Laboratory Test Utilization Management
General Principles and Applications in Hematopathology

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KEYWORDS

• Test utilization • Clinical value • Guidelines • Algorithms • Infrastructure • Multidisciplinary • Intervention • Strategy

ABSTRACT

As the cost of health care continues to rise and reimbursement rates decrease, there is a growing demand and need to cut overall costs, enhance quality of services, and maintain as a top priority the needs and safety of the patient. In this article, we provide an introduction to test utilization and outline a general approach to creating an efficient, cost-effective test utilization strategy. We also present and discuss 2 test utilization algorithms that are evidence-based and may be of clinical utility as we move toward the future of doing the necessary tests at the right time.

Key Features

- Test utilization is a strategy for performing appropriate laboratory and pathology testing with the goal of providing high-quality, cost-effective patient care.
- Test utilization is important for good patient care and good medical practice, and there is an economic demand for it.
- Test utilization is a complex issue: a good approach is likely multifaceted with a multidisciplinary effort.
- Pathologists should assume a leadership role in test utilization given their training experience in laboratory testing, and administrative and managerial skills.

OVERVIEW

The explosive growth of medical knowledge, imaging and technologies, access to medical care, and laboratory tests has led to a vast array of diverse information for medical practitioners to know and manage. As a result, practitioners may have difficulty efficiently navigating the enormous assortment of testing options thereby leading to medical testing overuse, misuse, and/or underuse.[1,2] Adding further to any potential confusion about which test(s) is/are the right one(s) to order, is that laboratories often set up tests without much help or guidance provided to the ordering individual as to which tests provide what information regarding a certain disease process. From a laboratory perspective, an opportunity therefore exists to collaborate with our clinical colleagues and share our collective expertise with regard to which tests might not be necessary and which tests might be necessary.[3]

There are 2 fundamental components that underlie a laboratory test utilization management

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program: founding principles and an implementation strategy. A high-level overview of test utilization principles and strategies for implementation comprises the first half of this article. The second half provides 2 evidence-based, data-driven examples of test utilization practice in the discipline of hematopathology.

TEST UTILIZATION MANAGEMENT PRINCIPLES

Test utilization management principles are key and vital components of the current and future success of the practice of medicine. Three basic principles supporting a test utilization approach include good patient care, sound medical practice, and economic demand. Importantly, these principles resonate not only with 1 or 2 medical specialties but rather with and influence all clinical medicine disciplines (**Box 1**).

Good patient care is an essential tenet of an optimal test utilization practice. The needs of each individual patient come first, and as good stewards of health care, all those involved in health care delivery aim to "above all, do no harm." From the perspective of the laboratory, we aim to do the right test, at the right time, for the right patient and obtain the right result.[4] By embracing and adhering to this principle, one reduces unnecessary testing and saves time. Additionally, potential pitfalls of equivocal or false-positive results that could result in unnecessary additional tests or incorrect patient management are avoided.

There are many factors that constitute sound medical practice, including physician and other health care worker competency, practicing with standard-of-care principles and knowledge, working honestly and with integrity, and respecting all individuals involved in medical care. The test utilization component of good medical practice comes from the perspective of practicing competently and using diagnostic testing modalities correctly and judiciously. Laboratory professionals take pride in knowing the value they provide by performing and accurately reporting the right tests for each individual patient. It has been stated that more than 50% of medical decisions are made based on laboratory results; thus, it is imperative that the right tests are being performed and that the unnecessary tests are not.[5,6]

Box 1
Three key factors that support the importance of test utilization

1. Good patient care
2. Sound medical practice
3. Economic demand

With the continued economic challenges in health care, decreasing reimbursements, and limited resources, a test utilization strategy, as part of overall patient care management, is not just a reality but a necessity. Every year the annual cost of health care in the United States continues to increase. This is due, in part, to the increased cost of laboratory testing in general, but unnecessary, overused, and duplicative testing are also significant contributing factors.[1,6–9] Thus, there is a growing economic need for reforming current test ordering/utilization practices and embracing a test utilization management plan. As overall reimbursement rates continue to drop and the fee-for-service payment model shifts to a bundled payment model, any testing that is performed will be a cost to the laboratory. Therefore, bundled tests with increased operating costs may not be financially sustainable. As such, these options will force the laboratory to move to a cost-cutting/saving test utilization model so as to perform as efficiently and effectively as possible.[4] A targeted testing approach for each patient/disease entity will result in decreased, out-of-pocket expenses for the patient whose testing charges are not covered by a health insurance company, and decreased costs and improved efficiency for the laboratory.

