Combined Pathology-Driven Algorithmic Testing and Integrated Reporting for Bone Marrow Examination

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- **Context.**—The College of American Pathologists published guideline recommending bone marrow synoptic reporting for hematologic neoplasms.

  *Objective.*—To evaluate the impact of pathology-driven algorithmic testing (PDAT) with integrated reporting for bone marrow examination on test utilization, ability to render a specific World Health Organization diagnosis, and clinician satisfaction 1 year after implementation.

  *Design.*—We reviewed the hematopathology reports, integrated synoptic reports, and ancillary test results generated during a 12-month period. The initial diagnosis from the hematopathology report was compared with the final diagnosis on the integrated synoptic reports. Test utilization data were compared with a previous year in which ancillary testing was ordered at clinician discretion. Clinicians were anonymously surveyed to assess their satisfaction with PDAT and integrated reporting.

  *Results.*—Integrated reporting resulted in a World Health Organization diagnosis for 80 of 85 cases (94%) compared with 54 (64%) for the hematopathology report alone. Unnecessary testing decreased from 45% pre-PDAT (124 of 274 cases) to 0.7% PDAT (2 of 268 cases), and PDAT resulted in fewer omissions of necessary tests. Clinicians preferred PDAT and valued integrated reporting for a variety of reasons, including the ease of finding relevant prognostic information.

  *Conclusions.*—Pathology-driven algorithmic testing with integrated reporting improves the pathologist’s ability to render a specific World Health Organization diagnosis and improves test utilization. Clinicians prefer PDAT to clinician-ordered testing. This is the first study to examine how synoptic reporting can modify hematologic diagnoses.

**MATERIALS AND METHODS**

**Implementation and Design**

In July 2014, the University of Vermont Medical Center in Burlington implemented PDAT and IR for all BM samples collected by the hematopathology/oncology service at our institution. The pathologists in hematopathology and cytogenetics sought and received approval from laboratory compliance personnel to offer algorithmic testing. We developed a strategy to triage BM samples into 1 of 8 testing algorithms, referred to as tracks, based on clinical history and initial peripheral blood and BM findings (see supplemental digital content at www.archivesofpathology.org in the June 2019 table of contents). The tracks are based primarily on World Health Organization (WHO) and National Comprehensive Cancer Network guidelines and were vetted by the hematopathology and hematopathology/oncology services. A process was developed to review, update, and approve the algorithms semiannually at a transdisciplinary team meeting.

A BM collection protocol was developed to accommodate the testing needs based on the patient’s clinical history (Figure 1). A reflex order that included a clinical information section was added to the laboratory ordering in the electronic health record (EHR). In the laboratory, the hematopathologist, using the clinical informa-
tion, BM and peripheral smear morphology, and other data, triages the sample to the correct testing track, which directs the hematopathologist to order ancillary tests according to an algorithm. Patients can move from one track to another based on BM and ancillary test results. Patients can be assigned to 2 tracks if needed, such as the lymphoma track and cytopenia track when the degree of involvement by lymphoma does not explain the patient’s cytopenias, or if dyspoietic morphology is identified. Allowing patients to be placed on 2 tracks ensures that a patient is appropriately evaluated for multiple possible causes of his or her cytopenias.

Separate reports are issued for the BM morphology, flow cytometry, cytogenetics, molecular, and other ancillary tests. In cases where a new WHO diagnosis is rendered, a separate integrated report, referred to as a pathology summary report (PSR), is generated in the anatomic pathology reporting system (Figure 2). Pathology summary reports are ordered by the hematopathologist on all patients with a new diagnosis of a neoplastic disorder but can also be used at the discretion of the pathologist to summarize findings that exclude a neoplastic disorder or provide additional information on a preexisting neoplastic disorder. The reports are written using standard reporting templates that correspond to each of the testing algorithms. Each template includes the important cytogenetic, molecular, and biomarker results integral for the diagnosis, prognosis, and monitoring of the patient. As the ancillary test results become available, they are manually entered into a working draft of the report. Pending PSRs are tracked manually using a patient list function in the EHR, similar to the patient lists used by clinicians. Once all results are completed, a 1- to 1.5-page PSR is issued that includes a final diagnosis, ancillary test results, and a comment section summarizing the diagnostic and prognostic significance of the findings. This includes information such as National Comprehensive Cancer Network risk stratification for acute myeloid leukemia and revised international prognostic scores for myelodysplasia.20 Most of the elements found in the College of American Pathologists cancer protocol templates for BM21 and plasma cell neoplasms22 are included, but the PSRs do not specify the biopsy site or quality of the specimens, unless they were unsatisfactory, and a complete list of immunohistochemical and flow cytometric immunophenotype results is also not included.

