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Global Cytopathology-Hematopathology Practice Trends

A Cyto-Heme Interinstitutional Collaborative Practice Survey of Intradepartmental Collaboration and Challenges in Pathology

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ABSTRACT

Objectives: Small-volume biopsy—fine-needle aspiration biopsy (FNAB) with or without core biopsy—is in increasing use in diagnosis and management of lymphoma patients. Our objective was to survey the current practice in small-volume biopsy diagnosis of lymphoma, focusing on the interaction among hematopathologists and cytopathologists and the integration of FNAB, core biopsy, and flow cytometry studies at sign-out.

Methods: This study used a cross-sectional survey design employing the RedCap database distributed via nine pathology professional society email listservs. The survey consisted of 25 multiple-choice questions and several free text fields. In total, 128 pathologists participated.

Results: Most respondents indicated that FNAB specimens in which lymphoma is a diagnostic consideration (FNAB-L) are seen daily or weekly (68/116; 58.6%). However, most institutions have separate hematopathology and cytopathology services (72/116; 62.1%) with inconsistent communication. When communication occurred, respondents were frequently inclined to reconsider their original diagnoses. Barriers identified included lack of communication, inadequate access to diagnostic studies, no formal subspecialty training, and various opinions regarding FNAB in diagnosing lymphoma.

Conclusions: This survey showed that FNAB-L specimens are common, with a lack of uniformity in how complementary fine-needle aspiration and core biopsy specimens or flow immunophenotyping results are shared across hematopathology and cytopathology services.

KEY POINTS

- Fine-needle aspiration biopsy (FNAB) with or without concurrent core biopsy in the diagnosis and management of lymphoma patients is a common specimen and is encountered frequently by pathologists.
- Communication between hematopathology and cytopathology departments is inconsistent; however, when communication occurs, pathologists often reconsider their original diagnoses.
- There is no uniformity in how components of a small-volume specimen (FNAB, core biopsy, and flow immunophenotyping) are handled across cytopathology and hematopathology service lines.

KEY WORDS

Cytopathology; Hematopathology; Fine-needle aspiration; Flow cytometry; Lymphoma

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INTRODUCTION

Fine-needle aspiration biopsy (FNAB) remains a frequently used procedure in the screening and diagnosis of a plethora of lesions throughout the body. The benefits of FNAB are well known and include minimal invasiveness, a low risk of adverse events, a rapid turnaround time, and cost-effectiveness. However, the diagnosis of lymphoma by FNAB is controversial, and opinions regarding its diagnostic utility among pathologists and oncologists vary.[1-3] Advocates for FNAB in this specific clinical context emphasize its utility in triaging patients, particularly when the patient has a prior lymphoma diagnosis.[4] FNAB with concurrent flow cytometry has also been shown to have utility in reassuring select patients when they present with benign lymphadenopathy.[5] Conversely, the limitations in the diagnosis of specific lymphoma types by FNAB have been acknowledged in the literature; however, evidence-based data are lacking. With the increasing subtypes of hematolymphoid neoplasms in the newest edition of the World Health Organization classification system, it is important to identify and define clinical scenarios and subsequently FNAB adequacy criteria for specific lymphoma diagnoses. Equally as necessary to recognize are clinical situations in which a core or excisional biopsy would be most prudent.[6] This survey aims to evaluate the current state of cytopathology and hematopathology cooperation in the workflow and sign-out of these oftentimes highly complex cases.

MATERIALS AND METHODS

This study used a cross-sectional survey design. Study data were collected and managed using REDCap electronic data capture tools hosted at Stanford University.[7,8] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing an interface for validated data capture; audit trails for tracking data manipulation and export procedures; automated export procedures for seamless data downloads to common statistical packages; and procedures for data integration and interoperability with external sources. This study was reviewed and approved by the institutional review board of Stanford University.

Email invitations to complete the survey online were sent to multiple pathology organizations to distribute to their membership database. These organizations included the European Association for Haematopathology, Society for Hematopathology, American Society of Cytopathology, World Association of Societies of Pathology and Laboratory Medicine, International Academy of Cytology, College of American Pathologists Cytology Committee, Brazilian Pathology Society, and the Chinese Hematopathology Society. The American Society for Clinical Pathology invited pathologists to participate in the survey via Twitter. The survey closed in February 2020.