STRATEGY FOR TEST UTILIZATION MANAGEMENT IMPLEMENTATION

A test utilization management system has value for patients, physicians, and health care overall, but implementation can be challenging and time-consuming. A successful strategy includes a multipronged approach, including support from the institution, identification and inclusion of the key stakeholders (eg, institutional leadership, clinicians, health care workers, managers, laboratorians, and pathologists), a careful and methodical approach, a data-driven process, and a recurring review process to ensure continued current medical applicability and appropriate updating.[1,3,9,10] **Box 2** outlines key components that could underlie one approach toward developing a test utilization implementation strategy.

To begin the work toward successful implementation of a laboratory test utilization management program, it is critical that there is full support by institutional leadership and an adequate organizational infrastructure. Senior administration and institutional/hospital leaders provide the highest level of oversight for the strategic planning and

Box 2
One approach to developing a test utilization implementation strategy

1. Ensure institutional leadership support and presence of adequate infrastructure
2. Define the problem with the current standard of practice and establish the need to address it
3. Decide on a type of intervention that will address the problem defined above (see **Box 3**)
4. Establish the clinical indications, overall value, and application of a diagnostic test for a certain disease
5. Review the current clinical practice guidelines
6. Formulate a data-driven, evidence-based strategy
7. Consider your stakeholders, especially your clinical colleagues, and share the proposed strategy with them
8. Launch your test utilization strategy
9. Audit laboratory and clinical personnel
10. Reevaluate your strategy on an annual basis

operational logistics of an institution.[11] With the backing of the institution, laboratorians then work with clinical colleagues and key health care personnel to effect the right outcome.[1,12–14] Pathologists, who have administrative leadership experience, laboratory management responsibilities, and knowledge regarding laboratory testing, are uniquely positioned to be leaders in this process.[1,15,16]

Next steps include identifying an area of the practice that would benefit from laboratory test utilization implementation. This identification process also includes taking into consideration the clinical, financial, and operational impacts.[1,13] Once a problem area is identified and agreed on as requiring intervention, a type of intervention that will address the problem is delineated (**Box 3**).

The development of a laboratory test utilization guideline or algorithm as an intervention occurs as a multistep process. The clinical indications, overall value, and application of a diagnostic test for a certain disease are established.[9] Subsequently, the laboratory team performs a retrospective review and correlation of in-house test results with the patient clinical status.[17] Simultaneously, other team members review the current literature regarding the diagnostic test and disease in question, including national and international guidelines (for example, the National Comprehensive Cancer Network guidelines), recommendations, published best practices, and peer-reviewed journals.[10] After identifying appropriate tests, supported by current standard of practice guidelines, a data-driven, evidence-based guideline or analytical algorithm can be formulated.[13]

At the appropriate point(s) in this process, all stakeholders should be included. For example, clinical colleagues and geneticists who are part of the disease-oriented group(s) relevant to the test utilization strategy are critical collaborators.

Box 3
A nonexhaustive list of the different types of interventions that can be used in test utilization strategies

- Restrict ordering to clinicians with certain credentials
- Changes to computerized provider order entry:
  - Using pop-ups
  - Removing tests from quick-pick screens
  - Removing research-only test
- Banning of certain tests:
  - Obsolete tests
  - Referral tests that are also offered in-house
- Send and hold specimens
- Add prerequisites/requirements that must be fulfilled before an order can be placed
- Requiring laboratory approval for specified tests
- Selective review process
- Test send-out review
- Test formularies
- Test guidelines
- Analytical algorithms
- Hard stops and gatekeeper functions
- Restrict the frequency of specified tests
- Real-time test-selection support
- Educational activities
- Utilization audits and report cards
- Required genetic counseling before approving test

