MAYO CLINIC

ORIGINAL ARTICLE

Quality Initiative in Clinical Practice: A Single-Institution Appraisal of Quality Metrics in the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma

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Abstract

Objective: To assess our adherence to treatment guidelines for diffuse large B-cell lymphoma (DLBCL) established by the American Society of Hematology in 2014 through implementation of a quality improvement initiative (QII) at our institution in 2015.

Patients and Methods: Patients with newly diagnosed DLBCL treated from January 1, 2006, through December 31, 2017, were identified. Electronic medical records were reviewed for documentation of American Society of Hematology Practice Improvement Module quality measures (eg, key pathologic features of DLBCL, lymphoma staging, and screening for hepatitis B virus [HBV] infection in patients receiving rituximab-based chemotherapy). We also reviewed assessment of prognosis by revised International Prognostic Index score, testing for hepatitis C virus, HBV, and HIV, chemotherapy education, and the addition of rituximab in the treatment regimen of $CD20^+$ DLBCL.

Results: Following QII implementation, we saw improvements in most metrics, including reporting of key molecular features (fluorescence in situ hybridization for *c-MYC*, *BCL2*, and *BCL6*, from 45.5% [75 of 165 patients] before QII to 91.7% [22 of 24 patients] after QII; $P<.001$), screening for HBV (41.8% [69 of 165 patients] to 91.7% [22 of 24 patients]; $P<.001$) and HIV infections (33.9% [56 of 165 patients] to 87.5% [21 of 24 patients]; $P<.0001$), providing chemotherapy education (92.7% [153 of 165 patients] to 100%), and use of rituximab for $CD20^+$ DLBCL (83.6% [138 of 165 patients] to 100%; $P=.05$). All patients had positron emission tomography–computed tomography for DLBCL staging, and there was significantly lower use of bone marrow biopsy ($P=.011$).

Conclusion: Implementating a QII and employing standardized metrics can aid in improving quality of care for patients with newly diagnosed DLBCL and allow opportunities to build and ensure better adherence to evolving patient care guidelines.

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of curable non-Hodgkin lymphoma (NHL), accounting for 30% to 40% of all lymphomas.[1] It shows a predominance for the male sex and typically presents at a median age of 64 years.[2] In the United States and England, the incidence is roughly 7 cases per 100,000 person-years.[3,4] The incidence of DLBCL is higher in patients with HIV. Diffuse large B-cell lymphoma is most commonly associated with expression of pan–B-cell markers (CD19, CD20, CD29, and CD45). CD30 expression is positive in 25% of cases and is associated with a more favorable outcome.[5] B-cell lymphoma 6 protein expression is reported in 70% of cases independent of *BCL6* gene (for expansion of gene symbols, see www.geneames.org) rearrangement, which occurs in only 30% to 40% of cases. B-cell lymphoma 2 protein, CD10, and MUM1/IRF4 are also commonly expressed.[3,5] Diffuse large B-cell lymphoma tumors have varying genetic features ranging from *MYC* gene rearrangements or

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t(14;18) translocations seen in follicular lymphoma to more rare translocations involving the *ALK* and clathrin genes.[6] The use of gene expression signatures has further empowered the identification of prognostic subclasses of DLBCL with distinct genotypic, epigenetic, and clinical characteristics and provides a potential nosology for precision medicine strategies in DLBCL.[7] The heterogeneity of DLBCL was acknowledged in 2016 by the World Health Organization, distinguishing a variety of clinicopathologic entities now considered to be individual diagnostic categories while also calling attention to several overlap categories.[8]

The National Comprehensive Cancer Network has issued well-established guidelines for the management and treatment of DLBCL.[9] The 2014 American Society of Hematology Practice Improvement Module (ASH-PIM) for NHL was designed for physicians to evaluate the quality of their clinical practice by assessing 6 quality metrics including pathologic diagnosis, staging, hepatitis B virus (HBV) testing before rituximab therapy, vaccination status, use of granulocyte colony-stimulating factor (G-CSF), and fertility counseling.[10] The ASH-PIM proved to be feasible and reliable while qualitatively assessing key aspects of patient care.[10] Its development has served as a guide for institutions to identify areas of care needing improvement.

