BACKGROUND

In patients, allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative option that can be used to treat hematologic malignancies and disorders. In 2016 in the US, the three most frequent indications for allo-HSCT included acute myeloid leukemia (AML), myelodysplastic syndromes (MDS) and acute lymphoblastic leukemia (ALL) [1]. Success of allo-HSCT is primarily influenced by human leukocyte antigen (HLA) matching between the donor graft and the recipient and a mismatch significantly increases the probability and severity of graft-versus-host disease (GVHD) [2]. Severe GVHD can be a life-threatening complication of allo-HSCT. Among unrelated donor allo-HSCT, approximately 10% of deaths are related to GVHD [1]. As a result, mismatched allo-HSCT, although potentially curative, is generally only utilized in healthier, fit patients to reduce the risk of serious complications. Diagnosis and definition of GVHD can vary across studies, but it is generally understood that a large proportion of allo-HSCT patients will experience GVHD, with 30-70% reported as having acute GVHD [3]. GVHD, aside from its clinical implications, is also believed to produce a humanistic burden as well as a significant economic burden to the healthcare system.

OBJECTIVES

We reviewed published evidence to assess quality of life (QOL), healthcare resource use and costs associated with GVHD post-allo-HSCT.

MATERIALS & METHODS

A systematic literature review (SLR) was conducted in November 2018 for all records published between 2008-2018 using key biomedical literature databases: Embase®, MEDLINE® and Cochrane databases.

Conference abstracts from the last three years were systematically reviewed (AMCP, ASCO, ASH, ISPOR). Additional bibliographic and string searches were also conducted to gather further relevant evidence.

The patient population included any patients with hematologic malignancies who experienced GVHD. Regarding interventions, any patient who underwent allo-HSCT was included.

Outcomes of interest included measures of cost, healthcare resource utilization and QOL related to GVHD.

Non-English studies, case studies, case reports and case series were excluded.

The SLR followed the Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1), using the Population, Intervention, Comparators, Outcomes and Study Design (PICOS) criteria following the Cochrane Collaboration Guidelines for Systematic Reviews and Meta-Analyses. Each citation underwent screening by two independent reviewers who used PICOS-based criteria to reject non-relevant publications.

Inconsistencies between reviewers were resolved through roundtable discussion with a third reviewer.

RESULTS

- A limited amount of published evidence was identified: 2 QOL and 3 economic studies.
- Two studies measured QOL (Table 1) and both found that GVHD was associated with QOL reductions.
- Significant and clinically meaningful (>10 point) reductions of all QOL domains were reported in GVHD patients as two studies measured QOL (Table 1) and both found that GVHD was associated with QOL reductions.
- GVHD was also associated with increased costs and healthcare resource utilization (Table 2).
- A US claims database analysis found that allo-HSCT patients with acute GVHD experienced greater healthcare costs compared to those without GVHD (>100,000 additional cost per patient; p<0.01) and also experienced 3 additional weeks of hospitalization after 1 year of follow-up [6].
- A US population analysis estimated that $5.2 billion would be used from 2015-2025 to treat chronic GVHD in 44,450 patients and $27 billion would be lost in wages and work productivity, demonstrating significant economic burden for health plans and from a societal perspective [7].
- A Japan-based cost study found that grade III-IV GVHD was associated with longer hospitalization (p=0.01); a significant driver of increased costs [8].
- The limited amount of evidence regarding the humanistic and economic burden of GVHD demonstrates a need for additional research.
- The reductions in quality of life and increased costs of GVHD based on the available evidence also support a need for treatment strategies that minimize the risk of GVHD in allo-HSCT patients.
- Novel treatment strategies to reduce GVHD, besides the clinical benefit, would have the potential to alleviate substantial economic burden to the healthcare system and to society (as described by the $26 billion in lost wages and productivity in the US) allowing for optimal use of healthcare resources in a scarce environment.
- The humanistic and QOL benefit of novel treatment strategies would have to be validated in additional value-based analyses (e.g. cost-effectiveness analyses) however, this collection of evidence demonstrates a gap in efficiency where patients are suffering at a large cost to the system.

CONCLUSIONS

GVHD is associated with reductions in QOL and increased healthcare/societal costs, with longer hospitalization as one of the main drivers. Superior treatment strategies to prevent and treat GVHD are warranted to reduce significant humanistic and economic burden.

LIMITATIONS

- One of the limitations of this collection of evidence is that the outcomes are not stratified by disease area.
- It is plausible that the costs and quality of life decrements would have enough variance between different diseases to justify targeting particularly burdensome indications for future therapies before expanding into other areas.
- Another limitation is due to the nature of QOL data and different scales, it can be difficult to conduct naïve comparisons without further transforming data into utilities.
- Lastly, few studies were identified in the search, and caution should be exercised when using data from a small number of samples or studies to generalize to a larger population; however, this is useful to identify the need for further research into the burden associated with GVHD.

REFERENCES