Data from Refs.[3,11,15,82]

Laboratory personnel, management, and specialists in information technology should also be consulted to ensure that the proposed strategy is a feasible one from the laboratory and operational standpoints. At times, it may be necessary to actively engage your stakeholders and this can be done using various educational tools that may include recorded videos, Grand Round presentations, and publications.[9]

Once an algorithm/implemented guideline is in place, it is necessary that it be audited on a routine, at least annual, basis. Auditing a test utilization guideline or algorithm supports sustained success of the strategy, helps to ensure compliance, confirms that a standardized approach is working, and is a critical step in efficient test utilization. Key concepts during an audit include assessment that the testing being performed remains relevant, that there are/are not new technologies or tests that should be considered and finally, that the diagnostic approach to the disease entity is unchanged. The data from auditing highlight comparative differences/similarities between practicing individuals, provide information on how a test(s) is being used, indicate whether the intended outcome was achieved, and help to identify problem areas that need updating, modifying, or reeducation.[3,4,9,13]

Beyond just the scope of one's local clinical and laboratory practice, implementation of efficient and successful test utilization strategies demonstrates our broader value to health care organizations and insurance companies as the economic environment continues to change. Ongoing comparison of disease workup under the previous model of care with a new test utilization strategy highlights standardization, decreased unnecessary testing, and improved targeted diagnostics. Thus, we prove evidence of added value while still putting the needs of the patient first and creating a sustainable and operational laboratory.

THE PRACTICE OF HEMATOPATHOLOGY AND TEST UTILIZATION

The discipline of hematopathology increasingly embraces the concept of utilization management as evidenced by a growing number of peer-reviewed publications, educational seminars and workshops, and presentations at pathology national meetings on this topic. As a direct result of these efforts, data-driven, effective, test utilization algorithms have been proposed and exist in some practices.[18–26] Algorithms incorporate important clinical parameters, comparative studies of testing modalities, practice data, published literature, and national and international guidelines (where applicable). They may vary slightly between individual pathology practices based on case mix, clinical trial enrollment, and practice expertise. However, in general, algorithms hold true to the principles of the right test(s) at the right time for the right diagnosis.

In this section, we present 2 examples of test utilization approaches for hematologic conditions: (1) the initial workup and diagnosis of myelodysplastic syndromes and (2) bone marrow testing in the staging for involvement by lymphoma diagnosed in an extramedullary site. A key point to remember with the consideration of implementation of an algorithm into routine clinical practice is that these approaches are meant for most patient cases (80%). They are by no means meant to be exclusive or "one size fits all." Outlier cases are well known to pathologists and in no way should deter testing that may be necessary in the evaluation of such a case. In general, our approach has been the "80/20 rule" wherein 80% of cases can be successfully managed with the algorithm. A second key point, as mentioned previously, is that medicine and technologies continually evolve and therefore algorithms need to be reviewed and updated on a regular basis or whenever a transformative event occurs. Algorithms, as a whole, provide an excellent framework within which to begin the assessment of a case and ensure that best practices are followed.

ALGORITHMIC APPROACH TO THE INITIAL WORKUP AND DIAGNOSIS OF MYELODYSPLASTIC SYNDROME

Myelodysplastic syndromes (MDSs) are a heterogeneous group of clonal stem cell myeloid disorders with a predilection for evolution into acute myeloid leukemia.[27–33] Pathologically, MDS is diagnosed by morphologic dysplasia in a bone marrow specimen in the setting of persistent cytopenias and adequate exclusion of non-neoplastic mimickers of dysplasia (eg, nutritional deficiency, toxin/drug exposure). On occasion (fewer than 5%–10% of all cases), bone marrows performed for unexplained persistent cytopenias show no diagnostic dysplastic features; however, a clonal MDS-associated abnormality (eg, chromosomal analysis, fluorescence in situ hybridization [FISH], and molecular mutations [Next Generation sequencing]) may be detected. These cases represent situations of clonal hematopoiesis of uncertain significance or clonal hematopoiesis of indeterminate potential.[27,34–36] Flow cytometry is another useful technique in the evaluation of

myeloid disorders, but its role currently as a diagnostic tool in MDS remains supportive.[37–40]