Nonetheless, the ASH-PIM fails to consider several other features of DLBCL that can affect the overall outcome of patients. These features include routine testing of all patients to assess HIV and hepatitis C virus (HCV) status,[11-14] the integral role of nurses in patient education,[15] the use of combined positron emission tomography (PET)—computed tomography (CT) using [18F]-fluorodeoxyglucose to stage patients before chemotherapy initiation, the frequency of bone marrow biopsies (BMBs) in these patients, and evaluation of response to therapy at treatment completion.[16] Therefore, to assess and improve institutional quality of care for patients with newly diagnosed DLBCL at our institution, we implemented a quality improvement initiative (QII) in July 2015 that incorporated metrics from the ASH-PIM such as pathologic diagnosis, staging, HBV serologic testing before rituximab therapy, and use of G-CSF and expanded these metrics to include HIV and HCV status before therapy, chemotherapy education, PET-CT before therapy, and frequency of BMB. Recent studies have reported that these additional metrics, alongside those incorporated in the ASH-PIM, have both prognostic and therapeutic implications that significantly impact the outcomes of patients with DLBCL.[14,17-20]

PATIENTS AND METHODS

This study was reviewed and approved by the Institutional Review Board of Virginia Mason Medical Center (VMMC). The VMMC Tumor Registry was used to identify a longitudinal cohort of patients with histologic confirmation of DLBCL by using the *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* diagnosis code 200.7 for the years 2006-2015 and code C83.3 from the *International Classification of Diseases*, *Tenth Revision*, *Clinical Modification* for the years 2016 and 2017. All patients in whom DLBCL was diagnosed and who received chemotherapy at VMMC from January 1, 2006, through December 31, 2017, were included. Patients who did not have a confirmed diagnosis of DLBCL and who did not receive at least one cycle of chemotherapy at VMMC were excluded from this study.

Before QII intiation, a multidisciplinary group of dedicated hematopathologists, radiologists, and hematology/oncology staff physicians reviewed cases and incorporated recommendations into Cerner Oncology DLBCL order sets (Cerner Corporation) including stage of disease, and histologic and molecular techniques were templated into pathology reports of all DLBCL assessments. For each identified patient, the electronic medical record (EMR) was reviewed for documentation of the following quality metrics (Table).

(1) Pathology reports were assessed for description of the diagnosis of DLBCL. This evidence included description of immunohistochemistry for the presence or absence of expression of CD10, CD20, *c-MYC*, *BCL2*, or *BCL6*, cell of origin by Hans criteria (germinal cell vs non—germinal cell), fluorescence in situ hybridization to identify *c-MYC*, *BCL2*, and *BCL6* rearrangements, and Epstein-Barr virus—encoded small RNA-1

Mayo Clin Proc Inn Qual Out ■ December 2019;3(4):485-494 ■ https://doi.org/10.1016/j.mayocpiqo.2019.08.004
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in situ hybridization for latent Epstein-Barr virus infection.[21]

(2) Staging of DLBCL was assessed by reviewing whether patients had either CT of the chest, abdomen, and pelvis or whole-body PET-CT, with or without BMB and aspiration.

(3) Risk category was assessed using the revised International Prognostic Index and the presence of high-risk markers including *BCL2* and *BCL6* and/or *c-MYC*.[22]

(4) Serologic tests before rituximab therapy established previous exposure to HBV (serum hepatitis B surface antigen, antibody to hepatitis B surface antigen, total hepatitis B core antibodies), HCV (serum HCV antibody), and HIV (HIV-1/HIV-2 antigen and antibody).

(5) Clear and concise language in the clinical note of the treating physician and/or nurse was used to assess whether patients received chemotherapy education.

(6) Patients' clinical notes, chemotherapy orders, and medication administration records were reviewed to assess whether they received rituximab infusion for $CD20^+$ DLBCL.

(7) For patients 65 years of age or older, records were reviewed to determine if G-CSF was given prophylactically beginning with the first cycle of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapy to minimize risk of neutropenic fevers.

