A clinical compilation of lymph node pathologies comparing the diagnostic performance of biopsy methods

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Abstract

Purpose It is critical to obtain sufficient tissue, both in quality and quantity, in biopsy applications for histopathological review. Our aim was to compare fine-needle aspiration cytology (FNAC) and core needle biopsy (CNB) techniques in terms of their diagnostic performance in lymph node biopsies. This was a clinical compilation, and histopathological results from biopsies were also evaluated.

Methods A total of 242 patients and 246 lymph nodes were prospectively evaluated. All histopathologic specimens were obtained through ultrasonography-guided biopsies performed at our institute between April 2015 and October 2017. Histopathological results were grouped according to diagnostic performance, and the mean performance scores of the two methods were compared.

Results For FNAC, the mean diagnostic score was calculated to be 1.63, whereas for CNB, the mean diagnostic score was calculated to be 1.89. The difference between diagnostic scores of the two techniques was statistically significant ($p < 0.01$).

Conclusion We recommend that interventional radiologists perform vacuum-assisted biopsies if there are no financial hindrances or evidence of psychological issues in patients. We recommend this not only for lymph nodes of malignant appearance but also for those that appear benign.

Keywords US-guided biopsy · Fine-needle biopsy · Core needle biopsy · Lymph nodes

Sommario

Scopo È un requisito importante della biopsia linfonodale ottenere un campione sufficiente in termini di qualità e quantità per la diagnosi. Il nostro obiettivo è stato confrontare tecniche di citologia con ago sottile (FNAC) e biopsia con ago (CNB) in termini di prestazioni diagnostiche nelle patologie linfonodali.

Metodi Sono stati valutati prospetticamente un totale di 242 pazienti e 246 linfonodi. Tutti i campioni cito-istopatologici sono stati ottenuti eseguendo una biopsia ecoguidata nella nostra istituzione dall'aprile 2015 all'ottobre 2017. I risultati cito-istopatologici sono stati confrontati in base alle prestazioni diagnostiche ottenute: in particolare sono stati confrontate le medie degli score diagnostici delle due metodiche (FNAC vs CNB).

Risultati Per FNAC il punteggio diagnostico medio è stato di 1,63, mentre per la CNB di 1,89. La differenza tra i punteggi diagnostici delle due tecniche era statisticamente significativa ($p < 0.01$).

Conclusioni Lo studio dimostra la necessità di eseguire CNB ecoguidata per la diagnosi differenziale tra linfadenopatie maligne e benigne, fatte salve problematiche di costi o di rifiuto da parte dei pazienti.

Introduction

Lymph node pathologies are common and can be seen in various conditions. There is a broad spectrum of disorders (infectious, metabolic, neoplastic, physiological, etc.) that may affect their size and appearance. According to the literature, abnormal lymph nodes are spherical in shape, with a short-to-long-axis ratio (S/L ratio or roundness index) > 0.5 ,

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and there is an absence of central echoic hilum. They have an irregular cortex, ill-defined borders, and vascular signals outside the hilum [1].

When a lymph node is encountered that appears pathological, the next step is to define the underlying disease. It is critical to obtain sufficient specimens in both quality and quantity from biopsy applications for thorough histopathological examination.

Image-guided lymph node biopsies are normally performed using two different methods: fine-needle aspiration (FNA) and core needle biopsy (CNB). FNA uses a thin, hollow needle attached to a syringe to remove a small amount of fluid and very small pieces of tissue from the target tissue. The performer can aim the needle while palpating the lesion if it is near the surface of the body. If the target lesion is deeper inside the body and cannot be felt, the needle can be guided via an imaging method such as ultrasonography (US) or computed tomography (CT) scan. CNB needles used in core biopsies are slightly larger (about 14G–20G in diameter and 0.5 in. long) than those used in FNA. They remove a small cylinder of tissue. Both biopsy techniques can be performed using local anesthesia [2].