Although morphology plays the key diagnostic role in MDS at the present time, prognostication in MDS is influenced by multiple factors. These factors include, but are not limited to, blast count in the peripheral blood and bone marrow, presence of Auer rods, degree of cytopenias, and number and type of chromosomal abnormalities.[33,41–43] Recent data indicate that certain molecular alterations also may now play a prognostic role in MDS.[35,44–46]

Given that morphology drives the diagnosis of MDS and that a variety of tools (clinical features, morphology, complete blood cell count values, chromosomal and molecular genetic findings) drive MDS prognosis, a data-driven, test utilization strategy for the initial workup of MDS can be proposed (**Fig. 1**). As mentioned previously, such a strategy is not intended to be dogmatic, nor does it preclude one from deviating in exceptional circumstances, but is meant to assist in the efficient and appropriate workup of a particular disease entity. A robust algorithm is evidence-based and integrates and incorporates findings from practice data, peer-reviewed published literature, clinician expertise, national guidelines (eg, National Comprehensive Cancer Network) and international recommendations (eg, international prognostic scoring system for MDS).[41–43,47,48]

Typically a bone marrow examination to assess for MDS is initiated by a clinician based on his or her clinical suspicion. This initial evaluation includes morphologic review and chromosomal analysis. Bone marrow morphologic requirements should include a peripheral blood smear in addition to complete blood cell count data, particulate, Wright-Giemsa–stained aspirate smears, and an adequate, hematoxylin-eosin–stained, bone marrow core biopsy. If morphologic review renders a firm diagnosis of MDS, the chromosomal study provides additional prognostic and therapeutic (eg, lenalidomide treatment for deletion 5q) information.[41–43,45,49–52] If the chromosomal study yields 20 adequate metaphase spreads and there is a resultant resolved karyotype, then FISH studies for the commonly recurring genetic abnormalities (−5/5q, −7/7q, +8, del20q, del17p, −13/13q) are not generally needed.[53–56] If the chromosomal study yields fewer than 20 adequate metaphases and/or the karyotype is unresolved, additional FISH testing should be considered for possible prognostic assessment. These general practice principles are based on the findings of the chromosomal study and apply not only to cases of morphologic MDS but also to cases in which the morphology is either equivocal or not diagnostic of MDS. The finding of MDS-associated abnormalities in those latter instances is of uncertain significance in the absence of unequivocal features of MDS.[27,57]

The recent and rapid discovery of recurring molecular mutations in MDS is yet another tool that is set to transform our diagnostic and prognostic approach to MDS.[35,45,46,58–61] However, it is still too early in this process to be able to carefully and methodically assess the test utilization principles for this technology at this point (see **Box 1**). An MDS algorithm is a good example of the critical value that an annual review and reassessment of the test utilization guideline has so as to determine what the evolving/current best practices and/or new technologies are and whether the guideline/algorithm needs updating. Given all the advances and innovation that continue to occur in medicine, our approach to MDS for best medical practice will undoubtedly evolve.[45,58]

ALGORITHMIC APPROACH TO THE EVALUATION OF BONE MARROW SPECIMENS PERFORMED FOR STAGING OF LYMPHOMA

Bone marrow biopsies are routinely performed to stage concurrently diagnosed Hodgkin and non-Hodgkin lymphoma in an extramedullary tissue