Because data recording errors are common, a standard process for review was developed for each metric in order to maintain data integrity.[23] We (A.M.B. and D.M.A.) independently reviewed patient data within the EMR and recorded the information in a de-identified, password-protected database. We initially reviewed pathologic diagnosis and then assessed staging metrics. Clinical notes confirmed the date of treatment initiation and determined the use of rituximab. This step was followed by assessment of serologic studies and chemotherapy education metrics. Clinical notes and medication history were subsequently reviewed, starting with the initial consultation through completion of chemotherapy. To ensure data integrity, once the metrics from the EMR were abstracted, 20 patients were selected at random, and their data were cross-verified by 3 of us (A.M.B., D.M.A., and P.V.) to confirm validity and accuracy.

The numbers of patients were recorded, and percentages were calculated for each of the aforementioned metrics before and after the quality initiative (2015). Comparisons were made between pre-QII and post-QII cohorts. The χ^2 test was performed to assess the differences between the 2 groups. The Fisher exact test was used if a sample size was less than 5. SAS statistical software, version 9.4 (SAS Institute) was used for statistical analysis. $P<.05$ was considered statistically significant.

RESULTS

We initially identified 207 patients for inclusion in the study and then excluded 18 because they either did not receive chemotherapy at VMMC or died before beginning chemotherapy. Thus, our analysis included a total of 189 eligible patients, 165 (87.3%) of whom were in the pre-QII cohort and 24 (12.7%) in the post-QII cohort. The median patient age was 67 years in the pre-QII cohort and 68.5 years in the post-QII cohort. Male and female patients were equally distributed across both cohorts: 51.5% (85) men and 48.5% (80) women in the preintervention cohort and 50.0% (12) each in the postintervention cohort (Table).

Hematopathologists' reporting of prognostic markers of DLBCL changed significantly in the post-QII group as illustrated in Figure 1. Trends in performing immunohistochemistry for *c-MYC*, *BCL2*, and *BCL6* increased gradually over the years from 81.2% (134 of 165 patients) to 100% (24 of 24 patients) ($P=.015$), whereas fluorescence in situ hybridization for c-*MYC*, *BCL2*, and *BCL6* increased rather swiftly from 45.5% (75 of 165) to 91.7% (22 of 24) ($P<.0001$) after implementation of the QII. Similarly, Epstein-Barr virus–encoded small RNA-1 in situ hybridization reporting also increased from 36.4% (60 of 165) to 87.5% (21 of 24) ($P<.0001$; Figure 2A).

Most patients in the pre-QII cohort (147 of 165 [89.1%]) and all 24 in the post-QII cohort underwent PET-CT for staging of DLBCL (Table and Figure 1). Figure 2B also shows a decrease in the number of BMBs for staging

TABLE. Patient Demographic Characteristics, Disease Features, and Assessment of Quality Metrics[a,b]

Variable	Metric	Pre-QII (N=165)	Post-QII (N=24)	*P* value
Demographics	Age (y), median (range)	67 (18-84)	68.5 (48-75)	NA
	Male	85 (51.5)	12 (50.0)	.90
Diagnosis: reporting of *c-MYC*, *BCL2*/*BCL6*, and EBER on tumor tissue biopsy	IHC: *c-MYC*, *BCL2*, *BCL6*	134 (81.2)	24 (100)	.02[c]
	FISH: *c-MYC*, *BCL2*, *BCL6*	75 (45.5)	22 (91.7)	<.0001
	EBER1 ISH	60 (36.4)	21 (87.5)	<.0001
Staging work-up	PET-CT/CT	147 (89.1)	24 (100)	.16[c]
	BMB	101 (61.2)	8 (33.3)	.011
Prognostication	r-IPI, *c-MYC*, *BCL2*, *BCL6*	130 (78.8)	24 (100)	.02[c]
Viral serology prior to chemoimmunotherapy	HBV	69 (41.8)	22 (91.7)	<.001
	HCV	61 (37.0)	10 (41.7)	.61
	HIV	56 (33.9)	21 (87.5)	<.0001
Patient education	Patient education prior to starting chemotherapy	153 (92.7)	24 (100)	.05[c]
Rituximab	Administration of rituximab for $CD20^+$ DLBCL	138 (83.6)	24 (100)	.05[c]
Use of G-CSF with chemoimmunotherapy	Administration of G-CSF starting from first cycle prior to neutropenia	37 (22.4)	5 (20.8)	a
	Administration of G-CSF after first cycle due to neutropenia	91 (55.2)	12 (50.0)	.61
	Did not receive G-CSF with chemotherapy	37 (22.4)	7 (29.2)	.44

