To the editor:

Prognostic impact of elevated pretransplantation serum ferritin in patients undergoing myeloablative stem-cell transplantation

Armand and colleagues suggest a possible link between pretransplantation ferritin levels and outcome after myeloablative hematopoietic stem cell transplantation (HSCT), especially in patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). In general, treatment-related mortality after HSCT is mostly caused by either graft-versus-host disease (GVHD) or infection-related complications. It is of note that the negative impact of iron overload on transplantation-related mortality was not attributable to a higher incidence of acute GVHD. Therefore, it would be interesting to know what the causes of death were in this group of patients. One suggestion is that these patients experienced fatal infections more frequently. The nature (bacterial versus fungal) could have also implications on prophylaxis and surveillance regimens after transplantation. Nevertheless, our concern is that the transfusion load as mirrored by ferritin level is rather a reflection of the disease stage. High ferritin levels and a long history of transfusion support are closely correlated with a longer interval from diagnosis to HSCT. At the same time, the duration and depth of disease-associated neutropenia might have been longer, leading to a higher frequency of opportunistic infections. Therefore, we would like to ask the authors to incorporate duration of neutropenia (absolute neutrophil count [ANC] < 1.8 × 10^9/L [< 1800/µL]) as well as time from diagnosis to HSCT into the proportional hazard model in order to confirm the ferritin level as an independent risk factor in this setting.

In addition, our conclusion from the presented data might be different from that of Armand et al proposing appropriate iron chelating therapy in these patients. We think that the current decision model of when to perform a HSCT in an individual patient must be rather extended, taking also into account the duration and frequency of transfusion support, which has also a negative impact of disease-free survival regardless of International Prognostic Scoring System (IPSS) score. This could disentangle into earlier intervention strategies proposing transplantation in a patient (eg, with INT-1–risk MDS in case of severe red cell transfusion dependency before clinical manifestation of iron load or transformation to higher IPSS stage).

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References


Response:

Further analysis of the relationship between pretransplantation serum ferritin and transplantation outcome: cause-of-death analysis and impact of disease duration

We appreciate the insightful comments of Platzbecker and colleagues on the possible confounders of the relationship between serum ferritin and transplantation outcomes, and on the conclusions that can be drawn from our analysis. At their suggestion, we analyzed the impact of elevated pretransplantation serum ferritin on cause of death, focusing in particular on infection-related deaths (including viral, bacterial, and fungal causes) and pulmonary-related deaths (including diffuse alveolar hemorrhage [DAH], idiopathic pneumonia syndrome [IPS], and respiratory failure). Patients with an elevated ferritin (in the upper quartile) showed a trend toward more infectious deaths in univariate and multivariate analysis (multivariate odds ratio = 1.9, P = .18). The numbers were too small to allow a distinction between pathogen classes. In contrast, there was no evidence of an increased likelihood of dying of pulmonary causes (multivariate OR = 1.0, P = .9). It should be remembered that cause of death is an unreliable variable, particularly in retrospective studies, and we would therefore urge caution when interpreting these results.

In our study, we did not have access to duration of disease-related (pretransplantation) neutropenia, and hence cannot comment on its relationship to ferritin levels. We repeated our
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