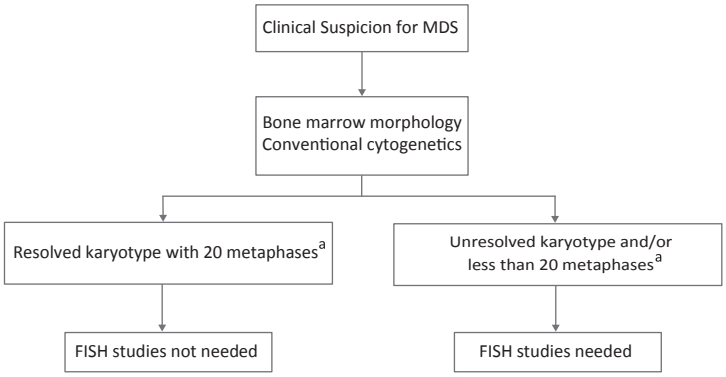

Fig. 1. Algorithmic approach to test utilization in MDSs. MDS FISH does not increase the detection of MDS if chromosome analysis is successful and 20 metaphases are analyzed. Thus, MDS FISH studies should be ordered at the discretion of the cytogeneticist if <20 metaphases are identified, if there is an unresolved karyotype, or if only 1 abnormal metaphase is identified. [a] Consider Next Generation Sequencing testing for select gene mutations, as clinically warranted.

biopsy. Staging for lymphoma in the bone marrow may be important for prognostication and therapeutic options.[62,63] Similar to other tissues biopsied to assess for a hematologic neoplasm, there is an extensive suite of ancillary studies that are at a pathologist's disposal to further clarify and classify a disease process. These testing modalities include morphology/step section levels, immunohistochemistry, flow cytometry, molecular testing, chromosomal analysis, and FISH testing. Each of these testing modalities has well-recognized value in the diagnosis and prognosis of lymphoma in tissues. However, in the context of evaluating bone marrows performed to stage diagnosed lymphoma, the utility of and value added from performing these testing modalities should be clarified.

Multiple, peer-reviewed articles have systematically reported on the utility of the available testing modalities in the evaluation of a bone marrow performed for the purpose of staging lymphoma (morphology/step section levels, immunohistochemistry, flow cytometry, molecular testing, chromosomal analysis, and FISH testing).[64,65] The utility of these various testing modalities in the bone marrow staging of lymphoma is controversial; however, most would agree that the highest impact modality is morphologic review of an adequate and generous biopsy specimen (**Fig. 2**). The patterns of bone marrow involvement by Hodgkin and non-Hodgkin lymphoma are well-recognized and documented.[64,66] With this knowledge, pathologists readily determine the presence or absence of morphologic involvement of the bone marrow by lymphoma.

Flow cytometric immunophenotyping is a useful ancillary tool in the diagnosis and classification of B-cell and T-cell lymphomas. In bone marrow specimens obtained for the purpose of staging extramedullary diagnosed lymphoma, the role for flow cytometry has also been investigated. Although its role is controversial among several peer-reviewed published articles,[67–72] in general, flow cytometry does not add significant additional information beyond the bone marrow morphology in most cases (80%).[68,70,73] The concordance rate beyond bone marrow morphology and flow cytometry exceeds 80% in most studies. Hanson and colleagues[73] concluded that flow cytometric evaluation is not cost-effective in the setting of an adequate morphologic evaluation. In the study by Wolach and colleagues,[70] positive flow cytometry (FC) in the setting of negative bone marrow (BM) histology at diffuse large B-cell lymphoma (DLBCL) diagnosis did not significantly affect overall survival (OS) or progression free survival (PFS). Iancu and colleagues[68] found that 3-color flow cytometric immunophenotyping adds little information to the evaluation of staging BM specimens of follicular lymphoma (FL) patients. Concordance between the 2 methods was detected in 411 (85%) cases (27% BMB+/FC+; 58% BMB−/FC−), whereas discordance was present in 75 (15%) ($P<.001$): 58 cases (12%) were BMB+/FC− and 17 (3%) were BMB−/FC+ in the study by Merli and colleagues.[69] Given the incidence of monoclonal B lymphocytosis and occasional cases of subtle bone marrow involvement by marginal zone lymphoma and intrasinusoidal lymphoma, it is not surprising that discrepancies exist.[74] It is therefore of utmost importance to determine in which very specific scenarios would flow cytometry contribute valuable information in the setting of a morphologically normal bone marrow.