[a]BMB = bone marrow biopsy; DLBCL = diffuse large B-cell lymphoma; FISH = fluorescence in situ hybridization; G-CSF = granulocyte colony-stimulating factor; HBV = hepatitis B virus; HCV = hepatitis C virus; IHC = immunohistochemistry; ISH = in situ hybridization; NA = not applicable; PET-CT = positron emission tomography–computed tomography; QII = quality improvement initiative; r-IPI = revised International Prognostic Index. For expansion of gene symbols, see www.genenames.org.

[b]Data are presented as No. (percentage) of patients.

[c]Fisher exact test.

of lymphoma in the post-QII cohort: only one-third of patients (8 of 24) underwent a BMB compared with 61.2% of patients (101) in the pre-QII cohort (Figure 1).[20]

There was an improved effort to assess prognosis and risk of recurrence by using the biological features of lymphoma (ie, *BCL2*, *BCL6*, and *c-MYC*) and revised International Prognostic Index in the post-QII cohort: 100% compared with 78.8% (138) previously (*P*=.02) (Figures 1 and 2B).

Screening for HBV and HIV infections increased significantly from 41.8% (69 of 165 patients) and 33.9% (56 patients), respectively, in the pre-QII cohort to 91.7% (22 of 24 patients) (*P*<.001) and 87.5% (21 patients) (*P*<.0001) in the post-QII cohort, whereas there was no such change seen in screening for HCV infection (37.0% [61 patients] to 41.7% [10 patients]; *P*=.61) (Figures 1 and 2C).

The rate of chemotherapy education before starting treatment was 92.7% (153 patients) in the pre-QII cohort and 100% in the post-QII cohort (*P*=.05) (Figures 1 and 2D).

The incorporation of rituximab, an anti-CD20 monoclonal antibody, to the treatment regimen of $CD20^+$ DLBCL increased from 83.6% of patients (138) pre-QII to 100% post-QII (*P*=.05) (Figures 1 and 2D).

In both the pre-QII and post-QII cohorts, the percentage of patients aged 65 years and older receiving G-CSF before the first cycle of chemotherapy remained unchanged at about 22%. Of 110 patients 65 years of age and older, 36 received prophylactic G-CSF starting from cycle 1 of chemotherapy, while