In this study, vacuum-assisted biopsy (VAB) was the preferred core needle technique. Our aim was to compare VAB and FNA in terms of their diagnostic performance. A contribution to the literature was expected since there are no articles in the literature reporting on this exact comparison.

Methods

A total of 242 patients and 246 lymph nodes were retrospectively reviewed from our pathology database. All histopathologic specimens were obtained by performing US-guided biopsies at our institute between April 2015 and October 2017. The ages and genders of all patients were noted. Since this study was a clinical compilation, all lymph node biopsy results were taken from a specific time interval. Biopsy procedures were performed using FNA in 135 lymph nodes and VAB in 111 lymph nodes. All histopathological results were recorded. Histopathological examinations were performed on lymph node regions as follows: 102 axillary, 37 inguinal and 107 cervical.

Inclusion–exclusion criteria

Lymph nodes meeting any of the criteria mentioned in the first paragraph of the introduction were included in the study. Eighteen of the biopsy results were excluded from the study because the results were not consistent with lymph node diseases. There are several pathologies, such as parotid tumors, parathyroid masses, and dense abscesses, that mimic pathologic lymph nodes in US examination. Accordingly,

Fig. 1 Vacuum-assisted biopsy device

Fig. 2 Vacuum-assisted biopsy of a malignant-appearing lymph node

some patients were referred to the interventional radiology department for lymph node biopsy, but after the results were obtained, it was understood that their problem was not in the lymph nodes.

Biopsy procedure

Before the procedure, each patient was questioned regarding contraindications such as anticoagulant medications or anxiety that would have precluded the procedure. Informed consents were obtained.

After necessary sterilization was provided, a topical 10% lidocaine solution (Vemcaine Pump Spray; Nobel Farma Medical) was sprayed as a pre-anesthetic to reduce pain at the procedure site. For CNB procedures, an additional 5–10 ml of bupivacaine (Marcaine solution; Pfizer) was used as an injectable local anesthetic.

The US device was the Aplio 500 (Toshiba Medical Systems Europe). The probe chosen was a 7.2–14 MHz linear probe covered with a sterile, disposable, and transparent plastic material.

In FNA, a 22G needle attached to a syringe was used. For VAB, an 18G vacuum biopsy needle was used (Fig. 1).

Figure 2 shows a vacuum-assisted biopsy of a malignant-appearing lymph node.

All procedures were performed by the same interventional radiologist with 5 years of experience. Evidence of bleeding under the skin was controlled with the US after homeostasis. Following the procedure, all patients were observed for a short period of time.

Histopathologic examination

Four to eight spreading slides were used for FNA cytology. Half of the preparations were fixed with 95% ethanol solution and stained with Papanicolaou (PAP). The other half were dried with air and stained with Giemsa. Cell blocks were prepared from the material obtained in the root of the needle. Sections from paraffin blocks 3–4 microns in thickness were stained with hematoxylin–eosin.

For VAB, paraffin cell blocks were stained with hematoxylin–eosin, as with the FNA material.

Diagnostic inadequacy criteria of fine-needle aspiration cytology (FMAC)

1. An absence of 40 lymphoid cells in every 40× enlargement area when there was an absence of granuloma and metastasis.
2. Preparations showing a presence of common blood and severe crushing artifacts.
3. The lymph node could have few cells where lymphomas with fibrosis, sclerosis, and carcinomas show a desmoplastic reaction. This also occurs when the lymph node is occupied with a non-cell matrix material such as mucin, colloid, amyloid, etc.

Diagnostic inadequacy criteria of vacuum-assisted biopsy (VAB) cytology

1. Small amount of tissue not adequate for immunohistochemistry (IHC) and molecular studies.
2. Presence of crush and handling artifacts.
3. Presence of fragmented and fibrotic tissues [3, 4].

Histopathological results were classified as diagnostic, suspicious (further procedures recommended), or non-diagnostic. The results were noted and calculated as a frequency in percent. (clinical, biochemical, and excisional biopsies were recommended for further evaluation.)