Survey development began with discussions among members of the Cytology-Hematology Interinstitutional Collaboration (CHIC) group led by Dr Dita Gratzinger at Stanford University. CHIC is a consortium of hematopathologists, cytopathologists, and lymphoma oncologists whose aim is to optimize the role of small-volume biopsy in lymphoma patient care. Questions were created and refined from these discussions to determine the overall current state of practice regarding fine-needle aspiration (FNA) cytology in diagnosing lymphoma with a focus on interdepartmental workflow and communication. A primary goal of the survey was to identify how specimens that overlap between cytopathology and hematopathology services are handled and what barriers may exist to integrated review of the patient's biopsy specimens by both services. The survey consisted of 25 multiple-choice questions with additional free-text questions to examine select responses in greater detail (see Supplementary Figure; all supplemental materials can be found at *American Journal of Clinical Pathology* online).

RESULTS

This survey presents data from 128 respondents from across the world. Most surveys were completed in their entirety (89; 69.0%). Geographic areas represented include North America—United States (41/113; 36.3%), the European Union (EU) (23/113; 20.4%), Asia (20/113; 17.7%), Europe—non-EU (7/113; 6.2%), Australia and Oceania (6/113; 5.3%), North America—Canada (5/113; 4.4%), South America (5/113; 4.4%), sub-Saharan Africa (2/113; 1.8%), the Middle East and North Africa (2/113; 1.8%), Central America and Caribbean (1/113; 0.9%), and North America—Mexico (1/113; 0.9%) FIGURE 1.

Most respondents included hematopathologists (HPs) (64/117; 54.7%), followed by surgical pathologists (SPs) (58/117; 49.6%), cytopathologists (CPs) (46/117; 39.3%), other pathology subspecialties (11/117; 9.4%), and other (1/117; 0.9%) FIGURE 2. Many respondents indicated more than one specialty (47/117; 40.2%). Specialty combinations included HPs and SPs (14/117; 11.9%); CPs and SPs (13/117; 11.1%); CPs, HPs, and SPs (8/117; 6.8%); HPs and other (3/117; 2.6%); CPs and HPs (2/117; 1.7%); CPs, SPs, and other (2/117; 1.7%); HPs, SPs, and other (2/117; 1.7%); CPs, HPs, SPs, and other (2/117; 1.7%); and CPs, HPs, and other (1/117; 0.85%). Distribution of respondents by practice setting included primarily those in an academic hospital or medical center (79/112; 70.5%) or nonacademic hospital or medical center (19/112; 17.0%). Fewer pathologists practicing in federal government facilities, local government facilities, central hospital laboratories, independent reference laboratories, and community-based practices responded (14/112; 12.5%). Most respondents were experienced pathologists with greater than 15 years of independent sign-out experience (45/116; 38.8%) or pathologists in practice for least 5 years and up to 15 years (45/116; 38.8%) FIGURE 3. The size of respondents' cytopathology and hematopathology services was surveyed. Most pathology departments were staffed by at least three cytopathologists (64/117; 54.7%), or cytopathology was included in the general anatomic pathology service (32/117; 27.4%). Similarly, hematopathology services were most often composed of at least three hematopathologists (46/115; 40.0%) with fewer numbers of departments staffed by one to two hematopathologists (36/115; 31.3%) or with hematopathology included as a part of the general anatomic pathology sign-out (25/115; 21.7%). FNAC specimens in which lymphoma or other hematolymphoid neoplasm was a diagnostic consideration were encountered commonly daily (32/116; 27.6%) or weekly (36/116; 31.0%) FIGURE 4.

