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ORIGINAL PAPER

Prolonged gut microbial alterations in post-transplant survivors of allogeneic haematopoietic stem cell transplantation

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Summary
Dysbiosis of the gut microbiota has been reported to increase early complications after allogeneic haematopoietic stem cell transplantation (allo-HSCT). However, it remains unclear whether gut microbial alterations persist during late complications, such as chronic graft-versus-host disease (cGVHD) or secondary cancers. Here, we analysed the gut microbiota of 59 patients who survived for 1–21.7 years (median, 6.4 years) after allo-HSCT. Long-term survivors showed lower gut microbial diversity than the age- and sex-matched healthy controls. This decreased diversity was reflected in the reduced abundance of the butyrate-producing bacteria. Patients with a history of grade 3 acute graft-versus-host disease (aGVHD) exhibited higher *Veillonella* abundance than patients with a history of grade 1–2 or non-aGVHD cases. The abundance of *Faecalibacterium* showed no decrease only in limited cGVHD cases. Additionally, the microbial structure in the secondary cancer group was significantly different ($p < 0.05$) from that in the non-secondary cancer group. This study is the first to show that microbial dysbiosis is present over a 10-year lifetime after discharge following allo-HSCT. Our results suggest that these prolonged gut microbial alterations may be associated with the development and exacerbation of late complications in post-transplant survivors.

KEYWORDS
aGVHD, allogeneic haematopoietic stem cell transplantation, cGVHD, gut microbiota, second cancer

INTRODUCTION

The outcomes of allogeneic haematopoietic stem cell transplantation (allo-HSCT) have improved with the advent of new therapies and drugs.[1] Such improvements have led to an increase in the number of long-term survivors. Late complications after transplantation are associated with a high mortality rate and decline in quality of life and represent a major concern for long-term survivors. Chronic graft-versus-host disease (cGVHD) and secondary cancers are particularly concerning.[2,3] cGVHD occurs in 54% of patients following transplantation and accounts for 37.8% of post-transplant, non-relapse mortality.[4,5] The pathogenesis of cGVHD involves uncontrolled B-cell activation, immune activation of specific T-cell subsets, and a deficiency of regulatory T cells.[6]