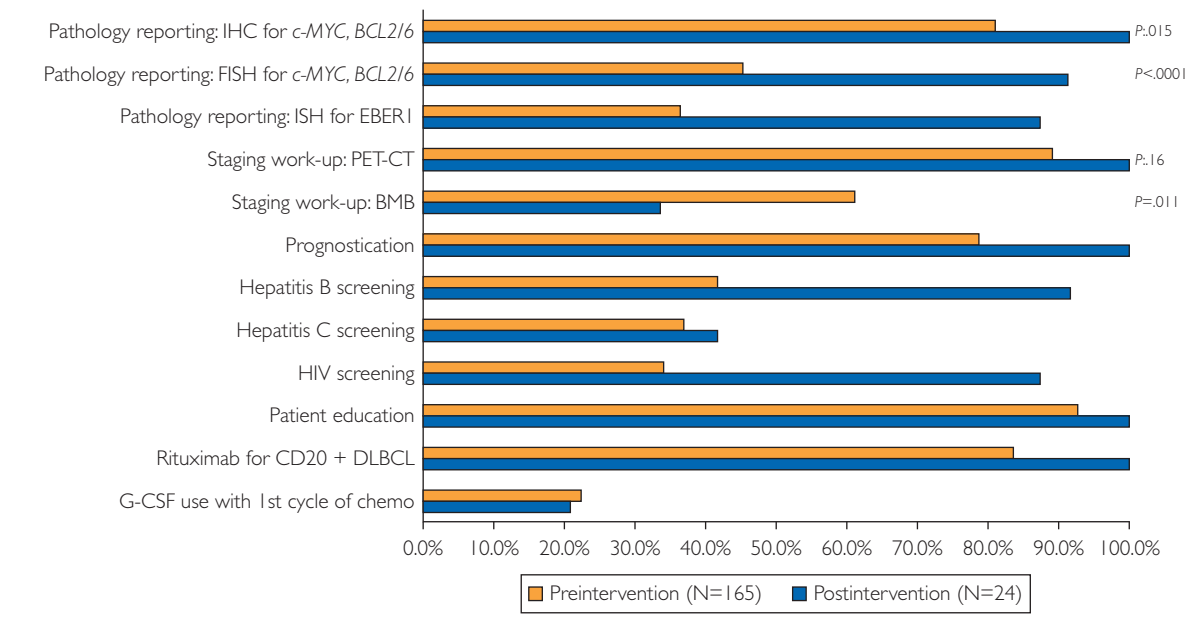

FIGURE 1. Performance improvement with implementation of quality improvement initiative. BMB = bone marrow biopsy; DLBCL = diffuse large B-cell lymphoma; EBER1 = Epstein-Barr virus–encoded small RNA-1; FISH = fluorescence in situ hybridization; G-CSF = granulocyte colony-stimulating factor; IHC = immunohistochemistry; ISH = in situ hybridization; PET-CT = positron emission tomography–computed tomography.

67 received G-CSF after neutropenia had developed following the first or the subsequent cycles of chemotherapy (Figure 2D).

DISCUSSION

Quality metrics can be used to identify treatment improvement opportunities and track the effectiveness of improvements over time as a first step toward a shift to value-based cancer care.[24] To evaluate gaps between recommended DLBCL practice guidelines and our institution's clinical practice, we implemented a QII to analyze our adherence to recognized quality metrics of lymphoma care and identify areas for institutional improvement. In this appraisal of the QII implemented at our institution, we found notable improvement in several of these metrics.

The ASH-PIM was developed as a Web-based self-evaluation tool to help guide physicians through medical record abstractions and system inventory to aid in establishing a robust practice performance assessment for various conditions.[10] The medical record abstraction tool was provided to institutions free of charge on the American Society of Hematology website and focused on key outcomes and process of care related to DLBCL. The key metrics for DLBCL included in this Web-based self-evaluation tool included pathologic diagnosis, staging, HBV testing before rituximab therapy, vaccination status, use of G-CSF, and fertility counseling. This Web-based Practice Improvement Module took 5 to 10 hours to complete, depending on how records were being reviewed, and proved to be a reliable and feasible tool for addressing areas of improvement at the institutional level.

For the implementation of our QII, we adopted metrics included in the ASH-PIM and selected additional metrics based on emerging evidence that would implicate positive or negative outcomes of DLBCL-associated therapy. Metrics of interest were determined at our twice-monthly hematopathology tumor board at which a multidisciplinary group of dedicated hematopathologists, radiologists, and hematology/oncology staff physicians review cases and incorporate recommendations into standard work, including the latest histologic and molecular techniques in DLBCL assessment. Helpful in implementing several of these metrics was

