Curr Hematol Malig Rep (2015) 10:199–204
DOI 10.1007/s11899-015-0264-3

HEALTH ECONOMICS (N KHERA, SECTION EDITOR)

Optimizing Quality and Efficiency of Healthcare Delivery in Hematopoietic Cell Transplantation

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Published online: 24 May 2015

Abstract Hematopoietic cell transplantation is a complex and resource intense procedure that can be associated with high risks of treatment failure due to disease relapse or complications. There also exists considerable variability among transplant centers with respect to the number of procedures performed, available resources and personnel, patient selection, transplant practices, and supportive care. Hematopoietic cell transplantation as a specialty has been a pioneer in incorporating the constructs of quality and efficiency routinely in patient care. However, several challenges still remain. Harmonization of data collection and reporting, use of innovative technological tools, evidence-based practice supported by clinical trials, better efforts towards care coordination and transition of care, and reduction of variation will facilitate these efforts and will lead to improved experience and outcomes for hematopoietic cell transplant recipients.

Keywords Hematopoietic cell transplantation · Health economics · Relapse · Complications

Introduction

Approximately 20,000 hematopoietic cell transplantation (HCT) procedures are performed in the USA every year for high-risk hematologic malignancies and other blood disorders [1]. HCT is a complex procedure that is limited to selected transplant centers in the country with the necessary expertise and resources. Although many patients are cured of their underlying disease with transplantation, the rate of non-relapse mortality (NRM) is higher than what is typically experienced in other areas of hematology and oncology. Within the first 3–6 months post-transplantation, 2–5 % of autologous HCT recipients and 10–30 % of allogeneic HCT recipients will die due to complications such as organ failure, infections, bleeding, or graft-versus-host disease (GVHD) [1]. Furthermore, relapse is not uncommon given the high-risk nature of diseases for which HCT is performed. There also exists significant practice variation in HCT, due to the variability and complexity of patients who are considered for transplantation, rapid evolution in the science and technology for transplantation, and a general lack of randomized clinical trials to guide practice [2–5, 6••]. Recognizing these challenges, the field of HCT has been a pioneer in integrating quality as part of routine patient care. This article will review examples of quality measures that are routinely applied in HCT practice and will discuss challenges that still remain in optimizing the quality of healthcare delivery for HCT recipients. Since healthcare systems vary considerably among countries, this review will focus primarily on HCT performed at US centers. However, several principles will apply to other countries as well.

Quality and Efficiency in HCT: Stakeholders and Outcomes

In most instances, the transplant process begins with a patient's hematologist-oncologist making the decision to refer a patient for consultation to a transplant center. If the patient is indeed a candidate for transplantation, the transplant specialist physician can decide to proceed with transplantation right away or may recommend additional therapy. Before the

This article is part of the Topical Collection on *Health Economics*

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transplant process can begin, transplant centers have to review the patient's transplant benefits and get approval from the patient's health insurance provider. In the meantime, centers also conduct a donor search to determine the best available donor for patients who are being considered for an allogeneic HCT. Patients then undergo an evaluation process to confirm their suitability for transplantation. Because of geographic distribution of HCT facilities or insurance contract arrangements, patients frequently have to travel and relocate near a transplant center for at least 2–3 months. It is not infrequent for patients to be hospitalized initially for up to 4 to 6 weeks for pre-transplant conditioning therapy, the transplant procedure itself, and for supportive care after transplantation while waiting for hematopoietic cell engraftment and recovery. On discharge, patients are followed for a period of time to ensure stable recovery and to monitor for complications of transplantation such as GVHD and infections. Depending on patient and physician preference, patients may continue to follow up long-term at the transplant center or may be referred back to their community providers.

In this context, several stakeholders have an interest in ensuring that patients get the highest quality care with the best outcomes at the transplant center. These stakeholders and some examples of relevant outcomes or indicators for quality and efficiency are listed below.

