

prevent a selection bias.

Finally, despite having similar underlying mechanisms and close relationships to heart failure, we don't have enough evidence to recommend intravenous ferric carboxymaltose therapy in atrial fibrillation patients without established ID anemia.

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Iron deficiency and atrial fibrillation

Dear Editor,

We read the article by Keskin et al. about iron deficiency in patients with atrial fibrillation (AF) with great interest. It was reported that iron deficiency was more frequent in patients with AF than in a healthy control group and that iron deficiency and anemia were more common in the permanent AF group.^[1]

The major cause of iron deficiency is blood loss; it is most often caused by excessive menstrual bleeding in women of childbearing age and bleeding of the gastrointestinal tract in the remaining population.^[2] The main reason for the difference in the prevalence of iron deficiency and anemia between healthy controls and AF patients could be related to anticoagulant medication use or as a result of increased occult bleeding.

Another important point is that medications can affect the absorption and metabolism of iron. There are emerging data suggesting an association between chronic proton pump inhibitor (PPI) use and iron deficiency.^[3] Patients treated with anticoagulation more often use a PPI when compared with the normal population. Therefore, we think that PPI use should be taken

into account in this study. Additionally, digoxin may affect some genes related to iron metabolism and can cause iron deficiency and anemia.^[4] Digoxin use could be another reason for iron deficiency in AF patients.

Finally, the duration of anticoagulation was not assessed. Patients with permanent AF may be under warfarin treatment longer than other groups. This longer duration of anticoagulation may be another reason for the difference in anemia and iron deficiency between the groups.

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heart failure: clinical data analysis and drug-gene interaction network. *Oncotarget* 2017 Aug 22;8:57003–11.

Authors' reply

Dear Editor,

We thank the authors for their important comments on our article. We agree that long-term anticoagulant use may result in increased occult bleeding and iron deficiency (ID) in patients with atrial fibrillation (AF). Patients with any history for treatment of anemia or ID in the prior 12 months had been excluded from our study, but patients with occult blood loss may have remained undetected. We have to keep in mind that all patients in the study group were using oral anticoagulants, and prevalence of ID was not different among the controls and paroxysmal AF, only slightly higher in persistent AF and significantly higher in permanent AF. Contrary to ID, prevalence of anemia among the AF patients with and without ID was relatively low (33.3% vs. 18.9%). The significant association of ID with hs-CRP in univariate analysis indicates that not only occult loss but also other mechanisms, especially inflammation should play a role in the increased frequency of ID.

The authors' comments on the associated medications and iron metabolism are important. We had excluded the patients with overt gastrointestinal bleeding, however, we haven't analyzed proton pump inhibitor usage separately, which is known to decrease iron absorption and lead to ID anemia.^[1] The patients with

systolic heart failure had been excluded from the study, which may be a cause for low digoxin usage among the study population (6.9% of all patients). Besides, in regression analysis the digoxin use was not associated with ID. Larger studies are required to reveal any possible effect between concomitant medications and ID in AF patients. Finally, we agree with the authors' statement about the association between oral anticoagulation usage duration and ID. Due to the retrospective design of the study, we could not reliably determine the duration of AF and drug usage. This might have been stated as a limitation. Nevertheless, we stratified the patients according their AF patterns and this categorization may reflect the duration of AF and indirectly oral anticoagulation usage duration.

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