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# Hematopoietic cell transplantation: Training challenges and potential opportunities through networking and integration of modern technologies to the practice setting

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### Abstract

Hematopoietic cell transplantation (HCT), particularly allogeneic HCT, is a complex and a high-risk procedure requiring expertise to manage potential treatment complications. Published data supports the value of quality management systems in improving post-transplant outcomes; however, there are no universally established, or agreed upon, criteria to assess adequacy of training of physicians, transplant or nontransplant, and supporting staff, among others. It is of paramount importance for transplant centers to identify the needed area(s) of expertise in order to seek appropriate training for their staff. Moreover, transplant physicians need to keep up-to-date with the rapidly occurring advances in the field. Outcomes of patients undergoing HCT are affected by various factors related to patient, disease, procedure, preventative, and supportive strategies, among others. Accordingly, availability of databases is necessary to collect information on these variables and use to benchmark future prospective clinical trials aiming at further improving clinical outcomes. Twinning with leading centers worldwide is helping to not only bridge the survival gap of patients diagnosed with cancer in the developing vis-à-vis the developed world, but eventually closing it. The advent of the World Wide Web and revolution in telecommunication has made access to information more readily available to various sectors including healthcare. Telemedicine is enabling healthcare delivery to remote and underserved geographic areas. In the setting of HCT, ensuring compliance to

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prescribed therapies and post-transplant surveillance are some areas where implementing telemedicine programs could fulfill an unmet need.

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# 48 Introduction

Despite increasing availability of smart antineoplastic thera-49 pies in recent years, hematopoietic cell transplantation 50 (HCT) remains an optimal treatment modality for various 51 hematologic malignancies [1-3]. High-dose chemotherapy 52 and autologous HCT (auto-HCT) are potentially curative in 53 54 certain types of relapsed chemosensitive lymphomas and have improved outcomes of other subtypes when offered as 55 frontline consolidation [4-7]. Availability of tools to prog-56 57 nosticate the significance of existing comorbidities (and their severity) on post-transplant outcomes has helped liberalize 58 prior empirically established cutoffs which were used to dis-59 qualify patients from receiving the procedure, based merely 60 on age [8]. This is also the case for allogeneic HCT (allo-HCT) 61 which represents the only possibility of cure for a variety of 62 63 hematologic malignancies and some benign blood disorders [9]. The curative potential of auto-HCT is primarily derived 64 65 from administering myeloablative doses of chemotherapy 66 or chemoradiotherapy resulting in organ toxicity and infec-67 tious complications, among others. In the case of allo-HCT, 68 risks associated with the procedure emanate from a variety of causes including host immune suppression, alloreactivity 69 of donor effector cells, chemotherapy and/or radiotherapy 70 71 toxicity, untoward effects of therapies used for prevention of acute graft-versus-host disease, and potential side effects 72 of other supportive therapies. This is further complicated by 73 the possibility of resurgence of serious, and even lethal, 74 75 opportunistic infections at times requiring preemptive therapeutic interventions [10,11]. Hence, HCT, particularly allo-76 77 HCT, is a complex and high-risk procedure which requires a 78 level of expertise to manage potential treatment 79 complications.

Implementation of quality management systems (QMS), 80 originally developed by the Foundation for the Accredita-81 82 tion of Cellular Therapy in the United States, and expanded to different parts of the world by the Joint Accreditation 83 84 Committee-ISCT and European Society for Blood and Mar-85 row Transplantation (EBMT), aims at establishing a threshold for excellence in cellular therapy including HCT [12]. 86 The presence of QMS is of particular importance in allo-87 HCT owing to the complex interplay of different subspe-88 cialties needed to cover the various facets of the proce-89 dure ranging from search and identification of suitable 90 91 donors, assessing patient eligibility, hematopoietic cell 92 procurement and processing, administration of chemotherapy and/or radiotherapy, and management of peri- and 93 postallograft complications. While published data supports 94 the value of QMS in improving post-transplant outcomes 95 96 [13,14], there are no universally established, or agreed 97 upon, criteria to assess adequacy of training of physicians, transplant or nontransplant, and supporting staff, among 98 99 others.

Technologic advances through availability of the World Wide Web has resulted in increased and easy access to essential information needed to optimize care of patients with cancer, including recipients of HCT. Telemedicine is already a reality and is certainly helping facilitate the management and care of patients, including those living in remote rural areas, by means of telecommunication technology [15].

In the following sections we evaluate ways to pursue training and gain experience in the care of HCT patients. We also explore the immense potential of integrating telemedicine to enhance not only physician-patient but also physician-physician and center-center interactions aimed at improving quality of care and also advancing the field.

## Training and experience

Data from the Center for International Bone Marrow Trans-116 plant Research (CIBMTR) shows a continuous increase in the 117 number of autologous and allogeneic HCT procedures per-118 formed over the past 20 years [16]. Moreover, availability 119 of better supportive therapies and specific tools to prognos-120 ticate the adverse impact of existing comorbidities are allow-121 ing expanding the procedure, auto-HCT, and more so allo-122 HCT, to patients who were deemed ineligible in the past. 123 Specifically to allo-HCT, emergence of reduced-intensity 174 conditioning and nonmyeloablative conditioning has also 125 increased the number of allo-HCT recipients older than 60 126 years. This has definitely created a challenge to staff HCT 127 programs with the needed number of adequately trained 128 physicians and other supporting personnel. Gajewski et al. 129 [17] described results of a study by the American Society 130 for Blood and Marrow Transplantation, using membership 131 records, showing a projected shortage of over 1300 new 132 HCT physicians by the year 2020. Interestingly, approxi-133 mately 60% of the current HCT physician workforce is  $\geq$ 50 134 years of age [17]. 135

This challenge is further compounded by development of 136 novel approaches using mismatched related or unrelated 137 donors, including haploidentical donors or cord blood, 138 expansion of allo-HCT to other indications, and also an 139 increased number of transplants performed in older patients 140 [18-21]. A patient's age is a known risk factor for worse non-141 relapse mortality, hence requiring closer attention during 142 the procedure [22]. These aforementioned situations may 143 require additional expertise pertaining to selection of opti-144 mal cord blood unit(s), haploidentical donors, management 145 of comorbidities and transplant-related complications in 146 elder patients, and understanding the risks associated with 147 existing organ impairment as is the case of iron overload in 148 patients with thalassemia in need of allo-HCT as an example 149 [23,24]. 150

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