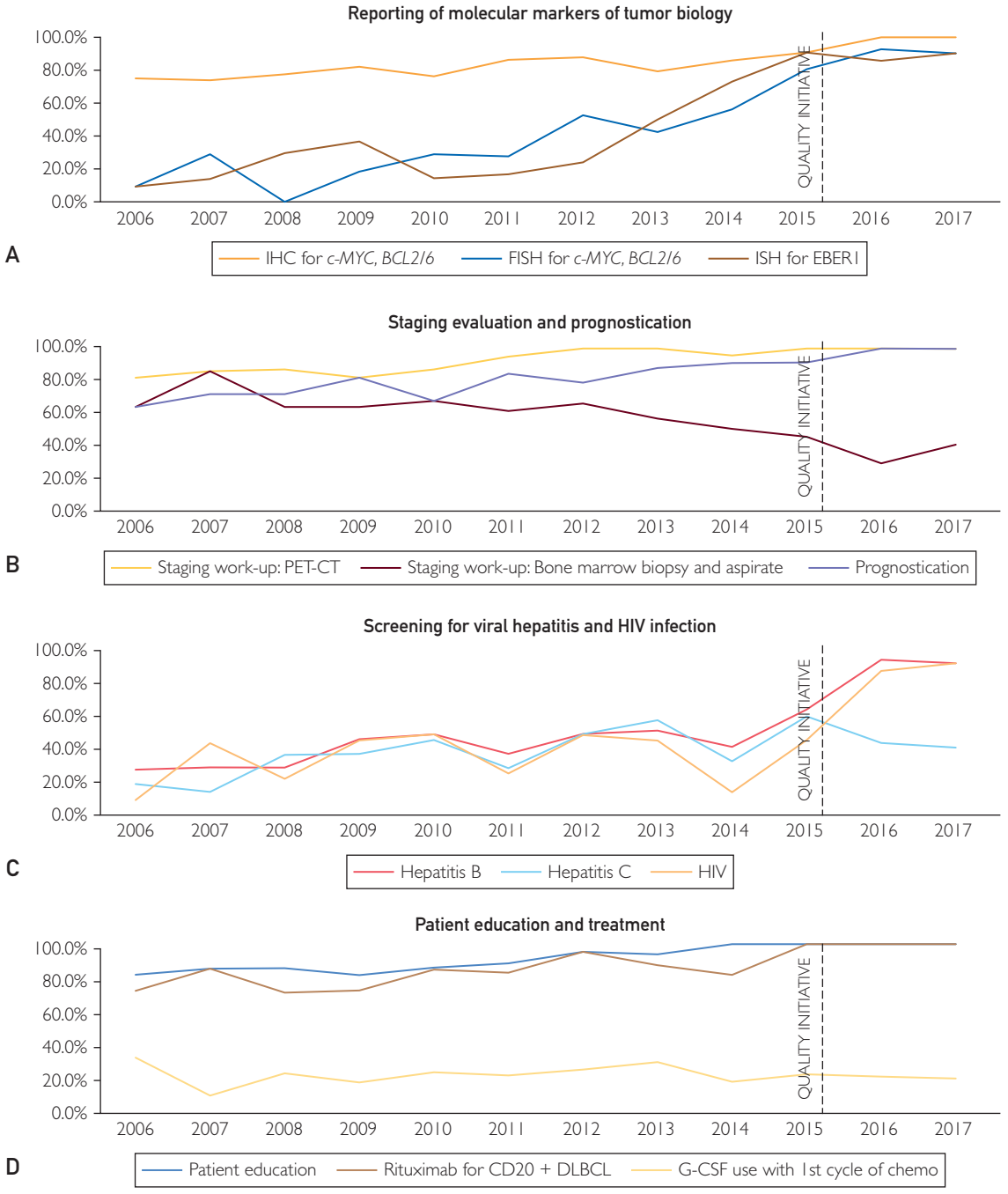

FIGURE 2. Trends in performance of quality metrics from 2006 to 2017. DLBCL = diffuse large B-cell lymphoma; EBER1 = Epstein-Barr virus–encoded small RNA-1; FISH = fluorescence in situ hybridization; G-CSF = granulocyte colony-stimulating factor; IHC = immunohistochemistry; ISH = in situ hybridization; PET-CT = positron emission tomography–computed tomography.

our ability to leverage Cerner Oncology, an EMR specifically designed for the practice of clinical oncology that was procured by our institution in 2016. With the help of EMR technical support staff, we customized R-CHOP and dose-adjusted rituximab, etoposide, doxorubicin, vincristine, cyclophosphamide, and prednisone chemotherapy order

Mayo Clin Proc Inn Qual Out ■ December 2019;3(4):485-494 ■ https://doi.org/10.1016/j.mayocpiqo.2019.08.004
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sets, wherein we were able to include HIV and HBV status as necessary fields to be populated when ordering the first cycle of chemotherapy. Use of G-CSF was built into the R-CHOP and rituximab, etoposide, doxorubicin, vincristine, cyclophosphamide, and prednisone chemotherapy order sets according to the American Society of Clinical Oncology clinical practice guideline update.[25] Education was provided to all hematology/oncology physicians about the incorporation of quality metrics for all patients with DLBCL receiving lymphoma care at VMMC.