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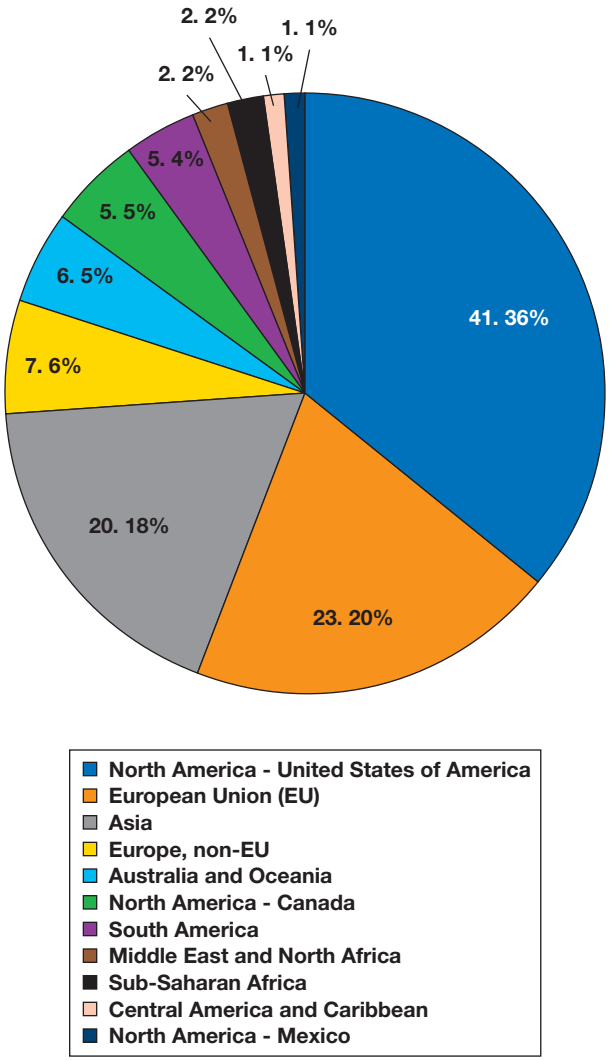

FIGURE 1 Geographic location of home/practice institution (n = 113).

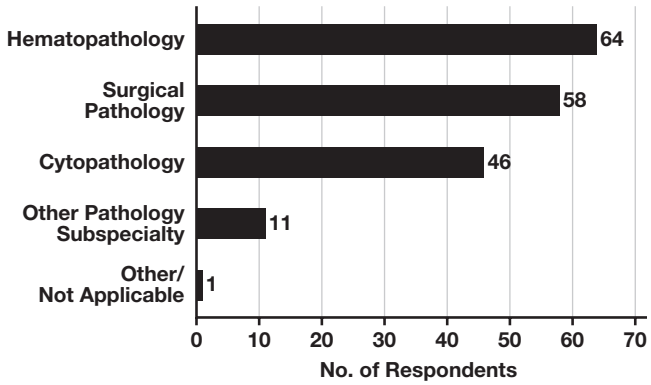

FIGURE 2 Professional specialty of respondents (n = 117).

Communication Between Hematopathology and Cytopathology Services

Most respondents indicated that their institutions have separate hematopathology and cytopathology services (72/116; 62.1%). More than three-fourths of respondents indicated that their hematopathology and cytopathology services were in close proximity either in the same or connected building (82/107; 76.6%) or within a 10-minute walk from each other (83/106; 78.3%). A minority of hematopathologists and cytopathologists sought out each other's opinions frequently on a daily (30/107; 28.0%) basis and more on a weekly (36/107; 33.6%) or monthly basis (11/107; 10.3%). Conversely, some practices rarely (18/107; 16.8%) or never (3/107; 2.8%) sought out diagnostic opinions from their respective hematopathology or cytopathology departments FIGURE 5. Following communication between hematopathology and cytopathology colleagues about a case, respondents were frequently inclined to reconsider their original diagnoses sometimes (31/89; 34.8%) often (10/89; 11.2%), or always (7/89; 7.9%). A similar finding was observed with interdepartmental consultations regarding the FNAC and separate core biopsy or concurrent flow cytometry FIGURE 6.

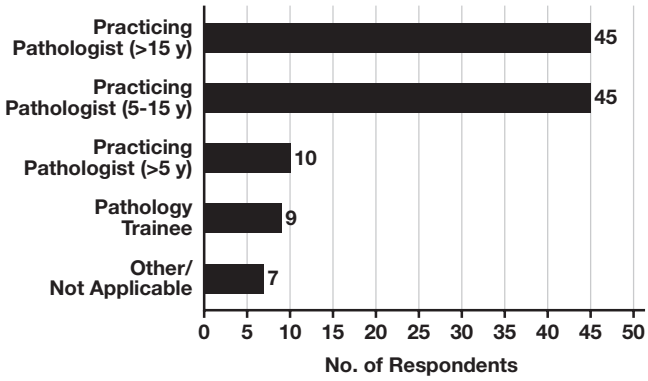

FIGURE 3 Pathologist experience level (n = 116).