- *Patients*: Patients are the focus for all quality and efficiency measures during the transplantation process. Ultimately, they want to obtain the best treatment for their disease and achieve the best possible outcomes. These outcomes can include survival, disease control, absence of complications, good quality of life, and a high degree of satisfaction with the care received. They also want care that is affordable and does not cause undue financial hardship. Factors relevant to patients that can impact the quality and efficiency of care can include sociodemographic factors (e.g., distance to the transplant center, healthcare disparities, insurance status, and availability of caregivers), disease-related factors (e.g., disease risk and stage, comorbidities, transplant type being considered, and need for additional treatment prior to transplant).
- *Referring Physicians*: Hematologist-oncologists who refer their patients to a transplant center, either internally from the same institution or from an outside institution, are interested in obtaining the best possible outcomes for their patients. They also value advice on optimal timing of transplantation or additional therapy that may be needed before transplant can proceed for their patient. In addition to patient-relevant outcomes such as survival, absence of complications, and good quality of life, quality and efficiency measures important to them include communication from the transplant center, experience of previously referred patients, center reputation, and accreditations.
- *Payers*: Private payers and government payers (e.g., Medicare and Medicaid) have similar interests as patients and referring physicians. Among various stakeholders, they are probably the most interested in high-value transplant care, that is, patients under their coverage have the best possible outcomes at the lowest possible costs. Given their population health perspective, they frequently look at objective metrics for transplant center quality and efficiency of care delivery, such as accreditation status with appropriate agencies (e.g., Foundation for Accreditation for Cellular Therapy [FACT] and AABB), ability to provide care to complex patients (e.g., unrelated donor transplantation), center survival rates, resources available at the center, and transplant volume.
- *Other Community Healthcare Providers*: Included in this stakeholder category are primary-care providers (e.g., internal medicine and family medicine) and specialist physicians (e.g., gynecology, ophthalmology, oral medicine) who may participate in the care of transplant patients. They are especially relevant as patients transition back to their community from the transplant center. During this survivorship phase, care transition and coordination and communication between the transplant center and these providers can determine the quality and efficiency of care being provided.
- *Professional and Patient Organizations*: Professional societies such as the American Society for Blood and Marrow Transplantation (ASBMT) can be considered a stakeholder in providing high-value care to transplant recipients. In fact, the ASBMT has several initiatives that directly or indirectly focus on improving quality (e.g., through the Committee on Quality Outcomes) and on providing evidence-based guidance to providers and centers for the optimal care of transplant recipients (e.g., through the Committee on Practice Guidelines). Patient advocacy organizations can also be included in this category, as they are vested in providing resources, support, and education to patients and their mission usually includes helping patients obtain the best care and outcomes.

An important question that needs to be considered is whether emphasis on quality within a transplant program can lead to improved patient outcomes. Studies from Europe have shown that allogeneic transplant survival improves as centers implement a quality management system in preparation for accreditation through the Joint Accreditation Committee ISCT EBMT (JACIE), an organization that sets standards for clinical, collection, and processing activities [7••, 8]. The construct of patient outcomes extends to endpoints other than overall survival, and it can be argued that the presence of a robust evaluation and improvement process within a

transplant program can positively impact other patient-relevant outcomes. One approach to considering outcomes in the context of quality in HCT can follow the tiered hierarchical model proposed by Porter [9••]. Generally, three tiers are defined, with the lower tiers contingent on successful outcomes in the higher tiers and the top tier being the most important (e.g., overall survival) and the third tier focusing on long-term consequences of therapy (Fig. 1).

Existing Mechanisms for Optimizing Quality of Care at Transplant Centers

HCT as a specialty recognized the need and has been a pioneer in establishing the principles for ensuring HCT recipients receive high-quality care from transplant centers. These standards and measures can focus on the following:

- *Structural Indicators*: That is, adequate infrastructure and resources are present at the transplant center to provide high-quality care. These indicators also focus on personnel, such that sufficient experienced clinical and non-clinical staffs are present at the center.
- *Process Indicators*: Measures included in this category pertain to the actual delivery of transplant care. Some examples are the minimum requirements and standard processes for donor selection and recipient evaluation, apheresis, cell processing and infusion, infection prevention, and survivorship care.
- *Outcome Indicators*: The most accepted metric in this category is overall survival. Other outcome measures are also important but are difficult to capture and analyze, such as disease control, complication rates, and quality of life.

