Review of: "Mortality and microbial diversity after allogeneic hematopoietic stem cell transplantation: secondary analysis of a randomized nutritional intervention trial"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

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This is the second data analysis from the previous randomized nutritional intervention trial during allogeneic hematopoietic stem cell transplantation. Patients received routine hospital food with optimized energy and protein intake (intervention group, n=23) or standard parenteral nutrition (control group; n=24). Collected patients' stools were used for microbiota analysis. The authors did not find any significant differences between both groups in investigated parameters. Although, they observed depletion of microbiota and SCFAs and changed markers of the gut barrier function after 3 weeks post-transplantation. They also propose the connection of higher one-year mortality with lower microbial diversity and with lower abundance of bacterial species Blautia.
It is quite a small study with a small cohort of patients, however, microbiome analysis is carefully and correctly done in detail.

There are some concerns with this study:
1) Bacterial abundances analysis was performed only with genera present in at least 50% of the individuals. It is known that each individual has a personalized gut microbiota containing a unique taxonomic composition with only a small shared group within humans, Approximately a third of intestinal resident microbes is shared by all individuals, the remaining part is unique for each host. Therefore, this limit to 50% abundance seems to be too strict and differences in the abundance of less abundant species may not be captured.

2) Authors found the reduction in OTUs number and Shannon diversity in both groups after the allo-HSCT (Fig. 1). This is not surprising, because the setting of allo-HSCT imposes a significant disruption on the gut microbiome homeostasis. And because SCFAs are produced by bacteria, also SCFAs decrease detected after the allo-HSCT is logical. However, it is important to note that the two groups did not differ in all parameters and therefore dietary measures do not seem to prevent the negative consequences of microbiome changes and clinical parameters after allo-HSCT.

Interesting seems to be finding that the relative abundance of Blautia genus was higher in survivors after 3 weeks post-HSCT. Blautia has potential probiotic functions and is able to produce bacteriocins that give *Blautia* the potential to inhibit the colonization of pathogenic bacteria in the intestine. Its lower abundance is often associated with various diseases and it can be used as a potential tool for the early diagnosis or treatment of diseases. However, one has to be very careful with drawing general conclusions at the genus level, because most of the functions and features are due to specific bacterial strains. Therefore, the differences and associations with single OTUs would be more meaningful.
(doi: 10.1080/19490976.2021.1875796)

3) Authors measured markers of gut barrier functions – plasma levels of I-FABP, LBP and sCD14. all analyzes and their statistical evaluation were appropriately performed. It is difficult to find suitable markers of gut permeability, although various markers are used in many studies. I-FABP is a marker of gut damage, but it is not very sensitive to small changes and its abundance is quite controversial in many studies. LBP represents a measure of internal exposure to bacterial lipopolysaccharide and its abundance has been associated with several chronic conditions and may be a marker of chronic inflammation; however, its reliability of this biomarker is also uncertain. sCD14 is a nonspecific marker of monocytes activation and an intermediate in the transfer of LPS to lipoproteins, resulting in neutralization of LPS. Some studies propose sCD14 as a marker of gut permeability, but it is more a sign of involvement of innate immunity cells after translocation of commensal bacteria.
None of the used biomarkers is optimal for the assessment of gut barrier function and the search for noble biomarkers should continue.

4) Figures 2 and 3: units at axes y and explanation in the legends are missing.