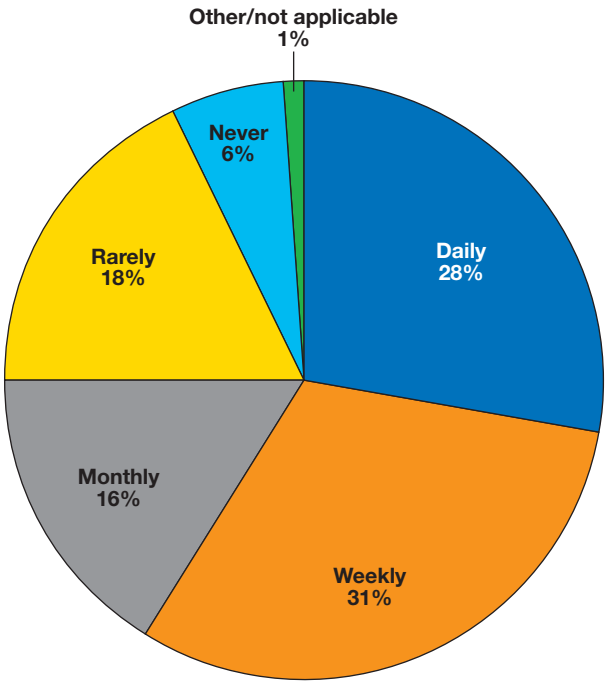

FIGURE 4 Frequency of fine-needle aspiration cases in which lymphoma is a diagnostic consideration (n = 116).

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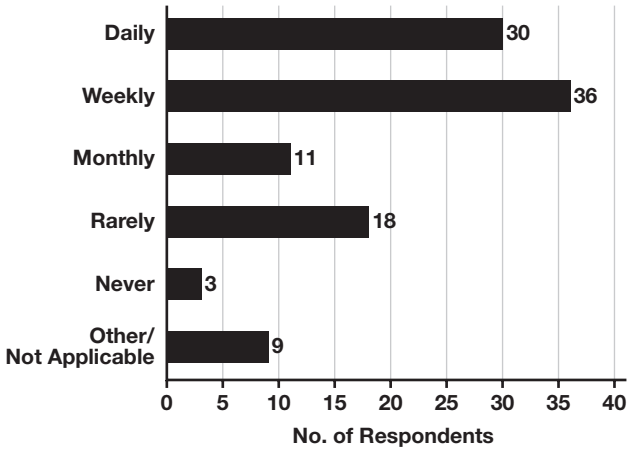

FIGURE 5 Frequency with which diagnostic opinions are requested from a hematopathologist or cytopathologist (n = 107).

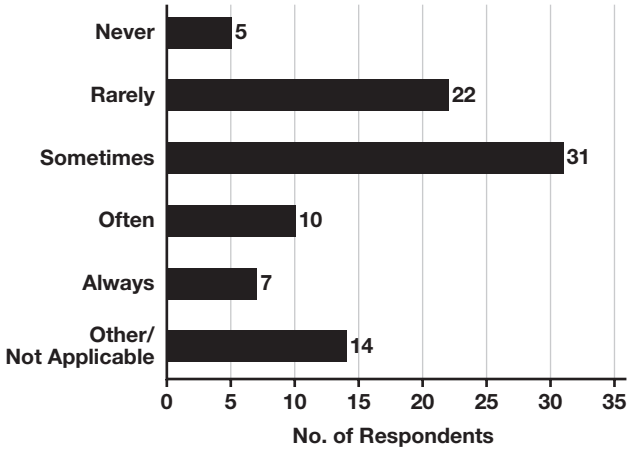

FIGURE 6 Frequency with which diagnosis is reconsidered following interdepartmental consultation (n = 89).

