

Peer review file

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Reviewer A

Comment 1: “According to the data shown in Table 1, significantly more patients with RHR > 100BPM received beta-blocker therapy (48% vs. 31.5%). The use of beta-blockers was also associated with a significant predictor of reduced adverse cardiovascular outcomes both in the univariate and multivariate logistics regression analyses. This finding seems to be against the conclusion that cancer patients with resting sinus tachycardia around cancer treatment are associated with increased adverse cardiovascular outcomes and mortality. The authors should give a further explanation in the discussion.”

Reply 1: Based on our data analysis, sinus tachycardia, which was adjusted for use of beta-blockers, was associated with increased adverse cardiovascular events. As demonstrated in Table 2, beta-blockers were identified as predictors of adverse cardiovascular outcomes. However, based on our models (both 1 and 2), sinus tachycardia was an independent predictor of outcomes, even when adjusted for variables such as beta-blockers. Hence, we arrived at our conclusions.

Changes in the text: NA

Comment 2: “It is also true that patients with RHR > 100BPM were significantly less Caucasian (60% vs. 77.8%). However, the white race appeared to be an independent predictor of increased adverse cardiovascular outcomes. The authors should give a further explanation in the discussion.”

Reply 2: Per our analysis (and included in Table 2), the white race was noted to be an independent predictor for adverse cardiovascular outcomes. Because of this, our models adjusted for the white race (Figure 1).

Changes in the text: Figure 1, Lines 115-124

Comment 3: “It looks identical between Figures 2(A) and 2(B). Is there a misplacement? If not, why did both models not show any difference in the prediction of mortality?”

Reply 3: The results from Figure 2A and 2B were similar. Due to the significant similarities, we have omitted Figure 2B for clarity.

Changes in the text: Figure 2, Lines 133-134

Reviewer B

Comment 1: “how far apart were these clinic visits?”

Reply 1: Patients were assessed in clinic on a weekly to monthly basis.

Changes in the text: Lines 56-57

Comment 2: “Interaction analysis with anemic, ckd, group on anticoagulation?”

Reply 2: Given the design of our study, we did not perform an interaction analysis. Rather, we adjusted for these variables in our models.

Changes in the text: NA

Comment 3: “univariate analysis has significant differences for anticoagulation and type of cancer unlike mentioned in table 2. Please explain. Show complete regression analysis in supplement”

Reply 3: We only included factors that we felt were clinically relevant. Nevertheless, these models adjusted for anticoagulation and type of cancer.

Changes in the text: NA

Comment 4: “does AHF include hypertensive heart failure episodes too?”

Reply 4: AHFE only included heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). This was clarified within the text.

Changes in the text: Lines 71-73

Comment 5: “Information for stroke volume, as increased heart rate might be due to decreased stroke volume to compensate for maintaining cardiac output?”

Reply 5: The authors believe this was beyond the scope of this manuscript. Moreover, because the included patients did not previously have a diagnosis of heart failure, most individuals did not have a baseline echocardiogram to ascertain this information.

Changes in the text: NA

Comment 6: “Perform subgroup analysis by including all groups excluded as mentioned in methodology and show using a kaplan meir curves where does mortality of increased heart rate cancer group stand in comparison to other groups excluded here.”

Reply 6: This was beyond the scope of this study, and the authors believe that this would be an excellent question to address in a separate study.

Changes in the text: NA

Comment 7: “Selection bias and residual confounding. Include E values if possible.”

Reply 7: Unfortunately, given the study design we were unable to account for both selection bias and residual confounding. This was included within the “Limitations” section of the text.

Changes in the text: Lines 186-187