

## Peer Review File

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### Reviewer A

This study investigates the impact of free triiodothyronine (FT3) levels within the normal range on new-onset atrial fibrillation (AF) in patients undergoing surgical coronary revascularization. The findings suggest that low-normal FT3 is associated with a higher risk of post-operative AF (POAF) and longer hospital stays, highlighting its potential as an independent predictor for identifying patients at greater risk of POAF following surgical coronary revascularization.

The study is interesting. However, there are several concerns as follows:

1. The term "Triiodoformylgenine" needs clarification, and a more SEO-friendly term, such as triiodothyronine, should be used.

**Reply:** The article has replaced "triiodoformylgenine" with "triiodothyronine". (see P1, Line 2 and Line 18; P2, Line 3 and Line 20; P3, Line 9 and Line 13; P9, Line 33 and Line 34 ).

2. The timing of thyroid function assessment (FT3, FT4, and TSH) on the first day of hospitalization requires clarification—whether pre-operative levels or on the first day after bypass surgery. Consider comparing with the work of Donmez et al. and addressing any differences.

See: Donmez K, Akca B, Erdil N. Is there a relationship between thyroid hormone change and postoperative arrhythmia in patients undergoing coronary bypass surgery? A prospective randomized controlled trial. *AZJCVS*. 2022;3(2):36-42 DOI: 10.5455/azjcv.2022.08.013

**Reply:** The timing of thyroid function assessment has been clarified. (P4, Line16-17). We have discussed work of Donmez et al. (P6, Line21-23 and Line 37-40; P7, Line 28-29 ).

3. Detailed data on surgery technique, machine time, inotropics use, ventilation time, inflammation/sepsis, and re-operation proportions/values are essential.

Discuss these factors in the context of the meta-analysis by Seo et al. in the Discussion section. See: Seo, E.J., Hong, J., Lee, HJ. et al. Perioperative risk factors for new-onset postoperative atrial fibrillation after coronary artery bypass grafting: a systematic review. *BMC Cardiovasc Disord* 21, 418 (2021). <https://doi.org/10.1186/s12872-021-02224-x>

**Reply:** We have discussed the preoperative and perioperative predictors in discussion. (P6, Line18-21; P7, Line 2-3 and Line8-12). Although surgery technique was related to AF, post-operative inflammatory factors and myocardial injury biomarkers were more important and were the response of operative aspects. Thus, we included postoperative inflammatory factors and myocardial injury markers in the present study.

4. Consider addressing the potential influence of euthyroid sick syndrome and provide comments on its exclusion.

**Reply:** We have discussed the CABG-related euthyroid sick syndrome exerts detrimental effects on the poor prognosis. Post-operative thyroid function were not tested in our department and were not regular. It is essential to explore the association between the levels of post-operative thyroid hormones and cardiovascular outcomes. (P6, Line 23-24; P7, Line 28-29).

5. The authors should compare their work with Cerillo, A.G., Bevilacqua, S., Storti, S., Mariani, M., Kallushi, E., Ripoli, A., ... & Glauber, M. (2003). Free triiodothyronine: a novel predictor of postoperative atrial fibrillation. *European journal of cardio-thoracic surgery*, 24(4), 487-492. to show similarities and differences, especially since Cerillo et al. performed a similar study two decades ago. This could provide more insight into the novelty of the authors' work.

**Reply:** We have compared our work with Cerillo, A.G. et al. (P7, Line 32-37).

6. Line 190: The authors state that "FT3 supplementation decreased the incidence of post-operative atrial fibrillation after cardiac operations (19)". However, other studies by the same group (Klamperer et al. NEJM) and by Bennet et al. (Bennett-Guerrero, E., Jimenez, J. L., White, W. D., D'Amico, E. B., Baldwin, B. I., Schwinn, D. A., ... & Wolfe, W. G. (1996) Cardiovascular effects of intravenous triiodothyronine in patients undergoing coronary artery bypass graft surgery: a randomized, double-blind, placebo-controlled trial. *Jama*, 275(9), 687-692.) failed to demonstrate the same results. Please comment on these studies in the Discussion section.

**Reply:** We have added the comments in discussion part. (P7, Line 13-17). In clinical practice, preoperative FT3 supplementation in patients with low-normal FT3 concentration is in debate and needs to be identified by large randomized cohort studies.

