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Methodological problems in the measurement of interleukin-33 concentrations in patients with heart failure with a reduced ejection fraction

To the Editor,

We have read manuscript entitled "The concentration of interleukin-33 (IL-33) in heart failure with reduced ejection fraction. Anatol J Cardiol 2019; 21: 305-13" with great interest (1). The study included 155 patients with heart failure and 60 healthy individuals to compare IL-33 levels (1). The authors pointed out that blood samples collected from patients on admission were stored at −80 °C until further use; however, they did not mention about blood sample storage time comparison between the patient and the control group. Storage time for blood samples may affect IL-33 concentration measurement and change results; for example, variable cytokine concentration levels were seen with different blood storage durations in the previous study (2).

The authors used the legend max human IL-33 kit manufacturer system as seen in the standard range of 15.6–1000 pg/mL, and the limit of detection is 4.14 pg/mL; it is not clear how values below this level are measured (3). However, the authors measured a healthy human concentration of 16.91 (0–81) pg/mL in Figure 1a, which we consider as an important problem as to how the kit measured levels below the limit of detection. Values between the limit of quantification and the limit of detection should be given qualitatively and calculated separately. Furthermore, we think that statistical measurement and interpretations made without value and corrections may affect the results.

Figure 1b is given as an interquartile range in figure legends, but that is not found in the text or figure. No numerical value was given in the text or figure for Figure 1c. In addition, the median was given in Figure 1d, and it was observed that the median value was below the limit of quantification.

Therefore, we think that the interpretations made on IL-33 in Figure 1a–1d are insufficient due to the methodological approach, and that the statistical comments about the values will seriously reduce the reliability. Furthermore, how values <4.14 are measured raises considerable doubt as they are below the minimum measurable limit.

The aim of the present study was to investigate the effect of cytokine expression on the course of the disease in patients with heart failure. However, case–control studies do not provide information about the course of the disease. These studies can only comment on the instant situation. To do this, we think that evaluation with longitudinal cohort studies would be a more appropriate method.

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