All histopathological adequacy results were evaluated by the same pathologist with 10 years of experience. Our pathologist was blinded to the origin of all preparations to optimize objectivity and the adequacy of the results.

The performance score

Each histopathological result was scored as 0 if the specimens were non-diagnostic.

It was scored as 1 if the specimens were suspicious and additional procedures were recommended.

It was scored as 2 if the specimens were diagnostic without question.

Statistical analysis

Microsoft Excel and Student's *t* tests were used for statistical comparison. Any *t* test *p* value of less than 0.05 was considered as significant.

Results

Of all 242 patients, 166 were female and 76 were male. The average age was 46.7 years (ranging from 9 to 86). The most common benign result we encountered was non-neoplastic lymphoid tissue, and the most common malignant result was breast carcinoma metastasis. All other benign and malignant results are shown in Table 1.

Distribution of the lymph nodes according to their regions and the techniques performed are shown in Tables 2 and 3.

Of the FNA samples, 3 specimens were non-diagnostic, 45 specimens were suspicious, and the remaining 87 were

Table 1 Distribution of benign and malignant histopathological results

	No. of nodes	%
Benign (149)		
Non-neoplastic lymphoid tissue	95	63.8
Reactive hyperplasia	37	24.8
Granulomatous lymphadenitis	12	8.1
Necrotic lymphoid tissue	5	3.4
Malignant (97)		
Breast cancer	40	41.2
Carcinoma from unknown origin	21	21.6
High-graded lymphoma	15	15.5
Thyroid cancer	8	8.2
Low-graded lymphoma	5	5.1
Nasopharynx cancer	2	2.1
Epidermoid cancer	1	1
Parotid gland mucoepidermoid cancer	1	1
Lung cancer	1	1
Stomach cancer	1	1
Anaplastic cancer	1	1
Neuroendocrine cancer	1	1
Total	246	

Table 2 Distribution of lymph nodes according to their regions

	No. of nodes	%
Region		
Neck	107	43.4
Axillary	102	40.9
Inguinal	37	15.7
Technique		
FNA	135	57.4
VAB	111	42.6

Table 3 Distribution of histopathological performance results

Technique	Non-diagnostic	Suspicious	Exact diagnostic
Fine-needle aspiration	3	45	87
Vacuum-assisted biopsy	0	12	99

Table 4 Comparison of the mean performance scores of FNA and VAB according to the regions and the pathology results

Total (<i>n</i> = 246)	FNA PS (<i>n</i> = 135)	VAB PS (<i>n</i> = 111)	<i>p</i>
Neck (<i>n</i> = 107)	1.57	1.79	0.02
Axillary (<i>n</i> = 102)	1.74	1.96	< 0.01
Inguinal (<i>n</i> = 37)	1.48	1.93	< 0.01
Malignant lymph nodes (<i>n</i> = 97)	1.58	1.92	0.03
Benign lymph nodes (<i>n</i> = 149)	1.64	1.72	0.09

diagnostic. The mean diagnostic score was calculated to be 1.63. For VAB, 12 specimens were suspicious, and the remaining 99 were diagnostic. There was no non-diagnostic result. The mean diagnostic score was calculated to be 1.89. The difference between the mean diagnostic scores of the two techniques was statistically significant ($p < 0.05$). There was also a statistically significant difference between the two methods' mean performance scores for malignant lymph nodes; however, the difference was not statistically significant for benign lymph nodes (Table 4).

Table 5 shows the distribution of the number of FNA and VAB techniques according to the histopathological results.