Analysis of Results

One year after implementation, we evaluated the effectiveness of PDAT and IR with respect to the ability to make a complete WHO diagnosis and appropriateness of test utilization. We evaluated clinician satisfaction with both PDAT and IR at 6 months.
postimplementation. The study received approval from the University of Vermont Institutional Review Board.

To evaluate the diagnostic efficacy of PDAT and its impact on test utilization, we retrospectively reviewed laboratory results from all BM examinations performed at inpatient and outpatient clinics at our institution from July 1, 2014, to June 30, 2015, which included the first year after implementation of PDAT with IR. To evaluate the diagnostic value of IR, we compared the final diagnosis on the hematopathology BM report with the final diagnosis in the PSR for all samples according to track assignment. Addendum reports were included and considered part of the final report. Completeness of the final diagnosis was classified into 3 categories: (1) definitive WHO diagnosis, (2) descriptive diagnosis offering a limited differential or a WHO diagnosis that became more specific with integration of ancillary test results, and (3) nonspecific descriptive final diagnosis with a broad differential. We also determined the percentage of integrated reports that contained significant diagnostic, prognostic, therapeutic, or monitoring information that was not included in the hematopathology BM report.

To evaluate the effect of PDAT on test utilization, we compared test orders during the first year of PDAT with test orders from BM studies collected at our institution from the pre-PDAT period of July 1, 2012 to June 30, 2013. We chose 12 to 24 months prior to implementation for comparison because in the year immediately prior to implementation of PDAT with IR, we had initiated IR for acute leukemia and had started to direct clinician test ordering in an informal manner using email and phone calls. For comparison, we retrospectively triaged the pre-PDAT cases into 1 of the 8 tracks based on information in the BM examination requisition, hematopathology report, and EHR. Appropriate ordering of ancillary tests was compared between pre-PDAT and PDAT periods. In both the pre-PDAT and PDAT groups, some patients were assigned to 2 tracks, and both testing tracks were included in the evaluation. Testing that was performed but not listed in the track algorithm was counted as excess testing. Testing that was indicated in the track algorithm but not performed was considered omitted. We considered a test appropriately performed if an order was placed and a proper sample was collected even if the testing could not be completed because of insufficient sample or analytical problems. The appropriateness of test orders was evaluated for each case and analyzed by track using descriptive statistics. Any ancillary testing that had been performed on BM or peripheral blood prior to the current BM examination was included. For the pre-PDAT group, testing done on BM or peripheral blood up to 1 month after the examination was included for analysis. Allowances were made for some tests such as calreticulin (CALR) and CCAAT/enhancer binding protein α (CEBPA) mutation analysis that were not readily available at our institution during the entire pre-PDAT period. Omission of these tests was not considered an incomplete evaluation during the pre-PDAT period but was considered incomplete during the PDAT period. Post-chemotherapy samples collected from patients who were treated for acute leukemia were excluded because of wide variation in local test ordering practice and lack of national testing guidelines.

To assess clinician satisfaction with both PDAT and IR, we surveyed hematology/oncology physicians, physician assistants, and nursing personnel 6 months after implementation. Surveys were anonymous and blinded.

RESULTS

From July 1, 2014, through June 30, 2015, 324 adult BM specimens were collected from inpatient and outpatient services at our institution. Physicians ordered PDAT in 100% of cases. Ten samples were assigned to 2 tracks, which included the cytopenia track and 1 other track.

IR Results

A total of 85 PSRs were issued in the PDAT period (Table 1). Pathology summary reports were completed on 80 of 88 cases (91%) with a new malignant diagnosis, 4 cases with a negative workup for a myeloproliferative neoplasm (MPN), and 2 cases of chronic lymphocytic leukemia in which the BM examination was performed for restaging. New diagnoses that did not have a PSR included 1 patient with acute myeloid leukemia who died shortly after admission to the hospital, 3 cases of smoldering myeloma or amyloid with insufficient numbers of plasma cells for ancillary testing, and 1 case of MPN, unclassifiable, that had a complete WHO...
diagnosis on BM report and mutation testing done on peripheral blood prior to BM examination.

