Improving Diagnostic Accuracy in Patients with Suspected Lymphoma

Picardi M, Gennarelli N, Ciancia R, et al. Randomized comparison of power Doppler ultrasound-directed excisional biopsy with standard excisional biopsy for the characterization of lymphadenopathies in patients with suspected lymphoma. J Clin Oncol 2004;22:3733–40.

Study Overview

Objective. To compare power Doppler ultrasound (PDUS)–directed excisional biopsy with standard excisional (SE) biopsy in patients with lymphadenopathy and clinical suspicion of lymphoma.

Design. Randomized prospective study.

Setting and participants. 152 patients with lymphadenopathy suspected of having lymphoma were randomized to PDUS-directed or SE biopsy. Patients with Epstein-Barr virus, cytomegalovirus, herpes simplex virus, rubella, or *Toxoplasma* or tuberculosis infection were excluded. All biopsies were performed by 3 surgeons experienced in nodal resection. In the SE group, biopsy was directed to the region containing the most superficial and/or largest node. In the PDUS group, patients underwent gray scale ultrasound exploration of all superficial nodal areas 24 hours prior to biopsy. Patients with abnormal nodes (in terms of size, shape, or hilus conformation) underwent PDUS to investigate the intranodal vascular pattern and select the optimal biopsy site. The lymph node with the highest mean resistive index of arterial vessels was selected for biopsy. Histopathologic examination was performed in a single pathology unit by 3 expert hematopathologists blinded to clinical condition, excision method, and the results of the other operators. Patients classified as having a histologic result negative for malignancy underwent close follow-up by clinicians blinded to excision method.

Main outcome measures. The percentage of cases of malignant involvement detected by PDUS-directed biopsy versus SE biopsy. Additional measures included the evaluation of biopsy-related complications and diagnosis of malignancy during the follow-up of patients who had negative initial biopsies. The overall diagnostic accuracy was defined as the rate of correct patient classification (ie, having or not having nodes positive for malignancy during follow-up).

Main results. 80 patients received SE biopsy, and 72 patients received PDUS-directed biopsy. A total of 116 nodes were removed in the SE group, whereas only 1 node was removed from each patient in the PDUS group. There was no significant difference between groups in terms of size of nodes removed. Patients in the SE group had slightly more cervical and inguinal biopsies, whereas patients in the PDUS group had slightly more supraclavicular and axillary biopsies. Malignancy was found in 64% of patients in the SE group (B-cell non-Hodgkin's lymphoma [NHL], 26 patients; Hodgkin's disease [HD], 23 patients; and metastatic carcinoma, 2 patients). 36% had lymph nodes negative for malignancy (benign lymphoid hyperplasia). In the PDUS group, 87% of patients had malignant nodes (B-cell NHL, 29 patients; T-cell NHL, 4 patients; HD, 29 patients; and metastatic carcinoma, 1 patient). Patients in the SE group had significantly more pain, numbness/paresthesia, and larger scars than patients who underwent PDUS-directed biopsy. Malignancy was detected in 14 of 29 patients in the SE group during follow-up (median, 11 months [HD, 7 patients; NHL, 5; melanoma, 1; and Rosai-Dorfman disease, 1]). In contrast, 0 of 9 patients in the PDUS group developed a malignancy during follow-up (median, 21 months; $P = 0.01$). The overall diagnostic accuracy of nodal status in the SE group was 82% (65 of 80 patients), with a sensitivity of 78% (51 of 65 patients with malignancy identified). In contrast, the overall diagnostic accuracy and sensitivity of the lymph node status in the PDUS group were 100%. There was a statistically significant difference between the 2 groups regarding diagnostic accuracy and sensitivity ($P < 0.001$).

Conclusion. PDUS is an accurate tool for screening lymphadenopathies to be removed by excisional biopsy in patients with suspected lymphoma.

Commentary

New lymphadenopathy is a common chief complaint in the clinic. Often, other accompanying historical and clinical find-

ings point to a probable nonmalignant diagnosis and plan of care. However, many patients will still ultimately require histologic evaluation to rule out a malignant process, such as lymphoma and, rarely, carcinoma. Fine-needle aspiration in expert hands can be a sensitive, if not specific, means of evaluation [1]. In the evaluation of lymphomas, excisional biopsy is preferred because a more adequate tissue specimen can be obtained for complete immunohistochemical analysis.

Excisional biopsy is routinely performed on the basis of physical examination alone. Imaging with ultrasonography or computerized tomography can help further define the nodal area prior to biopsy. PDUS is a technology that can enhance prebiopsy nodal evaluation in terms of anatomy, morphology, and vascularity [2]. Such evaluation may better select the optimal biopsy site of malignant tissue while limiting the biopsy field.

Picardi et al found that PDUS-assisted excisional biopsy was statistically more accurate and sensitive in identifying malignancy than SE alone and was associated with less morbidity. The overall rates of malignancy detected (at baseline and follow-up) were similar between groups (SE group, 65 of 80 patients; PDUS group, 63 of 72 patients). However, in patients with cancer, PDUS identified malignancy on the initial biopsy in every case.

This was a well-designed study at a single center in Naples, Italy, with surgeons skilled in nodal excisional biopsies. The groups were well-matched in terms of age and sex, and pathologists were appropriately blinded to group randomization. As well, clinicians in follow-up were blinded to assigned groups and were unlikely to be influenced in their surveillance. The results are impressive because PDUS was more accurate and safer than SE. However, the PDUS group had more axillary and supraclavicular biopsies than the SE group. This appears to be because PDUS was better able to identify these areas for biopsy than examination alone. It is possible that there was a discrepancy in the patients randomized to this group. Abnormal adenopathy in these regions may be more likely to initially present as malignancy than cervical or inguinal adenopathy. Second, this study may be more of a comparison between imaging and no imaging. Perhaps gray scale ultrasound was sufficient to account for the findings rather than PDUS (a technology that is not readily available). Finally, diagnostic accuracy may have improved in the standard group with longer follow-up. While it may be argued that earlier diagnosis in malignancy is prudent, there is no evidence that a delayed diagnosis in these patients led to inferior overall clinical outcomes. Despite these issues, PDUS can potentially enhance our ability to care for patients with new adenopathy and suspected malignancy and warrants further study.

Applications for Clinical Practice

PDUS can be an important tool in enhancing the diagnostic accuracy and safety of excisional biopsy in patients with lymphadenopathy. Presently, this technology is limited in its availability for routine clinical practice.

–Review by David R. Spigel, MD

References

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2. Bude RO, Rubin JM. Power Doppler sonography. Radiology 1996;200:21–3.