7. Discuss the debatable claim of FT3 being an independent predictor of POAF (line 190), considering operative aspects and age - conducting an interaction test in the multivariable regression analysis.

**Reply:** We have discussed the effect of age on POAF and the association between age and FT3 values. We have conducted the interaction test in the multivariable regression analysis and the results showed that there was no significant interaction in age and FT3 in multivariable regression analysis (HR=1.27, 95%CI, 0.59, 2.67, P=0.54).

In our study, 503 eligible patients who underwent surgery coronary revascularization, including off-pump coronary artery bypass graft and one-stop hybrid coronary revascularization, which avoid the negative effects of cardiopulmonary bypass. As a report from *Circulation*, they collected the intraoperative factor, operative time, and did not find the correlation between operative time and POAF(1). Similarly with the study, the same conclusions were conducted and the results showed that operative time did not associate with the risk of POAF(2-4). Additionally, intraoperative factors like cardiac index and fluid balance were no longer be accurately collected in the retrospective study. However, we included post-operative inflammatory factors and cardiac injury markers which were strongly related to cardiac operation and reported to be associate with the increased risk of AF. Compared with operative aspects, postoperative inflammatory response and cardiac injury were more important and reflex the intraoperative status. We further included the postoperative factors and thyroid function in the multivariable regression analysis and found preoperative FT3 levels, post-operative LDH levels were independently associated with the increased risk of POAF.

Additionally, some studies did not collect intraoperative factors in patients with OPCAB(5-7). This is the common shortcomings in the present studies. We will explore the effects of intraoperative factors combine with thyroid function in patients with surgical coronary

revascularization in prospective study.

8. Please evaluate redundancy between Figure 2 and Table 3.

**Reply:** Table 3 is the results of univariate and multivariable regression analysis. Figure 3 was the result of multivariable regression analysis to make the results more concise.

9. Ensure that discussion elements are appropriately placed in the Discussion section

**Reply:** We have carefully checked the text and ensure that discussion elements are appropriately placed in the discussion section.

### Reference

1. Antoniadis C, Van-Assche T, Shirodaria C et al. Preoperative sCD40L levels predict risk of atrial fibrillation after off-pump coronary artery bypass graft surgery. *Circulation* 2009;120:S170-6.
2. Akazawa T, Nishihara H, Iwata H, Warabi K, Ohshima M, Inada E. Preoperative plasma brain natriuretic peptide level is an independent predictor of postoperative atrial fibrillation following off-pump coronary artery bypass surgery. *J Anesth* 2008;22:347-53.
3. Gao M, Fan K, Yu W, Liu H, Wei Y, Yu Y. The effects of high-sensitivity C-reactive protein on the clinical outcomes in obstructive sleep apnea patients undergoing off-pump coronary artery bypass grafting. *BMC Cardiovasc Disord* 2021;21:366.
4. Smukowska-Gorynia A, Perek B, Jemielity M et al. Neopterin as a predictive biomarker of postoperative atrial fibrillation following coronary artery bypass grafting. *Kardiol Pol* 2022;80:902-910.
5. Fujiwara M, Nakano Y, Hidaka T et al. Prediction of atrial fibrillation after off-pump coronary artery bypass grafting using preoperative total atrial conduction time determined on tissue Doppler imaging. *Circ J* 2014;78:345-52.
6. Chamchad D, Horrow JC, Samuels LE, Nakhamchik L. Heart rate variability measures poorly predict atrial fibrillation after off-pump coronary artery bypass grafting. *J Clin Anesth* 2011;23:451-5.
7. Chia AXF, Pang PYK. Predicting postoperative atrial fibrillation after off-pump coronary artery bypass surgery-an ongoing story. *J Thorac Dis* 2023;15:5294-5296.

### Reviewer B

I have very much enjoyed reading your paper. It is a very intelligent theme and you have drawn the right conclusion, however I strongly recommend a proof reading of the article, especially the discussion part needs extensive grammar corrections and rewriting prior to being accepted.

**Reply:** We have rectified the manuscript especially the discussion part. Revisions for the manuscript were shown in yellow highlight and refreshed reference were shown in blue highlight, added discussion were shown in green.