For each specimen, we compared the PSR with the hematopathology BM report to determine the value of the PSR with respect to (1) the ability to reach a WHO diagnosis, (2) the specificity of the diagnosis or narrowing of the differential diagnosis, and (3) the presence of prognostic, therapeutic, or monitoring information (Table 2). Overall, PSRs resulted in a WHO diagnosis in 80 of 85 cases (94%) compared with 54 (64%) for the hematopathology report alone, with increases observed in the cytopenia, MPN, plasma cell dyscrasia, and lymphoma tracks. The ability to make a WHO diagnosis was unchanged in the acute leukemia and chronic myeloid leukemia tracks. Integrated reporting provided a more specific diagnosis or differential diagnosis in 35 of 85 cases overall (41%), with the most benefit found in the MPN, lymphoma, and acute leukemia tracks. Integrated reporting provided additional diagnostic, prognostic, therapeutic or monitoring information in 82 of 85 cases (96%) across all testing tracks (range, 67%–100%).

Test Utilization

The PDAT group (n = 268) was compared with 274 samples collected during the pre-PDAT period from July 1, 2012, to June 30, 2013. The pre-PDAT samples were retrospectively triaged into 8 testing tracks. Ten samples were assigned to 2 tracks that included the cytopenia track and 1 other. The distribution of hematologic disorders was similar in the pre-PDAT and PDAT groups. Review of pre-PDAT and PDAT cases revealed improved test utilization with respect to both unnecessary test orders and test omissions (Table 2). PDAT decreased test omissions, which improved the percentage of cases with a complete workup (94%) compared with 54 (64%) for the hematopathology report alone, with increases observed in the cytopenia, MPN, plasma cell dyscrasia, and lymphoma tracks. The ability to make a WHO diagnosis was unchanged in the acute leukemia and chronic myeloid leukemia tracks. Integrated reporting provided a more specific diagnosis or differential diagnosis in 35 of 85 cases overall (41%), with the most benefit found in the MPN, lymphoma, and acute leukemia tracks. Integrated reporting provided additional diagnostic, prognostic, therapeutic or monitoring information in 82 of 85 cases (96%) across all testing tracks (range, 67%–100%).

Table 1. Distribution of Pathology-Driven Algorithmic Testing Cases

<table>
<thead>
<tr>
<th>Track</th>
<th>Patients on Each Track</th>
<th>Patients on 2 Tracks</th>
<th>Malignant Diagnosis</th>
<th>PSRs</th>
<th>New Malignant Diagnosis</th>
<th>PSRs on New Diagnoses, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute leukemia</td>
<td>26</td>
<td>0</td>
<td>26</td>
<td>25</td>
<td>26</td>
<td>25 (96)</td>
</tr>
<tr>
<td>Treated acute leukemia</td>
<td>66</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cytophenias</td>
<td>58</td>
<td>10</td>
<td>18</td>
<td>9</td>
<td>9</td>
<td>9 (100)</td>
</tr>
<tr>
<td>CML</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2 (100)</td>
</tr>
<tr>
<td>MPN</td>
<td>39</td>
<td>0</td>
<td>29</td>
<td>19</td>
<td>15</td>
<td>14 (93)</td>
</tr>
<tr>
<td>Plasma cell dyscrasia</td>
<td>46</td>
<td>3</td>
<td>34</td>
<td>21</td>
<td>24</td>
<td>21 (88)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>89</td>
<td>5</td>
<td>42</td>
<td>9</td>
<td>9</td>
<td>9 (100)</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>334</td>
<td>10*</td>
<td>152</td>
<td>85</td>
<td>88</td>
<td>80 (91)</td>
</tr>
</tbody>
</table>

Abbreviations: CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasm; PSR, pathology summary report.

For each specimen, we compared the PSR with the hematopathology BM report to determine the value of the PSR with respect to (1) the ability to reach a WHO diagnosis, (2) the specificity of the diagnosis or narrowing of the differential diagnosis, and (3) the presence of prognostic, therapeutic, or monitoring information (Table 2). Overall, PSRs resulted in a WHO diagnosis in 80 of 85 cases (94%) compared with 54 (64%) for the hematopathology report alone, with increases observed in the cytopenia, MPN, plasma cell dyscrasia, and lymphoma tracks. The ability to make a WHO diagnosis was unchanged in the acute leukemia and chronic myeloid leukemia tracks. Integrated reporting provided a more specific diagnosis or differential diagnosis in 35 of 85 cases overall (41%), with the most benefit found in the MPN, lymphoma, and acute leukemia tracks. Integrated reporting provided additional diagnostic, prognostic, therapeutic or monitoring information in 82 of 85 cases (96%) across all testing tracks (range, 67%–100%).

