	0.005^{s}
	II FT4 value	III FT4 value	IV FT4 value	Test value (I FT4)	
Group A	11.91 (21.33%)	13.34 (11.88%)	14.39 (4.95%)	15.14	0.116^{ns}
Group B	11.95 (21.89)	13.45 (12.09%)	14.67 (4.11%)	15.3	0.132^{ns}
Group C	11.31 (24.75%)	12.90 (14.17%)	13.94 (7.25%)	15.03	0.094^{ns}

DISCUSSION

In this study, we assessed the effects of cardiopulmonary bypass (CPB) time on thyroid function and clinical parameters such as age, BMI, left ventricular function, aortic cross-clamp time, and postoperative recovery. The demographic and clinical characteristics, including age, gender, BMI, and left ventricular parameters (LVIDs, LVIDd, LVEF), were comparable across the three groups, indicating no confounding effects on thyroid hormone levels. These findings are consistent with previous research, which reported no significant differences in baseline characteristics among such cases [13]. The procedural parameters showed significant variation in aortic cross-clamp time among the groups (group A: 36.39±3.79 min, group B: 55.61±9.02 min, and group C: 69.28±5.82 min, $p<0.001$). This difference reflects increasing complexity and longer operative times in patients with more extended CPB durations. This is supported by studies that found a correlation between longer CPB durations and extended cross-clamp times, suggesting a more complex surgical procedure [14]. Interestingly, despite the differences in CPB duration, no significant differences were observed in ventilatory support or ICU stay times ($p=0.179$, $p=0.274$). This suggests that while CPB time may influence some aspects of recovery, it may not necessarily extend the need for mechanical ventilation or ICU care, which has been observed in similar studies [15]. The main aim of this study was to examine the impact of CPB time on thyroid function, particularly the changes in TSH, FT3, and FT4 levels. We observed no significant differences in preoperative TSH, FT3, or FT4 levels across the groups. However, significant reductions in TSH and FT3 levels were noted at the end of CPB (sample II), with group A showing the highest TSH values (2.05±0.61 mIU/L), followed by group B (0.76±0.77 mIU/L), and group C (0.52±0.57 mIU/L). These differences persisted on the first and third postoperative days, with groups B and C exhibiting more marked decreases in TSH and FT3 compared to group A. These findings are consistent with other studies that reported prolonged CPB durations resulted in significant drops in TSH and FT3 levels in patients undergoing cardiac surgery [16]. The reductions observed in TSH and FT3 levels were more pronounced in patients with longer CPB times, which further supports the notion that prolonged CPB leads to alterations in thyroid hormone levels [17]. The FT4 levels, however, remained relatively unchanged across all groups at all time points. This finding aligns with recent literature suggesting that FT4 levels are less affected by CPB compared to TSH and FT3. Other studies have demonstrated that FT4 levels remained stable despite significant changes in TSH and FT3 during cardiac surgery involving CPB [18]. The absence of changes in FT4 levels, in contrast to the fluctuations observed in TSH and FT3, may indicate that FT4 is less responsive to the acute stress induced by cardiopulmonary bypass (CPB). This could be because FT4 is primarily regulated through pituitary feedback mechanisms, while TSH and FT3 are more directly affected by peripheral conversion processes [19]. The observed reduction in TSH and FT3 levels during and after CPB is likely due to alterations in thyroid hormone metabolism. The decreased conversion of T4 to the more active T3 form, primarily due to suppressed 5'-deiodinase activity during CPB, may account for these changes. This hypothesis is supported by research indicating that reduced deiodinase activity during CPB leads to decreased T3 production [20]. Furthermore, the increased conversion of T3 to its inactive metabolite, reverse T3 (rT3), during CPB may contribute to the observed declines in FT3 levels. The significantly more pronounced drop in TSH and FT3 levels in the longer CPB time groups supports this mechanism, as prolonged CPB duration may exacerbate the effects on thyroid hormone metabolism [21]. This study confirms that prolonged CPB times significantly affect TSH and FT3 levels, while FT4 remains largely unaffected. These findings are consistent with recent studies, which suggest that CPB time is a critical factor influencing thyroid hormone levels, particularly TSH and FT3, during and after surgery. The underlying mechanism appears to be linked to alterations in thyroid hormone metabolism, especially the peripheral conversion of T4 to T3. Future research examining the role of deiodinases and other metabolic pathways may provide further insight into the molecular mechanisms driving these changes in thyroid function during CPB.

CONCLUSION & RECOMMENDATION

Patients undergoing cardiopulmonary bypass (CPB) for durations between 60 and 90 minutes showed a decrease in TSH and FT3 levels compared to those with CPB times under 60 minutes. Those with CPB times exceeding 90 minutes experienced a more significant reduction in TSH and FT3 levels than those with CPB times between 60 and 90 minutes. However, no clear association was found between CPB time (less than 60 minutes, 60 to 90 minutes, or greater than 90 minutes) and a decrease in FT4 concentration. Given the potential impact of prolonged CPB time on thyroid hormone levels, routine assessment of thyroid function is

recommended for effective patient management. Additionally, a larger prospective study is required to further validate these findings.

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