Association Between AID/FID with Incident CV Disease and Mortality

Hello, my name is Benedikt Schrage. I'm a cardiologist from Hamburg, Germany, also a cardiovascular researcher. I conducted the recently published study "Association of Iron Deficiency with Incident Cardiovascular Disease and Mortality in the General European Population".

The aims of the study

From trials in disease cohorts, for example, from heart failure trials, we do know that iron deficiency, and especially functional iron deficiency, is linked to the outcome.
Therefore, the morbidity and mortality of patients, and we also do know that interventions, so supplementation of iron in iron-deficient patients is linked to better symptomatic outcomes.
But this seems to be also true for functional iron deficiency, which means assessing the stored iron and the iron in circulation, instead of just assessing the absolute iron deficiency, which just uses the stored iron. However, in the general population, until now we have only investigated associations between absolute iron deficiency and outcomes, but not functional iron deficiency and outcomes.
Our aim was to provide a very comprehensive assessment of iron deficiency, functional iron deficiency, and absolute iron deficiency with mortality, cardiovascular mortality, and incident cardiovascular diseases in the general population.

Design and patient cohort of the analysis

For this study, we used the BiomarCaRE consortium. BiomarCaRE is the collaboration of several population-based study cohorts in Europe. And we were able to use data from three cohorts which provided baseline information on the iron status, which was needed to assess functional and absolute iron deficiency. In the end, this was a study of roughly 12,000 European patients, or participants, who were apparently healthy.
This was not a disease cohort, but participants randomly selected from the general population. And in this cohort of 12,000 participants, we then assessed the association between absolute and functional iron deficiency with the outcomes by applying Cox regression models. And we adjusted these for commonly known cardiovascular risk factors, such as age, sex, diabetes status, and cholesterol.

Key findings

The key findings of our study were that functional iron deficiency was not only associated with all-cause mortality, but also with cardiovascular mortality and incident coronary heart disease. There was a link between functional iron deficiency and the new onset of coronary heart disease and also cardiovascular and all-cause mortality. However, if we looked at absolute iron deficiency, we only saw the link between absolute iron deficiency and incident coronary heart disease, but not with mortality.
It seems as if functional iron deficiency would provide a more general and a broader assessment of the patient and iron deficiency as a risk factor than absolute iron deficiency would do.

Implications

This is an observational study, so we cannot draw a direct conclusion on the causal interaction between the iron deficiency and the outcomes we assessed.

There might be another factor involved. However, if we put this into the whole body of evidence on this topic, and especially if we go a step further and look at the trials on heart failure and other cardiovascular diseases where we show, especially for HF trial, that if we treat functional iron deficiency, we improve symptomatic outcomes of the patients. And we will soon also have outcome trials where supplementation of iron in functional iron-deficient patient is assessed on mortality endpoints.
I think there is a certain rationale to believe that functional iron deficiency is a relevant and valid risk marker and risk factor for participants or individuals from the general population. And I wouldn't go so far to say, now we should supplement iron in individuals with iron deficiency. However, this is certainly something which, A, needs to be studied in future research, and, B, it's specifically, one could think about conducting a randomised trial on this topic and to compare different measures of iron supplementation. For example, oral supplementation might be enough in these individuals, but there's also the means to intravenously provide iron in individuals with iron deficiency to see if this really, on the population level, also improves outcomes.

Take-home messages

I think the take-home message of the study is that functional iron deficiency, but not absolute iron deficiency, seems to be a relevant risk marker also at a general population level. And it seems very worthwhile to investigate this further and conduct more research on this topic.