Discussion

It is important to obtain adequate specimens, both qualitatively and quantitatively, and to refer them to the pathology section for inspection at the cellular level of apparently abnormal lymph nodes with imaging methods. CNB (in this study VAB) can be preferred in cases where more solid

Table 5 Distribution of FNA and VAB results

	Benign lymph nodes	Malignant lymph nodes
FNA (<i>n</i> = 135)	101	34
VAB (<i>n</i> = 111)	48	63
Total (<i>n</i> = 246)		

specimens are needed. However, the two main disadvantages of using core needle techniques are that the needle used is thicker (more traumatic) than a fine needle, and it is more expensive [5]. According to market data from our country, a vacuum-assisted device costs around \$20, while a fine needle syringe costs less than \$1. On the other hand, the complication frequency was also evaluated for both procedures, and no major complication was experienced with either method. The only minor complication was bleeding under the skin, and this was only rarely seen (3 out of 242 patients, or around 1% frequency), so both methods can be considered safe. Patients were questioned concerning anxiety to prevent unexpected and dangerous results such as panic attacks, and cardiac arrhythmias. In one case, the patient fainted during the procedure, but he woke spontaneously after a few seconds. Neither FNA nor VAB can be defined as painful or posing a high risk of complications since local anesthetics and imaging guidance are being used [6, 7]. In our experience, patients nearly always were comfortable with pain at the procedure site.

There were three anatomical regions evaluated, namely the axillary, cervical, and inguinal regions. This study was a compilation from our interventional radiology department, and the lymph node biopsies were performed from those regions. From the beginning, inter-observer variability was planned to be excluded, so all biopsy procedures were performed by the same interventional radiologist, and all histopathological results were evaluated by the same pathologist.

In our study, US was used for imaging guidance. Ultrasonography is the preferred method because it shows superficial structures clearly, does not use ionizing radiation, is non-invasive, and allows real-time examination at low cost [8]. A vacuum-assisted device (VAB) was used in CNB. This provides for better needle control, especially for the range of fire. Once the target tissue is reached with the biopsy needle, the device does not shoot further for the duration of the procedure. While sampling is performed, the needle stays at the same point; only the cylinder part of the needle turns to an empty pipe. For this reason, the possibility of damage to adjacent regions is significantly reduced. One feature common to all lymph node regions is that they are rich in vascular and nerve structures, so VAB was our choice in terms of protecting nearby anatomical

structures from traumatic damage. The reason we prefer VAB is that although some articles have concluded that FNA has a comparable satisfactory success rate as a surgical technique, a larger amount of specimen and solid material is acquired with CNB [9, 10].

According to our results, the most common malignant result overall was breast carcinoma metastasis. Breast cancer is the most frequently diagnosed malignancy and the second leading cause of cancer death among women worldwide [11]. Consequently, malignant results from the axillary region were mostly breast carcinomas. In the same region, we also had two lymphomas and one epidermoid carcinoma as malignant results. When the cervical region was evaluated, more variable malignant results were seen. The majority were lymphomas and metastatic thyroid carcinomas, probably because of proximity. Two nasopharynx carcinomas and one parotid carcinoma were found. One lung carcinoma and one gastric carcinoma were found in the supraclavicular region (Virchow's node). There was also an anaplastic carcinoma, but its origin could not be defined because of severe cellular atypia. We also found a neuroendocrine carcinoma. Finally, in the inguinal region, the majority of the malignant results were lymphomas, with three being metastatic breast carcinomas. Twenty-one of the malignant lymph nodes were metastases with unknown origins. Although there were additional immunohistochemical results, it was impossible to identify the malignant cells and their origin.

A significant portion of the benign results consisted of non-neoplastic lymphatic tissue. This is the term our pathologist prefers for normal lymph nodules. There were also benign results, namely reactive hyperplasia, lymphadenitis, and necrotic lymph tissue, with decreasing prevalence.

