

Reviewer Comments

Comment 1: This is an interesting study reporting an investigation concerning the BV of NT-proBNP in 8 apparently healthy Turkish females, adhering to all the necessary preanalytical requirements outlined by the European Biological Variation. The experimental design of this study is sound and the results are original. The Authors should be congratulated for their effort.

Reply 1: We are grateful for the constructive feedback provided by the reviewer.

Comment 2: The NT-proBNP assay is recommended by all the international guidelines, especially for diagnostic, prognostic, and management of patients with heart failure. The patients with heart failure are more frequently adult individuals of both sexes who have an age > 55 years. Authors should comment on the Discussion of the revised manuscript as the biological variation was calculated in only 8 women, with a median age of 23.2 years (range 20-29 years), after the exclusion of data related to 12 men and 4 women from the total enrolled healthy population (i.e., only the 33.3% of the sample was taken into consideration in this study) should be clinically useful in the patients with heart failure.

Reply 2: We concur with the reviewer's observations. Unfortunately, we didn't have access to samples from older subjects, and we've acknowledged this as a limitation in our work. Moreover, in agreement with the reviewer's suggestion, we've incorporated the following statement in the discussion:

“The clinical relevance of NT-proBNP in the management of heart failure is well-acknowledged, with international guidelines emphasizing its significance in the diagnostic, prognostic, and therapeutic contexts. Specifically, it has become an indispensable tool for the evaluation of adult patients, primarily those over the age of 55, who suffer from heart failure (1). In the present study, we determined the BV of serum NT-proBNP in 8 healthy Turkish female individuals with a median age of 23.2 years (range 20-29 years). It is crucial to recognize the potential limitations this might pose. While the demographic investigated provided valuable insights, it is not entirely representative of the typical heart failure patient, often being older adults of both genders. This discrepancy could influence the generalizability of our findings to the broader patient population. However, it is noteworthy that understanding the biological variation in a younger, healthy demographic can provide a foundation upon which future studies can build. “