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Research Letter

Reticulocyte hemoglobin equivalent is an easily applicable marker for detecting iron deficiency in patients with acute decompensated heart failure

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Iron deficiency (ID) is associated with poor outcomes in patients with acute decompensated heart failure (ADHF) [1]. It is, therefore, relevant to identify ID to ensure appropriate treatment in ADHF patients with ID. However, various definitions of ID have been used [1–3] and there is a controversy over definitions of ID in patients with heart failure (HF) [1]. A most recent 2023 focused update of the 2021 European Society of Cardiology (ESC) Guidelines used a definition based on either transferrin saturation (TSAT) <20 % or serum ferritin <100 μg/L [3].

With regard to a marker for ID, reticulocyte hemoglobin equivalent (Ret-He) is considered to reflect the iron content in reticulocytes and we recently proposed that Ret-He has utility as a marker for ID in patients with HF [4]. However, definitions of ID in HF are various and there are limited data regarding Ret-He in patients with ADHF. Therefore, in this study, we aimed to assess Ret-He according to a definition based on 2023 focused update of the 2021 ESC Guidelines (TSAT <20 % or serum ferritin <100 μg/L) [3] to evaluate whether Ret-He is an easily applicable marker for detecting ID in patients with ADHF.

To this end, we studied 360 consecutive patients hospitalized for ADHF according to the Framingham criteria [5] between December 2017 and August 2019 at Hyogo Medical University Hospital. Patients with renal failure or receiving hemodialysis, hematological diseases, or active malignancies were excluded; eventually, 225 participants were included. Participants' baseline characteristics and laboratory and echocardiographic data were obtained on admission. Ret-He levels were determined using an automated hematology analyzer (Sysmex, Kobe, Japan). This study was approved by the ethics committee of Hyogo Medical University (authorization number: 3549), and informed consent was obtained from all participants.

Of the 225 patients with ADHF (median age: 79 years, proportion of men: 56 %, median left ventricular ejection fraction, hemoglobin, and serum iron levels: 37 %, 10.6 g/dL, and 7.1 μmol/L, respectively), the median Ret-He levels were lower in ADHF patients with ID than in those without ID (Fig. 1A,B). According to the ID definition of TSAT <20 %, the cut-off value of Ret-He for ID screening was 32.4 pg by receiver-operating characteristic analysis, and per the definition of serum ferritin <100 μg/L, the cut-off value was also 32.4 pg. The corresponding areas under the curve values for these definitions were 0.776 and 0.754, respectively (Fig. 1A,B). Additionally, according to World Health Organization criteria of anemia, the cut-off values of Ret-He for iron deficiency anemia screening were 32.4 and 31.0 pg by TSAT <20 % and serum ferritin <100 μg/L, respectively (Fig. 1C,D). As Ret-He is correlated with iron parameters [4], these results may reflect iron levels.

The distinctive result of the present study was that the cut-off value of Ret-He for ID screening was same for each definition based on TSAT <20 % and serum ferritin <100 μg/L in patients with ADHF. The measurement of Ret-He is inexpensive and cost-effective. Collectively, Ret-He levels may be a useful parameter for detecting ID in patients with ADHF.

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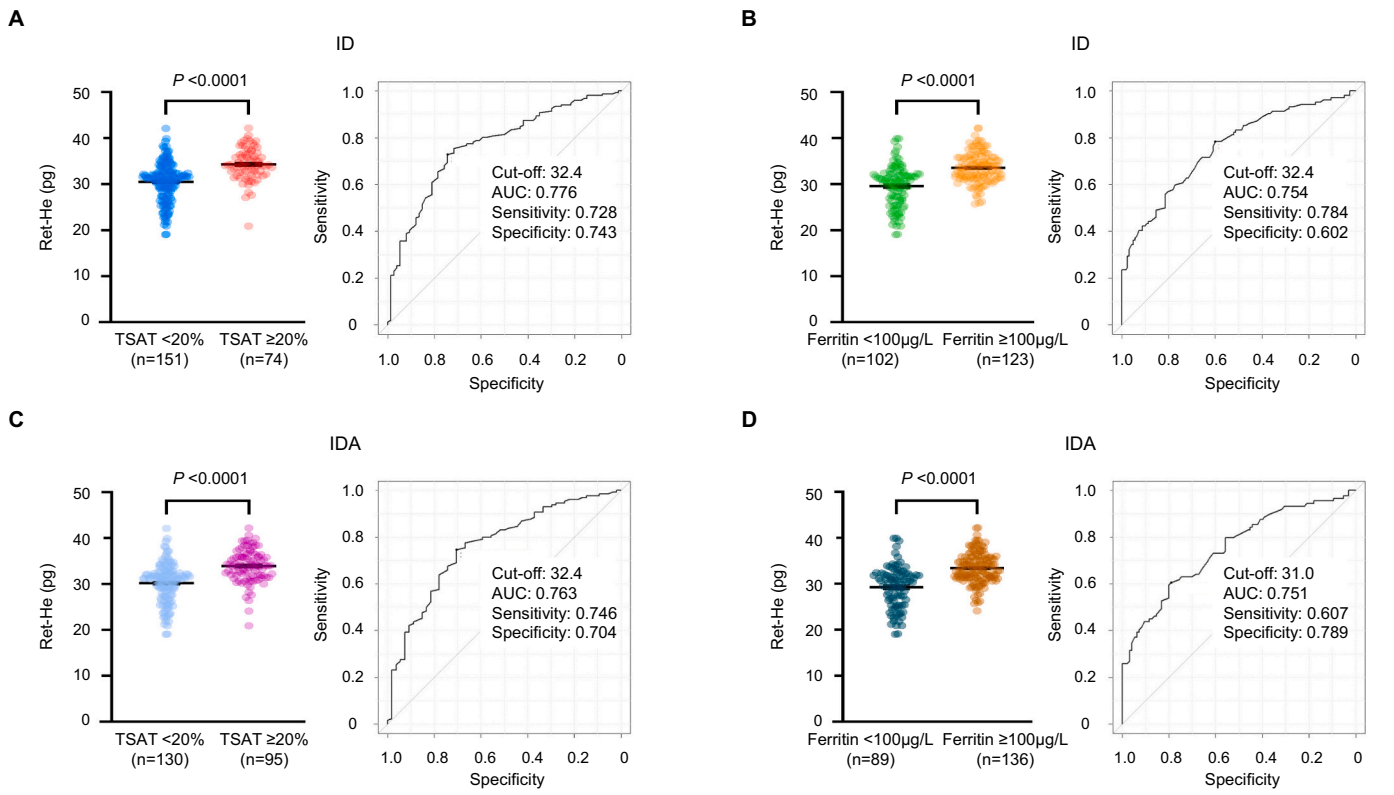

Fig. 1. Reticulocyte hemoglobin equivalent levels in patients with acute decompensated heart failure according to each definition of iron deficiency.
Ret-He levels and receiver-operating characteristic curve of Ret-He to screen for iron deficiency (ID) and iron deficiency anemia (IDA) according to **(A,C)** TSAT <20 % and **(B,D)** serum ferritin <100 μg/L in patients with acute decompensated heart failure. AUC indicates area under the curve. Statistical significance was evaluated by Student *t*-tests.

Declaration of competing interest

The authors declare they have no conflict of interest.

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