Documenting chemotherapy education delivery by our Oncology Nursing Society–certified nurses was accomplished through a broader effort to standardize practices across the entire section of medical oncology and hematology. During the patient education session, imformation was provided to patients by registered nurses using a standardized teaching booklet that addressed important issues about DLBCL, the goal of chemotherapy, and potential adverse effects and reactions including fertility counseling, symptom prevention and management practices, available community resources, and instructions for when to call for urgent problems including fever (temperature >38.1°C) and/or shaking chills, uncontrolled nausea and vomiting, persistant nosebleeds, bloody or black stools, increased bruising, new-onset shortness of breath or pain with breathing, and burning/pain or blood with urination. Instructions for when to call the nurse or physican for issues of less urgency were also reviewed including emergence of mouth sores, increased phlegm or change in its color, sore throat or more cough than usual, diarrhea or loose bowel movements lasting more than 2 days, new or increased pain not responsive to analgesics, and new-onset constipation that does not improve with usual treatment in 2 days. After each chemotherapy education session, the nurse, patient, and consulting physician were all required to sign a chemotherapy informed consent form that was scanned into the medical record and also reviewed by the oncology-based pharmacist before chemotherapy preparation. This effort was monitored by a thorough documentation of patient chemotherapy education in the EMR. Although our institution did not implement a fertility metric, fertility counseling was indirectly measured through chemotherapy teaching by nursing staff and was therefore not a measureable outcome. This effort also served as an additional metric for the American Society of Clinical Oncology Quality Oncology Practice Initiative certification process.[26]

The incidence of HIV-associated NHL has decreased drastically during the era of highly active antiretroviral therapy (HAART), while the survival of these patients has increased remarkably.[27] HAART substantially restores immune function, reduces opportunistic infections, and lowers plasma HIV viral RNA load, leading to reduction of AIDS-related complications.[28,29] Current National Comprehensive Cancer Network guidelines recommend that HIV-positive patients receive HAART in conjunction with chemotherapy, and therefore, assessing HIV status is crucial in dictating the clinical course during therapy.[30] Furthermore, oncologists and HIV clinicians along with HIV and oncology specialty pharmacists should review proposed cancer therapy and HAART guidelines for possible drug-drug interactions and overlapping toxicity concerns before initiation of therapy, bringing to light one of the unintended consequences of treating patients receiving immunotherapy.

Although the need for HBV testing before rituximab therapy has been well established because of risk of reactivation in up to 50% of HBV-seropositive patients, the management and monitoring of patients with HCV-associated DLBCL remains uncertain.[15] Hepatitis C virus can play a role in DLBCL etiology, showing a striking association between the oncogenic HCV nonstructural 3 protein and DLBCL.[15] Although the risk of reactivation is low, HCV-infected individuals typically have an extended duration of infection (15 years) and characteristically present with extranodal lymphoma affecting overall morbidity and mortality.[13,15] Following the QII, we had not yet incorporated routine HCV serology as a necessary metric for treatment initiation because these data emerged after the initiaton of our QII, and as such, there was no improvement in assessment of HCV infection during the pre-QII and post-QII intervals.

PET-CT using [^{18}F]-fluorodeoxyglucose is a noninvasive, 3-dimensional imaging modality

that has become widely used in the management of patients with malignant lymphomas. It has emerged as an indispensable clinical tool for staging and response assessment in aggressive lymphomas. This technology has been reported to be more sensitive and specific than either gallium scintigraphy or CT alone, providing a more accurate distinction between scar or fibrosis and active tumor.[16] PET has been evaluated in pretreatment staging, restaging, monitoring during therapy, posttherapy surveillance, assessment of transformation, and, more recently, as a surrogate marker in new drug development.[20] As we have recently reported, PET has a high sensitivity for evaluating bone marrow involvement in DLBCL and may, in certain circumstances, reduce the need to routinely perform a staging BMB and aspiration.[20] Incorporation of this finding led to a reduction in BMBs from 61.2% (101 of 165 patients) before QII to only 33.3% (8 of 24 patients) after QII (P=.011).