VAB had better performance, which was not surprising since there is no reason for FNA to show better performance. The diagnostic performance difference between the two methods was statistically significant, both regionally and in total. Mean performance scores were also compared in terms of histopathological results. The performance score difference for benign lymph nodes was not statistically significant, in contrast to malignant lymph nodes. There is an article concluding the opposite to our findings, but it focuses on salivary glands and adjacent lymph nodes. The authors concluded that the diagnostic accuracy of US-guided FNA was similar to CNB, but there was no actual comparison of the two techniques in their study. Instead, they calculated diagnostic accuracy for FNA and then compared the results to CNB from literature [12]. There are several articles drawing conclusions about the performance of FNA versus CNB [13–18]. All of these articles focus on a specific region (for example, axillary) or a specific disease (breast cancer, melanoma, etc.). To our knowledge, as a clinical compilation, our study should be the first of its kind.

We must point out some additional data about this study. The malignant results were more frequently obtained from VAB, with 48 benign results obtained with this technique. In comparison, 34 malignant results were obtained from FNA. In addition, evaluation of footnotes from pathology reports shows that pathologists tend to warn clinicians and recommend additional tests when they label a lymph node as “benign”, especially if the sample was obtained with FNA. This situation was a factor affecting the FNA mean performance score. We suppose that pathologists want to protect patients and themselves.

To summarize, image-guided CNB is increasingly replacing excisional lymph node biopsy in the diagnosis and subclassification of malignant lymphadenopathies and enlarged lymph nodes, with obvious advantages in terms of morbidity and cost. It is minimally invasive, well-tolerated, and has advantages over surgical techniques, including reduced costs, lower rates of post-procedural complications, and fewer delays in the diagnostic pathway [10, 19–23].

There were two limitations of this study. First was the malignant–benign distribution imbalance of the two techniques, which may have affected statistical significance. The other was scarcity of specimen data, especially from the inguinal region.

In conclusion, we recommend that interventional radiologists use VAB for lymph nodes, particularly vacuum-assisted biopsy when possible, provided there is no financial hindrance or evidence of psychological reasons for excluding patients. We recommend this not only for lymph nodes with malignant appearance but also for lymph nodes that appear benign, since there is always a possibility for lymph nodes to be malignant despite their appearance.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by our Institute's Research Ethics Committee. Date: 06.02.2018 No: 825.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Ying M, Bhatia KSS, Lee YH, Yuen B, Ahuja AT (2014) Review of ultrasonography of malignant neck nodes: greyscale,

