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Diagnosis of iron deficiency in ESRD patients

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## CORRESPONDENCE

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### DIAGNOSIS OF IRON DEFICIENCY IN ESRD PATIENTS

To the Editor:

The review article by Fishbane and Maesaka entitled "Iron management in end-stage renal disease"<sup>1</sup> is scholarly, interesting, and informative. We were pleased that our article concerning the search for the best laboratory method to diagnose iron deficiency in end-stage renal disease (ESRD) patients<sup>2</sup> was footnoted and that our results were discussed and compared with those of other studies. However, our study did not show that no level of serum ferritin concentration is of value in the diagnosis of iron-deficiency anemia. In fact, by using the bone marrow iron stores as the reference standard, we found that a serum ferritin level less than 200 ng/dL was highly specific but not sufficiently sensitive (specificity of 100% but sensitivity of only 41%) for this purpose. Thus, according to our data, any ferritin level less than 200 ng/dL is very reliably consistent with iron deficiency and no further studies are necessary to evaluate the iron status. However, a serum ferritin concentration of more than 200 ng/dL cannot rule out iron deficiency because of low sensitivity. Moreover, we showed that a serum transferrin saturation ratio of less than 20% is a highly reliable test for iron deficiency and that the test could reach a sensitivity of 100% and a specificity of 80% if hypotransferrinemic patients are excluded.<sup>2</sup> Low transferrin, and subsequently, low total iron-binding capacity (TIBC) levels can occur because of non-iron-related factors such as malnutrition. In a recent study, we showed that TIBC levels are lowest in severely malnourished and highest in well-nourished dialysis patients.<sup>3</sup> Thus, in poorly nourished patients, the serum transferrin saturation ratio, calculated by serum iron concentration divided by TIBC level, can be erroneously normal to high, even though such a hemodialysis patient might suffer from iron deficiency:

$$\text{Transferrin Saturation } (\uparrow) = \text{serum iron/TIBC } (\downarrow)$$

This situation could lead to the false conclusion that an iron-depleted ESRD patient receiving recombinant human erythropoietin does not need iron supplementation. Our suggestion to exclude the patients with hypoproteinemia will improve diagnostic accuracy and does not make the test impractical for routine clinical use. In our study,<sup>2</sup> only five of 25 patients (20%) had hypotransferrinemia. For these patients, other laboratory parameters should be obtained to assess the iron status. By ignoring the non-iron-related changes in the serum TIBC level, most of these hypoproteinemic, malnourished patients would be falsely considered as having adequate iron

stores and would be deprived of needed iron supplementation. Thus, we suggest the enclosed algorithm (Fig 1) as a summary of our recommendations.

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#### REFERENCES

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Reply:

Kalantar-Zadeh and Luft suggest that the serum ferritin at a cutoff of less than 200 ng/mL is a reliable indicator of iron deficiency. Their data show a sensitivity of 41% and a specificity of 100%. Although in their hands the serum ferritin was quite specific (we have not found the same), the sensitivity was unacceptable for routine clinical use, because 59% of iron-deficient patients would be missed. Their suggestion to use the transferrin saturation by excluding patients with a low total iron-binding capacity is intriguing; however, I wonder if it would be practical for routine clinical practice.

We must remember the vitally important point that iron deficiency in dialysis patients is usually functional and would not be associated with absent marrow iron stores. Under the stimulation of intravenous erythropoietin (EPO) therapy, red cells are often made faster than iron can be supplied, even when iron stores appear to be adequate. Therefore, iron status cannot be defined by the bone marrow iron stores in patients treated with EPO. A study such as that by Kalantar-Zadeh et al, which defines iron deficiency based on the bone marrow findings, tends to significantly underestimate the prevalence of iron deficiency. The algorithm they propose, although interesting, is based on this flawed concept. It would lead to the underdetection of iron deficiency among dialysis patients.

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