Transplant centers have oversight mechanisms for ensuring they meet the standards that are accepted by the transplant community as required to provide high-quality care. In the USA, external and internal mechanisms are present at most transplant centers for this purpose. Studies from Europe have shown that external quality monitoring can lead to the improvement in transplantation outcomes, although similar studies in the USA are lacking.

- *External Mechanisms*: FACT (www.factwebsite.org) establishes the minimum required quality standards for

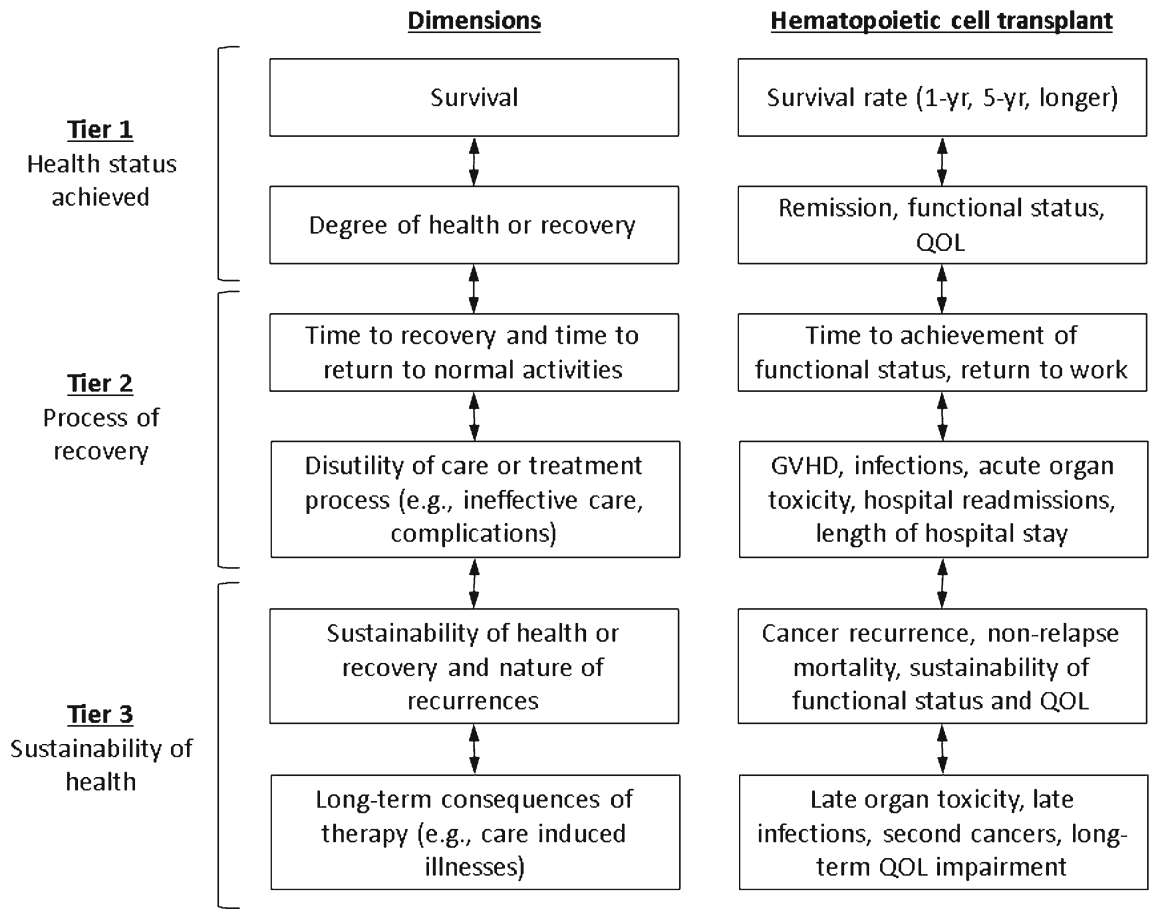

Fig. 1 Outcome hierarchies for hematopoietic cell transplantation (adapted from Porter [9])