Immunohistochemistry (IHC) is another useful tool in the hematopathology armamentarium for disease classification. However, its role in the setting of an adequate bone marrow morphology specimen in staging lymphoma is not clear. It is doubtful that in most cases IHC would make a meaningful contribution to the interpretation of a staging lymphoma bone marrow in otherwise straightforward concordant involvement or lack of involvement (see **Fig. 2**). Exceptions could be investigated as necessary on a case-by-case basis (eg, assessment for intrasinusoidal involvement by marginal zone lymphoma).

Conventional karyotyping is an optional ancillary study that may be performed in the setting of bone

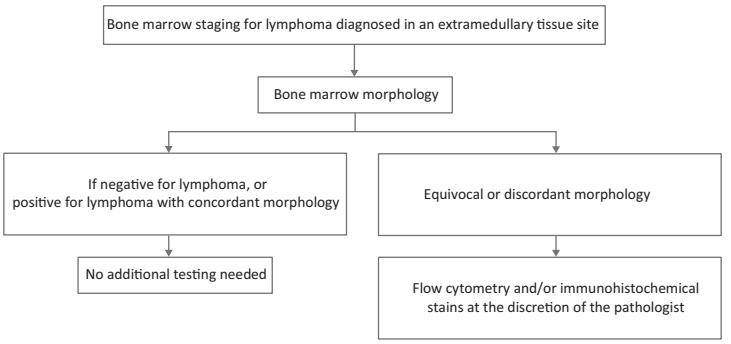

Fig. 2. Guideline for bone marrow testing performed for staging for lymphoma diagnosed in an extramedullary tissue site.

marrow staging for lymphoma. However, a routine cytogenetic study is costly, time-consuming, and labor intensive. Two, large, recent, independent retrospective studies have shown that routine cytogenetic studies in staging of extramedullary diagnosed lymphoma in the bone marrow provides no additional diagnostic information beyond the histomorphologic findings.[25,75]

FISH plays an important role in the prognostication and occasional diagnosis of non-Hodgkin lymphomas.[76–78] FISH studies, as a general rule, when needed for the latter purposes, should be performed on the primary diagnostic specimen. In the setting of a staging bone marrow for extramedullary diagnosed lymphoma, FISH is of doubtful utility whether there is morphologic evidence of marrow involvement by lymphoma or not. Although it could be argued that detection of a low-level abnormality could indicate occult bone marrow involvement by lymphoma, the true significance of such a finding in the absence of morphologic confirmation is unclear and could potentially be spurious.[79] Conversely, morphologic bone marrow involvement by lymphoma does not require confirmation by a FISH study.

Clonal immunoglobulin heavy chain gene (IgH) rearrangements may support the presence of a clonal B-cell population in the appropriate clinical, morphologic, and immunophenotypic setting. In bone marrows performed to stage extramedullary lymphoma, assessment for a clonal IgH gene rearrangement does not routinely contribute additional meaningful information. In the setting of morphologic bone marrow involvement by lymphoma, IgH gene rearrangement studies provide no additional diagnostic information. Conversely, in cases lacking morphologic bone marrow involvement by lymphoma, apparent IgH clonality detection could lead to a significant misinterpretation or misdiagnosis of bone marrow involvement by lymphoma. It is known that IgH clones may occur in reactive conditions and when there is a limited B-cell repertoire.[80] Detection of a clone in a morphologically negative bone marrow may have a prognostic role in follicular lymphoma,[81] but should be confirmed in larger studies.

SUMMARY

Efficient, cost-effective test utilization is a key component of sound medical practice, judicious management of health care resources, decreasing health care costs, ensuring patient safety, and improving the quality of health care services.[1,9] Pathologists and laboratorians must be engaged in this process along with clinical colleagues and all health care contributors. Utilization management also allows the laboratory to demonstrate value to insurance companies, provides justification for a sustainable and data-driven operation for patient care, and is an important parameter of evidence-based medicine. Pathologists are uniquely positioned to be at the forefront of test utilization and lead the efforts during this needed time of change. The field of hematopathology has been a leader in incorporating ancillary testing into the diagnostic classification of disease. As ancillary testing continues to evolve and transform our practice, hematopathology is a key area in which efficient test utilization can be and must be applied.

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