The American Society of Clinical Oncology guidelines recommend that prophylactic G-CSF be incorporated into the first cycle of R-CHOP for treatment of DLBCL in patients aged 65 years and older, particularly in the presence of comorbidities.[25] A single randomized clinical trial examined the benefit of G-CSF prophylaxis among older patients. The trial enrolled patients aged 65 years or older who had an Eastern Coperative Oncology Group score of 0 to 2 and either a solid tumor or NHL.[31] Patients received either pegfilgrastim starting with cycle 1 for all cycles or pegfilgrastim initiated after cycle 1 at the physician's discretion. Pegfilgrastim administered during all cycles reduced the risk of febrile neutropenia. Among patients with DLBCL, the risk of febrile neutropenia across all cycles was 37% in the physician discretion arm and 15% in the arm receiving pegfilgrastim in all cycles (P=.004), justifying the use of G-CSF as primary prophylaxis to prevent febrile neutropenia and hospitalization. It is worth noting that our institution did not implement a process for improving this metric, and therefore, the percentage of patients who received G-CSF did not change following implementation of our QII. This metric will be an additional area of focus moving forward, with plans to build G-CSF dosing into the Cerner Oncology order sets.

Limitations of our study include the small number of patients in the post-QII cohort and lack of longer-term follow-up data. Relying on the EMR for the availability of data further limits this study given that data are contingent on the EMR's accessibility and accuracy, which in turn are dependent on the consistency and compliance of the health care providers' documentation of clinical course and events. Hepatitis B virus status was assessed on the basis of whether the patient had undergone HBV testing at our institution. Testing could have occurred at any point in time, and therefore, this metric did not specifically measure HBV testing as part of the work-up for rituximab therapy. Lastly, our QII did not include a fertility or vaccination metric, both of which are commonly missed but have the potential to dictate patient outcomes and should be considered as metrics of interest in future QIIs.

CONCLUSION

Care of patients with lymphoma is swiftly moving toward patient-centered care models that include value-based practice incentives. Meaningful and feasible quality metrics need to be established with these models in mind. Several methodological challenges remain, but a collaborative effort among health care professionals, payers, and patient care navigators will foster ways to overcome the barriers for successful implementation of quality-focused cancer care programs. Periodic intervention with educational programs, appraisal of the quality initiative among physicians, and regular audit of quality metrics at an institutional level are all feasible, as found in this study. Yet, the impact on patient outcomes by implementation and measurement of such quality metrics should be prospectively evaluated. Further work is in progress to correlate process-to-outcomes and value in the care of patients with DLBCL.

Our initial experience with the ASH-PIM was a useful exercise designed to incorporate practice standards into the routine care of patients with DLBCL. Continued efforts to incorporate these standards in daily practice will help ensure that metrics continue to improve and goals are modified to reflect best practices in clinical care.

Mayo Clin Proc Inn Qual Out ■ December 2019;3(4):485-494 ■ https://doi.org/10.1016/j.mayocpiqo.2019.08.004
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ACKNOWLEDGMENTS

We thank Virginia M. Green, PhD, for her editorial assistance and preparation of the submitted manuscript.

Author contributions: conception and design—Drs Aboulafia and Vishnu; collection and assembly of data—Ms Bischin, Drs Vishnu and Aboulafia; data analysis and interpretation—Ms Bischin, Drs Vishnu, Aboulafia, and Chen; manuscript writing: Ms Bischin, Drs Vishnu, Aboulafia, and Knopf; final approval of the article—all authors; accountable for all aspects of the work—Ms Bischin, Drs Vishnu and Aboulafia.

Abbreviations and Acronyms: **ASH-PIM** = American Society of Hematology Practice Improvement Module; **BMB** = bone marrow biopsy; **CT** = computed tomography; **DLBCL** = diffuse large B-cell lymphoma; **EMR** = electronic medical record; **G-CSF** = granulocyte colony-stimulating factor; **HAART** = highly active antiretroviral therapy; **HBV** = hepatitis B virus; **HCV** = hepatitis C virus; **NHL** = non-Hodgkin lymphoma; **PET** = positron emission tomography; **QII** = quality improvement initiative; **R-CHOP** = rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone ; **VMMC** = Virginia Mason Medical Center

Potential Competing Interests: The authors report no competing interests.

Publication dates: Received for publication December 20, 2018; revisions received May 30, 2019; accepted for publication August 23, 2019.

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