Workflow Between Hematopathology and Cytopathology Services

Most institutions had separate FNA and core biopsy sign-out in cases in which a diagnosis of lymphoma was considered (61/93; 65.6%). Specific workflow models interrogated in which FNAB and concurrent core biopsies were performed include two separate reports with no discussion of the other interpretation (19/90; 21.1%), two separate reports with discussion of the other interpretation in one or both (40/90; 44.4%), one report signed out by the cytopathologist only (6; 6.7%), one report signed out by the hematopathologist only (13/90; 14.4%), one report cosigned by the cytopathologist and hematopathologist (or double specialist) (6; 6.7%), or one report signed out by a nonspecialized pathologist (1/90; 1.1%). The pathologist responsible for FNAB sign-out reviewed the core biopsy specimen prior to signing out the FNAB always (24/92; 26.1%), often (19/92; 20.7%), sometimes (16/92; 17.4%), rarely (15/92; 16.3%), never (11/92; 12.0%), or other, not applicable (7/92; 7.6%). Conversely, the pathologist responsible for core biopsy sign-out reviewed the FNAB slides prior to signing out the core sometimes (30/91; 33.0%), always (23/91; 25.3%), rarely (20/91; 22.0%), often (6/91; 6.6%), never (6/91; 6.6%), or other, not applicable (6/91; 6.6%) FIGURE 7. Various protocols for preventing or reconciling discrepancies in interpretation between FNAB and core biopsy diagnoses were indicated. These included review of all concurrent cases before sign-out (33/88; 37.5%), ad hoc review as cases come to attention (28/88; 31.8%), review of all concurrent cases after sign-out (3/88; 3.4%), review of a subset of concurrent cases before or after sign-out (2/88; 2.3%), and other/not applicable responses (22/88; 25.0%). Some respondents elaborated further on their workflows for discrepancy prevention in a free-text field. One respondent noted that immunohistochemistry is not performed on FNAB cell block material, and definitive lymphoma subtyping is typically deferred to the subsequent excision. A few respondents indicated that at their institutions, FNAB is typically not attempted in patients when lymphoma is a diagnostic consideration and a core biopsy is performed instead. One respondent commented that the hematopathology and cytopathology departments at his or her institution are completely separate without an integrated workflow or any communication between services.

FNAB and Concurrent Flow Cytometry

FNAB cases with concurrent flow cytometry results are frequently signed out as two separate reports (52/85; 61.2%) with mention of the interpretation in one or both reports (38/85; 44.7%) or without discussion of the other interpretation (14/85; 16.5%). One report encompassing the FNAB and flow interpretation is generated less often (14/85; 16.5%) and is signed out by a cytopathologist only (5/85; 5.9%), a hematopathologist only (2/85; 2.4%), both a cytopathologist and hematopathologist (6/85; 7.1%), a nonspecialized pathologist (1/85; 1.2%), or not applicable (19/85; 22.4%). For FNAB specimens, the flow cytometry was most often performed in house (48/85; 56.6%), sent out for technologic and professional interpretation (14/85; 16.5%), sent out for technologic interpretation only (8/85; 9.4%), or not applicable (15/85; 17.6%). In sign-out of cases in which there is involvement by both hematopathology and cytopathology, flow plots and FNAB slides are reviewed separately and impressions shared in the reports (27/81; 33.3%), are reviewed by both attending pathologists together (11/81; 13.6%), are reviewed by the trainee with both attending pathologists separately (6/81; 7.4%), are reviewed together at a regularly scheduled case conference (1/81; 1.2%), are reviewed by digital pathology (0; 0%), or are reviewed via another method or not applicable (36/81; 44.4%).

Barriers Between Hematopathology and Cytopathology Services

Access to Ancillary Studies

Some respondents indicated that their facility was not able to perform flow cytometric studies in cases that may derive benefit from it. Others noted that there was no access at all to flow cytometry either in house or as a send-out test. Lack of access to appropriate

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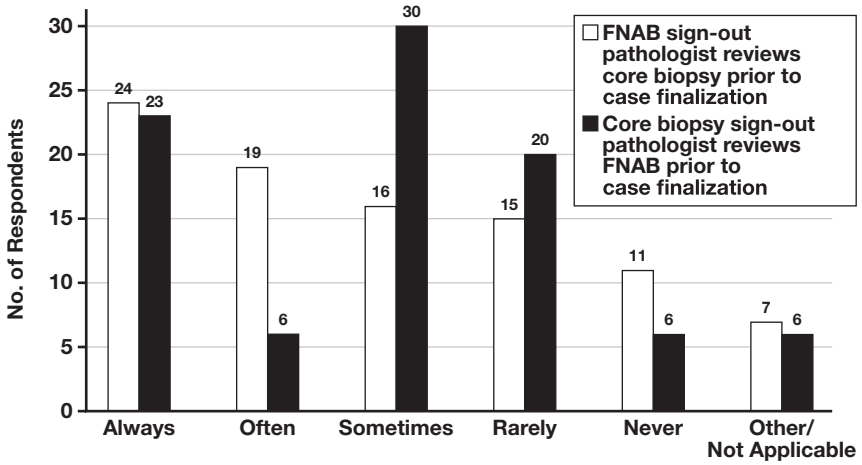

FIGURE 7 Review of fine-needle aspiration biopsy (FNAB) and core biopsy slides prior to sign-out.

immunohistochemistry for diagnosing lymphoma was also mentioned by one survey respondent.

