In this issue of *Journal of Cardiac Surgery*, Zhao et al. investigate the effects of subclinical hypothyroidism (SCH) on postoperative outcomes following CABG surgery and whether this contributes to the postoperative development of atrial fibrillation.[1] The effect of SCH in patients requiring cardiac interventions remains a controversial topic, with previous reports suggesting SCH to be associated with heart failure, stroke, atrial fibrillation and coronary insufficiency.[2–4] The converse however has also been reported, with some suggesting in fact a lower risk of atrial fibrillation in the SCH population.[5] However, the results of such studies must be interpreted with caution as flaws in methodology, limited sample sizes, and lack of appropriate control groups plague previous reports, precluding a definitive consensus of the effects of SCH following cardiac surgery. As a result, guidelines for preoperative pharmacologic treatment of SCH remain inconclusive and differ among recognized international societies thus further complicating the clinical management of this unique patient population.

Zhao et al. however address many of the previous limitations of prior studies in their retrospective, propensity matched analysis of SCH and euthyroid patients undergoing CABG procedures. Using advanced statistical analysis, intergroup imbalances, preoperative comorbidities and interventions were controlled between the SCH and euthyroid control group to account for confounding variables and bias inherent to the retrospective design of this study. While the primary outcome (that being the incidence of atrial fibrillation) was similar between populations, the authors report the SCH cohort to require longer durations of mechanical ventilation, greater ionotropic support, and increased wound complications compared to their euthyroid counterparts. The clinical utility of these findings is significant, however despite the sophisticated statistical analysis and extensive consideration of confounding variables, this study still has several minor limitations the clinician must consider in interpreting the results.

First, while the retrospective design of this study prohibited post-hoc modifications in methodology, using a single, isolated laboratory result to identify the SCH cohort could perhaps be problematic. It's well known that the effects of cytokines, inflammatory mediators, circadian timing of laboratory testing, concomitant medications and a host of other factors in hospitalized patients can transiently alter thyroid function values.[6,7] As the SCH cohort was categorized based on labs obtained on average six days prior to surgery, the stress response in these patients with likely decompensated heart failure undoubtedly influenced the hypothalamic pituitary axis, and possibly caused transient thyroid hormone imbalances that on repeat laboratory testing may have normalized. Thus, one could question whether all 545 subjects in the SCH cohort would be identified as such on repeat testing. Nevertheless, as the SCH cohort was identified in the immediate preoperative setting, one can be fairly confident that this cohort remained hypothyroid in the peri- and immediate post-operative states; therefore, the secondary outcomes reported remain significant.

An additional consideration must be made with respect to atrial fibrillation as its etiology is often complex and multifactorial. Thus, while the authors analyzed a multitude of preoperative and intraoperative factors, it's difficult to definitively conclude the lack of association between SCH and atrial fibrillation in absence of an exhaustive (and likely unrealistic) inclusion of every known potential confounding variable causing atrial fibrillation in both the pre, peri and postoperative settings. Nevertheless, given this limitation, the authors present a thoughtful and convincing argument that SCH has minimal effect on the postoperative development of atrial fibrillation.

Perhaps the most clinically significant findings of this study however are those of the secondary outcomes ascribed to the SCH cohort. The authors report nearly a three-fold increase in wound complications in the SCH cohort compared to the euthyroid population. In a surgery where mediastinitis and thoracic wound infections can have devastating complications, this finding alone may support the rationale for attaining preoperative euthyroid states in the SCH cohort. Alternatively, nutritional adjuncts and preemptive vitamin supplementation in the SCH cohort could potentially mitigate the higher incidence of wound complications and improve postoperative outcomes. Thus, further investigation is warranted to both clarify the mechanism of impaired wound healing in SCH, as well as the subsequent prevention therapies required to augment wound healing and optimize favorable outcomes.

Similarly, the reported increased ionotropic requirements as well as duration of both ionotropic support and mechanical ventilation in the SCH cohort are important secondary outcomes that should not be minimized. While institutional practices may vary in the pre, peri and postoperative settings, judicious fluid use, alternative anesthetic modalities and multi-disciplinary efforts in critical care management could potentially mitigate these outcomes in the SCH cohort. However, the clinician must remain cautious in interpreting these findings for while statistically significant, the clinical significance of a one-hour difference in mechanical ventilation in the absence of significant differences in ICU length of stay, or rates of tracheostomy or reintubation questions the utility of these findings if the clinical outcomes are equivocal between cohorts. Nevertheless, knowledge that SCH patients undergoing CABG have worse outcomes in these domains might prompt clinicians to mitigate these outcomes preemptively.

The reported outcomes of this study thus beckon the question of the utility of supplemental levothyroxine preoperatively to treat SCH and thereby prevent the postoperative complications observed in the SCH cohort. Unfortunately, it's not that simple however as clinical support of definitive benefits from levothyroxine supplementation remain inconclusive at this time.[8,9] In fact, should the spectrum shift to hyperthyroid states, the cardiovascular complications can be equally disastrous as the SCH counterparts, therefore further investigations are warranted to define the role of levothyroxine supplementation in this unique population.

Nevertheless, despite these minor criticisms, the authors should be commended for their impressively large sample size, well matched cohorts and statistical analysis all of which should lay the groundwork for further investigations on this topic. While further studies are warranted to further expand our understanding of the clinical significance and implications of the outcomes presented by the present study, the authors should be commended on a job well done in their scientific contributions to expanding our understanding of the effects of SCH in patients undergoing coronary bypass surgery.

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