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the order was unintentionally omitted in a patient who was also on a second track (1 case), or because there was inadequate sample (2 cases). The sources of incomplete orders in the pre-PDAT period could not be analyzed because of lack of documentation in the laboratory and EHR.

Analysis of test utilization revealed a decrease in unnecessary testing orders from 124 of 274 cases (45%) pre-PDAT to 2 of 268 cases (0.7%) with PDAT (Table 3). The greatest decreases were observed in the plasma cell dyscrasia track (32% pre-PDAT to 0% with PDAT) and the lymphoma track (85% pre-PDAT to 0% with PDAT). Both tracks improved primarily because cytogenetics was not ordered on samples where the BM morphology did not show significant involvement by plasma cells or lymphocytes.

Clinician Survey

A satisfaction survey was sent to clinicians 6 months after implementation of PDAT with IR. Nine of 18 clinicians (50%) responded to the survey, and respondents included attending physicians, hematology/oncology fellows, and nursing staff members of the hematology/oncology patient care team. Six of the 9 respondents (67%) preferred PDAT to clinician-ordered testing (3 had no opinion), 7 (78%) agreed that PDAT improved cost effectiveness, and 8 (88%) felt that it saved time. No one preferred clinician-ordered testing to PDAT in any category. All 9 respondents valued PSRs for their integrated prognostic information. Six (67%) used PSRs to review results before seeing a patient or ordering tests, 5 (56%) used them to provide information to patients or primary care providers, and 3 (33%) used them as an educational tool, to provide information to referral centers, and to enter data into study or clinical trials databases.

DISCUSSION

We implemented IR at our institution to address College of American Pathologists recommendations and as a service to our clinicians. Prior to PDAT, we had difficulty completing IRs because of the lack of appropriate ancillary tests being performed. PDAT was adopted to solve that problem and provide a clinician-friendly mechanism for appropriate test utilization. Pathology-driven algorithmic testing with IR ensures that our patients receive an appropriate BM examination with an integrated diagnosis.
Abbreviations: CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasm.

Table 2. Comparison of Pathology Summary Report (PSR) With Hematopathology Bone Marrow Report (HP) With Respect to Ability to Render a World Health Organization (WHO) Diagnosis, Specificity of the Diagnosis or Differential Diagnosis, and Presence of Additional Prognostic or Monitoring Information

<table>
<thead>
<tr>
<th>Track</th>
<th>PSR on New Diagnoses by Track</th>
<th>Ability to Render WHO Diagnosis, No. (%)</th>
<th>PSR Contribution, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HP</td>
<td>PSR</td>
<td>More Specific Diagnosis or Differential Diagnosis, No. (%)</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>25 (100)</td>
<td>14 (56)</td>
<td>35 (41)</td>
</tr>
<tr>
<td>Cytopenias</td>
<td>9 (56)</td>
<td>3 (33)</td>
<td></td>
</tr>
<tr>
<td>CML</td>
<td>2 (100)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>MPN</td>
<td>19 (37)</td>
<td>9 (64)</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Plasma cell dyscrasia</td>
<td>21 (181)</td>
<td>5 (24)</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>9 (56)</td>
<td>4 (44)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>85 (72)</td>
<td>80 (94)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasm.

We improved our ability to render a specific WHO diagnosis and enhanced reports with important prognostic information. Implementation of a standardized BM collection protocol helped ensure adequate specimen for testing. Although many institutions have protocols for how to collect a BM sample, preanalytic variables such as the quality and quantity of specimen available for testing continue to be problematic for some. Addressing preanalytic variables is critical for successful implementation of PDAT.

We believe our high satisfaction rating by clinicians is attributable to reducing the complexity of these BM evaluations and our ability to work with our clinicians to arrive at a unified ordering practice. Pathology-driven algorithmic testing improves compliance with recommendations for testing. In the pre-PDAT period, tests were often omitted when patients were admitted during a change in resident or attending coverage. This was particularly evident in patients presenting with acute leukemia. Pathology-driven algorithmic testing allows for seamless transfer of patients from the care of one clinician to another without excess or omitted testing. We reduced inappropriate utilization of routine chromosome analysis and fluorescence in situ hybridization. Modifying practice behavior in just these 2 areas accounted for the vast majority of savings.

Some institutions may achieve this by drawing a specimen to hold for cytogenetics. Our clinicians were strongly in favor of PDAT and IR, so the perceived benefit made agreement on PDAT relatively easy. Recent survey results from the College of American Pathologists confirm that lack of standardization of testing for acute leukemia samples is a common problem.