- Doppler, contrast enhancement and elastography. *Cancer Imaging* 13(4):658–669
2. American Cancer Society. <http://www.cancer.org/treatment/understanding-your-diagnosis/tests/testingbiopsy-and-cytology-specimens-for-cancer/biopsy-types.html>. Accessed 2017
 3. Joachim Harry L, Jeffrey Mederios L (2009) Joachim's lymph node pathology, 4th edn. Lippincott Williams & Wilkins, USA
 4. Koss Leopold G (2006) Koss diagnostic cytology, 5th edn. Lippincott Williams & Wilkins, USA
 5. Head and neck cancer guide. <http://www.headandneckcancerguide.org/adults/cancer-diagnosis/treatments/diagnosis/biopsies>. Accessed Mar 2017
 6. Nakano Y, Noguchi M, Yokoi-Noguchi M, Ohno Y, Morioka E, Kosaka T et al (2017) The roles of 18F-FDG PET/CT and US-guided FNACC in assessment of axillary nodal metastases in breast cancer patients. *Breast Cancer* 24(1):121–127
 7. Fleischman GM, Thorp BD, Difurio M, Hackman TG (2016) Accuracy of ultrasonography-guided fine-needle aspiration in detecting persistent nodal disease after chemoradiotherapy. *JAMA Otolaryngol Head Neck Surg* 142(4):377–382
 8. Burke C, Thomas R, Inglis C, Baldwin A, Ramesar K, Grace R et al (2011) Ultrasound-guided core biopsy in the diagnosis of lymphoma of the head and neck. A 9 year experience. *Br J Radiol* 84(1004):727–732
 9. Rautiainen S, Masarwah A, Sudah M, Sutela A, Pelkonen O, Joukainen S et al (2013) Axillary lymph node biopsy in newly diagnosed invasive breast cancer: comparative accuracy of fine-needle aspiration biopsy versus core-needle biopsy. *Radiology* 269:54–60
 10. Sharma G, Jung AS, Maceri DR, Rice DH, Martin SE, Grant EG (2011) US-guided fine-needle aspiration of major salivary gland masses and adjacent lymph nodes: accuracy and impact on clinical decision making. *Radiology* 259(2):471–478
 11. Siegel RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. *CA Cancer J Clin* 68(1):7–30
 12. de Kerviler E, Benet C, Brière J, de Bazelaire C (2012) Image-guided needle biopsy for diagnosis and molecular biology in lymphomas. *Best Pract Res Clin Haematol* 25(1):29–39
 13. Ganott MA, Zuley ML, Abrams GS, Lu AH, Kelly AE, Sumkin JH et al (2014) Ultrasound guided core biopsy versus fine needle aspiration for evaluation of axillary lymphadenopathy in patients with breast cancer. *ISRN Oncol* 4(2014):703160
 14. Ahn HS, Kim SM, Jang M, La Yun B, Kim SW, Kang E et al (2013) Comparison of sonography with sonographically guided fine-needle aspiration biopsy and core-needle biopsy for initial axillary staging of breast cancer. *J Ultrasound Med* 32(12):2177–2184
 15. Bohelay G, Battistella M, Pagès C, de Margerie-Mellon C, Basset-Seguín N, Viguier M et al (2015) Ultrasound-guided core needle biopsy of superficial lymph nodes: an alternative to fine-needle aspiration cytology for the diagnosis of lymph node metastasis in cutaneous melanoma. *Melanoma Res* 25(6):519–527
 16. Jankowski C, Hudry D, Vaillant D, Varbedian O, Mejean N, Guy F et al (2015) Evaluation of axillary involvement by ultrasound-guided lymph node biopsy: a prospective study. *Gynecol Obstet Fertil* 43(6):431–436
 17. Saha S, Woodhouse NR, Gok G, Ramesar K, Moody A, Howlett DC (2011) Ultrasound guided core biopsy, fine needle aspiration cytology and surgical excision biopsy in the diagnosis of metastatic squamous cell carcinoma in the head and neck: an eleven years experience. *Eur J Radiol* 80(3):792–795
 18. Zosimas D, Lykoudis PM, Vashisht R (2016) Preoperative ultrasound guided percutaneous axillary biopsy in breast cancer patients: fine needle aspiration cytology versus core biopsy. *Ann Ital Chir* 87:509–516
 19. Skelton E, Jewison A, Okpaluba C, Sallomi J, Lowe J, Ramesar K et al (2015) Image-guided core needle biopsy in the diagnosis of malignant lymphoma. *Eur J Surg Oncol* 41(7):852–858
 20. de Kerviler E, de Bazelaire C, Mounier N, Mathieu O, Brethon B, Brière J et al (2007) Image-guided core-needle biopsy of peripheral lymph nodes allows the diagnosis of lymphomas. *Eur Radiol* 17:843–849
 21. Gronckel L, Quaas A, Hallek M, Zander T, Weihrauch MR (2016) Ultrasound-guided core needle biopsies for workup of lymphadenopathy and lymphoma. *Eur J Haematol* 97(4):379–386
 22. Stigt JA, Boers JE, Boomsma MF (2015) Ultrasound-guided tissue core biopsies in supraclavicular lymph nodes in patients with suspected thoracic malignancies. *Respiration* 90(5):412–415
 23. Abe H, Schmidt RA, Kulkarni K, Sennett CA, Mueller JS, Newstead GM (2009) Axillary lymph nodes suspicious for breast cancer metastasis: sampling with US-guided 14-gauge core-needle biopsy—clinical experience in 100 patients. *Radiology* 250(1):41–49