centers to follow. FACT accreditation is now recognized as the desired state for transplant centers, as it demonstrates their commitment to meeting structural and process quality indicators for providing high-quality care. Since accreditation involves an active and continuous process for monitoring and meeting quality standards, it also assures other stakeholders (e.g., patients, referring physicians, and payers) about the quality of care provided at that transplant center. In addition, several other organizations directly or indirectly monitor structural and process quality indicators at transplant centers. For example, the National Marrow Donor Program requires that transplant centers meet certain standards before it can allow Be The Match® donors to be used for transplantation. Several payers have criteria for transplant centers for participation in their coverage networks. In addition, other organizations (e.g., State Department of Health) may also be involved in monitoring transplant center quality. The indicator that is most commonly used to assess transplant center outcomes is the center-specific survival report that is reported by the Center for International Blood and Marrow Transplant Research (CIBMTR) annually [10, 11]. This report focuses on all first allogeneic HCT reported by US transplant centers to the CIBMTR over a 3-year period and provides the observed and expected 1-year survival for a given center patient while adjusting for its patient case-mix. This metric is now a well-established measure of center performance and is being increasingly included within monitoring mechanisms by other organizations such as FACT and payers.

– *Internal Mechanisms*: Most centers in the USA have internal quality monitoring and improvement programs. This is partly mandated by external organizations that accredit and monitor transplant centers (e.g., FACT). In addition, most centers are committed to providing high-quality care to their patients and recognize the importance of having mechanisms to monitor their processes and outcomes.

Efficiency or timeliness of care delivery around HCT is a complex construct and difficult to monitor and standardize (see below).

Quality and Efficiency in HCT: Challenges and Opportunities

Despite existing mechanisms to ensure that patients receive high-quality and timely care, several challenges still exist. At the same time, as transplant centers evolve in the current healthcare environment in the USA, there also exist opportunities to better measure and optimize quality and efficiency of care delivery around transplantation. Some of these challenges and opportunities are discussed below.

– *Health Disparities*: There exist disparities in access to and outcomes of HCT, especially allogeneic HCT [5, 12–14]. Transplant centers may not be able to directly influence these societal challenges to appropriate and timely healthcare delivery, but they cannot ignore these issues particularly for patients who are referred to them and undergo a transplant. Centers have to be actively involved and use internal and external resources (e.g., patient financial grants from advocacy organizations) in tackling issues such as transportation, local lodging for patients who need temporary relocation, and providing culturally appropriate care. As more individuals obtain healthcare coverage under state Medicaid programs through the Affordable Care Act, healthcare disparity issues are going to become more relevant for transplant centers as they care for patients with limited social and economic resources. The NMDP, through its System Capacity Initiative Program, is evaluating resources required and is exploring innovate models of care delivery to address these disparities [15, 16].
– *Variation in Care and Practices*: There exists considerable variation in individual physician and center practices for transplantation. These can range from patient selection for transplantation, use of different conditioning and GVHD prophylaxis regimens, variability in supportive care practices, and treatment of transplant-related complications [2, 3]. This variation is in part because of the general lack of high-quality evidence in the form of prospective clinical trials to guide practice. Despite variation in practices among centers, survival outcomes at most centers do not differ substantially. This is best exemplified by the CIBMTR annual center-specific survival report, where most centers are within their expected 1-year survival target. Nevertheless, there is a need for eliminating "habits," conducting more clinical trials, and standardizing practices based on high-quality data from existing clinical trials and large well-conducted registry studies.
– *Variation in Resources and Personnel*: Similarly, transplant centers vary with respect to their infrastructure, capacity, and personnel available for performing HCT [4, 17]. This variation occurs due to several factors, such as the number of patients transplanted annually, the structure of the program, referral patterns, institutional priorities, and local models of care delivery. Irrespective, centers that are FACT accredited are required to demonstrate availability of a minimum number of personnel and infrastructure in order to meet its standards. In the present resource-constrained environment, it is imperative that centers continue to innovate and learn from their peers

in order to provide high-quality and efficient care using the infrastructure that is available to them.

