Best Practice & Research Clinical Haematology 27 (2014) 283–287

Contents lists available at ScienceDirect

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/beha

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Improved accuracy of acute graft-versus-host disease staging among multiple centers

John E. Levine, MD, MS, Professor of Pediatrics and Internal Medicine [a], William J. Hogan, MD, Assistant Professor of Medicine [b], Andrew C. Harris, MD, Assistant Professor of Pediatrics [a], Mark R. Litzow, MD, Professor of Medicine [b], Yvonne A. Efebera, MD, Assistant Professor of Internal Medicine [c], Steven M. Devine, MD, Professor of Internal Medicine [c], Ran Reshef, MD, Assistant Professor of Medicine [d], James L.M. Ferrara, MD, DSc, Ward-Coleman Professor of Cancer Medicine [e, *]

[a] *Blood and Marrow Transplantation Program, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, USA*
[b] *Blood and Marrow Transplant Program, Mayo Clinic, 200 First St. SW, Rochester, MN 55905, USA*
[c] *Blood and Marrow Transplant Program, Ohio State University, 300 W. 10th Ave., Columbus, OH 43210, USA*
[d] *Blood and Marrow Transplant Program, University of Pennsylvania, 3400 Civic Center Blvd., Philadelphia, PA 19104, USA*
[e] *Translational Research Center, The Tisch Cancer Institute, The Icahn School of Medicine at Mount Sinai Hospital, 1470 Madison Avenue, New York, NY 10029, USA*

Keywords:
bone marrow transplant
BMT
data entry system
guidance
graft-versus-host disease
GVHD
multiple centers
online
staging
standardization
web

The clinical staging of acute graft-versus-host disease (GVHD) varies significantly among bone marrow transplant (BMT) centers, but adherence to long-standing practices poses formidable barriers to standardization among centers. We have analyzed the sources of variability and developed a web-based remote data entry system that can be used by multiple centers simultaneously and that standardizes data collection in key areas. This user-friendly, intuitive interface resembles an online shopping site and eliminates error-prone entry of free text with drop-down menus and pop-up detailed guidance available at the point of data entry. Standardized documentation of symptoms and therapeutic response reduces errors in grade assignment and allows creation of confidence levels regarding the diagnosis. Early review

* Corresponding author. Tel.: +1 212 824 9339.
E-mail address: james.ferrara@mssm.edu (J.L.M. Ferrara).

http://dx.doi.org/10.1016/j.beha.2014.10.011

and adjudication of borderline cases improves consistency of grading and further enhances consistency among centers. If this system achieves widespread use it may enhance the quality of data in multicenter trials to prevent and treat acute GVHD.

Introduction

The clinical staging of acute graft-versus-host disease (GVHD) is inconsistent among transplant centers and highly prone to errors [1]. The very definition of GVHD remains variable, with the cumulative incidence of GVHD grade II–IV ranging from 40% to 80% following T-cell replete bone marrow transplant (BMT) [2–4]. Although this poor concordance between transplant centers has been recognized for over 25 years [5,6], different practices of long standing among centers pose formidable barriers to harmonization. These differences become glaringly apparent during the conduct of multicenter trials when it can be very difficult to decide whether a patient actually experienced GVHD. This article reviews some new approaches to multicenter efforts to improve GVHD grading that have been piloted in a consortium led by investigators at the University of Michigan to address these common problems using remote data entry system and near-real time adjudication.

Standardized, user-friendly data collection reduces needless variations

Data collection systems at BMT centers possess many idiosyncratic features as a result of practices that evolved over years, but they are familiar to their users. Uniform data collection systems that are fast and easy-to-learn are highly desirable; investigators at the University of Michigan have recently developed flexible, intuitive, web-based interfaces similar to online shopping sites in order to standardize data collection among BMT centers. Entries are completed by radio button mouse clicks and drop down menus rather than free text entry. The first layer of the data collection asks yes/no questions, eg, "was there a rash this week?" If no, no further entry is needed. If yes, additional questions appear to determine etiology, extent, and treatment. As an example of a desirable feature, detailed guidance is available at the point of data entry, appearing only when clicked, which keeps the form visually uncluttered, but makes reference to guidance easy. Logic checks warn users of missing or inconsistent data via pop-up alerts much the same way online shoppers are warned of incorrect credit card entries.

In our experience, physicians who are familiar with the data entry system are better equipped to troubleshoot problems, and thus both physicians and data managers were encouraged to participate in a data entry webinar where a lead data coordinator enters data from source documents while answering questions posed by participants. Following the webinar, data managers from each center entered data in an electronic "sandbox" populated with test patients. The time requirements to collect the data appear to be manageable. When patients have no new symptoms, data entry can be completed in less than 1 min; when new symptoms appear, the forms can still be completed in fewer than 5 min. Feedback from centers involved in the testing has been very positive.

Documentation of granular details improves consistency of GVHD staging

A 55% body surface rash is stage 3 skin GVHD, but "rash" does not distinguish active inflammatory erythema from inactive hyperpigmentation; thus, the above rash may be categorized by different observers either as a stage 2 or a stage 3, *changing the overall grade and the need to treat with systemic steroids*. Gastrointestinal (GI) staging is even more prone to inaccuracies because it requires accurate measurement of diarrhea volume. When diarrhea starts at home, patients almost always quantify by episodes, not volume, and estimation of volume based on history alone is inherently flawed. "Five episodes of diarrhea" can be staged as stage 1 or 2, *again changing the overall grade*. In order to address this type of problem, we created standardized GVHD guidance after a review of weekly GVHD grades that identified both common and uncommon sources of confusion. This guidance addresses important