There are some limitations to our study. We assumed that all patients who underwent a BM procedure would require a complete workup. One patient in the PDAT group with acute myeloid leukemia died shortly after the procedure, and the ancillary testing was cancelled. That evaluation was counted as incomplete, even though the testing done was adequate for the clinical situation. Because we were not able to account for incomplete evaluations because of clinical factors in the pre-PDAT group, we did not adjust for clinical factors in the PDAT group.

Pathology-driven algorithmic testing with IR may be used as an educational tool for medical students, pathology residents, hematopathology fellows, and hematology-oncology fellows. Pathology-driven algorithmic testing and IR are incorporated into our training programs and provide an active learning opportunity that is built into the workflow of the service. Our trainees are responsible for ordering

Table 3. Appropriate Use of Ancillary Testing Pre–Pathology-Driven Algorithmic Testing (PDAT) Compared With PDAT

<table>
<thead>
<tr>
<th>Track</th>
<th>Complete Workup Ordered, No. (%)</th>
<th>Misleading Test Orders, No. (%)</th>
<th>Unnecessary Test Orders, No. (%)</th>
<th>Total, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-PDAT, No. (%)</td>
<td>PDAT, No. (%)</td>
<td>Pre-PDAT, No. (%)</td>
<td>PDAT, No. (%)</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>13 (59)</td>
<td>25 (96)</td>
<td>10 (45)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Cytopenias</td>
<td>60 (98)</td>
<td>53 (91)</td>
<td>1 (2)</td>
<td>4 (7)</td>
</tr>
<tr>
<td>CML</td>
<td>8 (80)</td>
<td>2 (67)</td>
<td>3 (30)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>MPN</td>
<td>15 (83)</td>
<td>34 (87)</td>
<td>2 (11)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Plasma cell dyscrasia</td>
<td>30 (79)</td>
<td>44 (96)</td>
<td>7 (18)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>111 (91)</td>
<td>86 (97)</td>
<td>2 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (100)</td>
<td>7 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Treated acute leukemia</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Totalb</td>
<td>240 (88)</td>
<td>251 (94)</td>
<td>25 (9)</td>
<td>14 (5)</td>
</tr>
</tbody>
</table>

Abbreviations: CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasm; NA, not analyzed.

a The MPN data also include MPN/myelodysplastic syndrome and mast cell disorders. Other includes bone marrow samples for workup of nonhematologic conditions such as solid tumor malignancies and infectious diseases.

b Totals may exceed sum of values shown above because of some patients’ cases being assigned to more than one track.
ancillary tests and writing IRs. One-third of clinicians who were surveyed specifically used the IR for educational purposes, so it has value in the clinical teaching setting as well.

Although both PDAT and IR are popular with our clinicians, the process is time consuming for the pathologist. We developed our PSR as a separate report instead of an addendum to make it more visible in the EHR. Prior to PDAT with IR, clinicians had difficulty finding addended reports in the EHR and received multiple addended reports that were generated as ancillary test results became available. Replacing the old process with PSRs mitigated this issue and was appreciated by clinicians for ease of finding clinical laboratory data. As a separate report, the PSR documents the clinical pathology consultation requested by the hematology/oncology physician and has the added benefit of being billable under Current Procedural Terminology code 80500. During our first year of IR, 100% of reports were reimbursed.

The PDAT algorithms are easily modified or updated to incorporate changes in testing recommendations. For example, we were able to modify our tracks to add colony stimulating factor 3 receptor (CSF3R) mutation analysis for possible chronic neutrophilic leukemia, ensuring appropriate and consistent utilization of the test. We have also used PDAT to respond to changes in insurers’ reimbursement for certain procedures, thus avoiding direct patient billing. The initially cumbersome paper ordering system has been improved by instituting electronic ordering of ancillary testing in the anatomic pathology reporting system. An electronic dashboard system to enhance sample ordering and tracking is being considered.

Pathology-driven algorithmic testing with IR is the standard of care at our institution. Pathology-driven algorithmic testing with IR is in line with our state and health care system’s goal to convert from a fee-for-service to a pay-for-performance model, in which physicians would be paid based on outcomes instead of being paid for specific tests or procedures.26,27 Pathology-driven algorithmic testing with IR is now available to 4 rural hospitals in our health network. The network clinicians and pathologists requested the service to deal with the increasing complexity of sample collection and test ordering. We anticipate this united effort will decrease the number of repeat studies needed when patients are referred to our center and lead to overall lower cost and improved patient care.

References