- *Timely Referral to Transplant Center*: One of the biggest challenges to optimal transplantation outcomes is the delay in referral to a transplant center. For patients who may benefit from a transplant, HCT early in the disease course leads to the best outcomes [5]. However, even in the current era, referring physician perceptions about the efficacy and toxicity of transplantation continue to be a barrier to timely referral [18, 19]. Several transplant organizations (e.g., NMDP and ASBMT) are engaged in education and outreach to referring physicians to address this challenge. Transplant centers also need to engage their referring physicians in this effort so that an early transplant consult is considered for patients in whom a transplant may be a treatment option.
- *Care Coordination and Transition of Care*: Care coordination and communication with referring providers is an important component for providing high-quality care around transplantation. This is especially relevant in the pre-transplant phase so that patients can start the transplantation process at the right time in their disease course and in the late post-transplant phase when patients are being discharged back to non-transplant providers [20]. Several challenges exist in this area, including time and personnel constraints at centers, fragmented electronic health records that are not conducive for information transfer, and regulations that make it difficult to share patient information. Centers need to continue to explore technologies and avenues to enhance transition of care between the non-transplant providers and the transplant centers.
- *Measurement of Quality and Efficiency*: The majority of quality-related efforts in HCT focus on structural and procedural pathways. The CIBMTR center-specific survival analysis is the only validated and accepted metric for objectively measuring transplant center outcomes. However, one can argue that metrics other than overall survival are also important, such as disease-free survival, complication-related mortality, and quality of life. The measurement and analysis of these endpoints as a quality metric is not well established. Data collection methods to better capture these metrics are needed along with a continued exploration of analytic methods to include these endpoints in center outcome analyses.
- *Harmonization of Quality Measurement and Reporting*: Transplant centers have to report quality metrics and data to several external stakeholders, each with their own data requirements and data collection forms. Similarly, there is considerable variation among centers in the type and monitoring frequency of quality and efficiency indicators that are reviewed internally. This frequently leads to additional resource and personnel burden at centers to comply with the external and internal reporting requirements. Some harmonization of these efforts as well as exploration of technological tools (e.g., through electronic health records or mobile applications) to ease this burden will facilitate review and use of quality data at transplant centers.

The Affordable Care Act, through its several provisions, is going to positively impact the quality and efficiency of US healthcare, including HCT. There is considerable emphasis on improving access and quality and lowering costs and ultimately providing value-based care to patients. The law has established the Center for Medicare and Medicaid Innovation that has been tasked with testing innovative ways of delivering care to patients in order to improve the quality of care while reducing the rate of growth of healthcare costs for Medicare, Medicaid, and the Children's Health Insurance Program. Other aspects of the law focus on providing financial incentives to hospitals to improve quality of care, public reporting of hospital performance, incentives to form integrated health systems (e.g., Accountable Care Organizations), investigation of "bundled" payments and pay-for-value models, care coordination (e.g., Medical Homes), and broader implementation of electronic health records. Some of these concepts such as care coordination and bundled payments are well known to the transplant community.

Conclusion

Transplant centers have been at the forefront of routinely incorporating quality and efficiency metrics in patient care. Several challenges still remain in integrating these indicators in the care of patients receiving HCT. Harmonization of data collection and reporting, use of innovative technological tools, evidence-based practice supported by clinical trials, better efforts towards care coordination and transition of care, and reduction of variation will facilitate these efforts and will lead to improved patient experience and outcomes.

Compliance with Ethics Guidelines

Conflict of Interest Navneet Majhail declares no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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