Access to and Communication With Diagnostic Experts in Hematopathology/Cytopathology

This was a major theme in several comments by pathologists who completed the survey. Physical separation of the hematopathology and cytopathology departments represented a significant barrier to collaboration on lymphoma cases. Sparse or absent communication between departments was noted by many survey respondents as well. One respondent indicated a lack of cytopathology services entirely in his or her department.

Adequacy of FNA Specimen for Lymphoma Diagnosis

Some pathologists expressed concern regarding the adequacy of FNAB specimens to make a definitive diagnosis of lymphoma. One respondent indicated that when lymphoma is in the clinical differential diagnosis, FNAB is not used to make the diagnosis at his or her institution.

DISCUSSION

FNAB in the diagnosis of lymphoma is not uncommon and is an area of pathology in which prior and current studies have attempted to determine clinical utility.[9,10] Recently, Ingersoll et al[11] investigated its applicability in a variety of clinical contexts and showed that most cases included in their study were able to be successfully diagnosed without a subsequent excisional biopsy. Furthermore, they found a higher statistically significant diagnostic rate by FNAB in patients with a suspected lymphoma relapse vs in patients without a history of lymphoma. Overall, they found FNAB to be practical in the evaluation of most hematolymphoid neoplasms, including diffuse large B-cell lymphoma/high-grade B-cell lymphomas and other small B-cell lymphomas with rare exceptions. Conversely, Gupta et al[12] recently found that minimally invasive biopsies, either FNAB or core biopsy, have limited sensitivity in the initial diagnosis of nodular lymphocyte-predominant Hodgkin lymphoma and require an incisional or surgical biopsy for adequate evaluation. Importantly, both of these studies showed limited sensitivity of FNAB and core biopsy in the diagnosis of lymphoma when tumor cells are infrequent or evaluation of the architecture is essential for diagnosis.

Given practice preference heterogeneity, we were interested in determining the current state of practice as it pertains to workup and sign-out of these cases. We recognize that the diagnosis of lymphoma is complex and often requires incorporation of tissue histology, flow cytometry, and cytogenetic findings. FNAB specimens often consist of a fine-needle aspirate component, a needle core biopsy component, and a flow cytometry component. These specimen components are complementary and interrelated, yet in the experience of the authors and as seen per the results of this survey, in many instances these components are not reviewed in tandem by pathologists separately responsible for different components of the biopsy.

Through this survey, we discovered various barriers to lymphoma diagnosis via FNAB. Several pathologists indicated barriers to obtaining ancillary testing, including immunohistochemistry panels and flow cytometry, which are often critical for clinching the diagnosis. Another frequent issue from respondents pertained to communication about cases in which lymphoma is in the differential diagnosis. Communication was often hampered by physical distance of the cytopathology and hematopathology departments. Similarly, lack of access to diagnostic experts in either hematopathology or cytopathology was cited as a barrier by multiple respondents. Interestingly, we note that opinions varied regarding the appropriateness of the role of FNAB in lymphoma diagnosis in survey answers.

Overall, the findings in our study show that lymphoma is a common diagnostic consideration in FNAB across multiple institutions and internationally. However, many departments face barriers to making the diagnosis, most notably issues with access to ancillary testing and communication between the cytopathology and hematopathology departments. Volaric et al[13] emphasized this limitation in a recent publication that highlighted the need for pathology and laboratory services including the absence of subspecialty expertise and ancillary studies in low-resource settings. Exploring why opinions vary with regard t

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o adequacy of FNAB in lymphoma diagnosis could be valuable in addressing a specific pathologist's and oncologist's concerns. Additional follow-up questions of interest include determining the type of lymphoma sampled via FNAB or core biopsy. In particular, it would be of interest to explore the subtypes that were reconsidered following joint evaluation by cytopathologists and hematopathologists. In our experience, close collaboration on cases between departments has enhanced our ability to diagnose these oftentimes complicated cases as we acknowledge the vital role cytopathologists play in making diagnoses with limited cellular material while also noting hematopathologists' crucial expertise in lymphoma diagnostics. FNAB specimens in patients with lymphoma represent an area of pathology where it is critical for intradepartmental specialists to have an open-door policy, a low threshold for case dialogue, and access to ancillary studies such as flow cytometry studies.

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