Bone Marrow Transplantation (2014) **49,** 1455–1456

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EDITORIAL

A golden opportunity

Bone Marrow Transplantation (2014) **49,** 1455–1456; doi:10.1038/bmt.2014.185; published online 18 August 2014

In a previous issue of the journal, Allareddy *et al*.[1] report on the prevalence of acute respiratory failure from any cause in hospitalized SCT patients and the associated hospital costs. The authors utilized the Nationwide Inpatient Sample (NIS), which is the largest all-payer inpatient database in the United States, approximating 97% of all hospital discharges annually. This study provides valuable information from one of the largest cohorts of patients ($n = 6074$) hospitalized with respiratory failure following SCT. The authors confirm the well-documented finding that SCT recipients who develop respiratory failure have high in-hospital mortality.[2,3] They found that the prevalence of respiratory failure increased over the course of the study. They also demonstrated that the overall in-hospital mortality was greater than 50% and that continuous invasive mechanical ventilation (IMV) and prolonged IMV (>96 h) were independent predictors of mortality. The novelty of the authors' work is the assignment of a direct financial cost to hospital resource utilization associated with respiratory failure following SCT. The mean hospitalization charge was $620 765; total hospitalization expenditures for the entire cohort were a staggering $3.34 billion dollars. These costs did not include certain medications or loss of productivity and other indirect expenses associated with the hospitalizations and, therefore, likely underestimate true resource utilization.

Over the last decade advances in critical care medicine—the use of low tidal volume ventilation, positive end-expiratory pressure, and non-invasive positive pressure ventilation as well as early liberation from mechanical ventilation—have led to overall mortality reductions in patients requiring mechanical ventilation.[4,5] However, respiratory failure following SCT continues to be associated with high mortality. Prior to recent advances, respiratory failure requiring mechanical ventilation following SCT had mortality rates between 85–90%.[2] Allareddy *et al*.[1] found an overall mortality rate between 60.6 and 66.5% for SCT patients requiring mechanical ventilation. These numbers, although significantly improved compared with older studies, are still well above the $<30\%$ mortality reported for those requiring mechanical ventilation for respiratory failure in the general population.[5]

Passage of the Affordable Care Act and an increased focus on quality initiatives, such as the establishment of the Patient-Centered Outcomes Research Institute, has presented a golden opportunity.[6] The etiologies of respiratory failure following SCT are poorly understood, deadly and costly. They include early post-transplant complications such as infections, engraftment syndrome, diffuse alveolar hemorrhage (DAH) and idiopathic pneumonia syndrome (IPS), and late-phase complications due to infections, bronchiolitis obliterans syndrome (BOS) and cryptogenic-organizing pneumonia (COP).[7] We currently lack clinically proven effective therapies for DAH, IPS and BOS.[7] In order to better understand and study respiratory complications following SCT a multi-center approach is needed to standardize evaluation and management as well as acquisition of clinical data, which could provide a foundation for future clinical trials while emphasizing patient-centered outcomes. There are many questions that still need to be answered, such as the role of non-invasive mechanical ventilation (NIMV) in this cohort.[8–10] Intubation is often delayed in the SCT population based on older literature that suggested a mortality benefit from the use of NIMV to avoid endotracheal tube placement.[8] However, IMV was almost universally fatal during this time period ($>90\%$ mortality).[2,8] I suspect there is a role for NIMV in the SCT population, but its universal use for respiratory failure may be deleterious. For example, patients with IPS, who often have evidence of diffuse alveolar damage on histology, may be harmed by NIMV, which could allow excessive tidal volumes and increase the risk of barotrama.[4,7]

Other areas rife with opportunities for deeper understanding and the potential to improve the outcomes include characterization of the microbiologic role in respiratory failure, applications of lung imaging and a more comprehensive review of risk factors for disease development. Bhatt *et al*.[11] identified a novel pathogen, *Bradyrhizobium enterica*, associated with the development of cord colitis syndrome, a complication of umbilical-cord hematopoietic SCT—perhaps there are unidentified pathogens associated with the development of IPS. Our group has identified changes in the proximal airways associated with the development of BOS. We believe that there may be a role for the use of quantitative computed tomography and advanced imaging techniques in the characterization of SCT-related pulmonary complications.[12] Tran *et al*.[13] demonstrated that a smoking history was associated with an increased risk of early respiratory failure following allogeneic hematopoietic SCT. This raises the question of whether active tobacco use should be considered a contra-indication to SCT as it is currently for patients undergoing lung transplant evaluation.[13,14] These represent just a few of the many questions that still need to be answered.

The work of Allareddy *et al*.[1] demonstrates that the prevalence of respiratory failure following SCT continues to increase and is associated with an unacceptably high mortality and cost. As our health-care system has evolved there is an increased focus on patient-centered outcomes and providing cost-effective quality care. Respiratory failure following SCT provides a unique opportunity to improve patient care and reduce costs. A multi-center research approach is needed to build the infrastructure necessary to effectively study this devastating and far too often fatal complication of SCT.

CONFLICT OF INTEREST

The author declares no conflict of interest.

L Gazourian
Division of Pulmonary and Critical Care Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA
E-mail: lgazourian@partners.org

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