Research Article

Ultrasound-Guided Cervical Lymph Node Sampling Performed by Respiratory Physicians

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What Is It about?

Some respiratory diseases such as lung cancer and sarcoidosis are associated with neck lymphadenopathy. Sampling of neck lesions is frequently done by non-radiologists. In this study we retrospectively looked at the adequacy of ultrasound-guided sampling of neck lymph nodes performed by respiratory physicians compared to radiologists and found no difference. Respiratory physicians were able to obtain enough material for analysis in 91% of cases and a diagnosis was made based on these samples in 84% of cases.

Abstract

Background: A variety of disease processes investigated by respiratory physicians can lead to cervical lymphadenopathy. Ultrasound (US) has revolutionised respiratory investigations, and neck ultrasound (NUS) is increasingly recognised as an additional important skill for respiratory physicians. ***Objectives:*** We aimed to assess the feasibility of NUS performed by respiratory physicians in the workup of patients with mediastinal lymphadenopathy. ***Methods:*** This is a single-centre retrospective cohort study. All patients that underwent US-guided cervical lymph node sampling were included. The diagnostic yield is reported, and specimen adequacy is compared for respiratory physicians and radiologists. ***Results:*** Over 5 years, 106 patients underwent NUS-guided lymph node sampling by respiratory physicians compared to 35 cases performed by radiologists. There was no significant difference in the adequacy of sampling between the two groups (respiratory physicians 91.5% [95% CI 84.5–96%] compared to 82.9% [95% CI 66.4–93.4%] for radiologists [p = 0.2]). In the respiratory physician group, a diagnosis was achieved based on lymph node sampling in 89 cases (84%). Neck lymph node

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sampling was the only procedure performed to obtain tissue in 48 cases (45.3%). **Conclusion:** NUS and sampling performed by respiratory physicians are feasible and associated with an adequacy rate comparable to that of radiologists. It can reduce the number of invasive procedures performed in a selected group of patients. Guidelines for training and competency assessment are required.

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Introduction

Endobronchial ultrasound (EBUS) has revolutionised the assessment of intrathoracic lymphadenopathy but is relatively expensive and in many jurisdictions remains difficult to access in routine clinical practice. Cervical lymph nodes are frequently involved by the same pathological processes associated with hilar and mediastinal lymphadenopathy. In lung cancer, for instance, patients with mediastinal lymphadenopathy have been reported to have cervical lymph node involvement in 40–50% of cases when neck ultrasound (NUS) was routinely performed [1, 2]. The presence of metastatic disease within the supraclavicular lymph nodes represents N3 disease and M1b disease if the upper cervical lymph nodes are involved with a major impact on treatment decisions [3]. The clinical and radiological assessment of neck adenopathy can suggest involvement; however, sampling of the nodes is necessary to definitively confirm involvement. In addition, the basic principles of cancer assessment advise sampling the site of disease that provides the most clinical information regarding staging and diagnosis in a single clinical setting [4]. Moreover, other conditions frequently investigated by respiratory physicians such as sarcoidosis, tuberculosis, mediastinal lymphadenopathy due to metastatic extrapulmonary malignancy, and lymphoma are also associated with neck adenopathy [5, 6].

Respiratory physicians are increasingly familiar with the use of ultrasound (US). It is now an integral component in the assessment of the pleural space and EBUS is by far the greatest advance in lung cancer staging over the last two decades. Finally, NUS is also frequently performed by respiratory physicians in working critical care units to guide central line insertion.

In this paper we report our experience with NUS-guided lymph node sampling performed by respiratory physicians and compare it to the results obtained from procedures performed by radiologists within the same institution.

Methods

This is a retrospective cohort study performed in the interventional respiratory unit of Galway University Hospitals over a 5-year period (March 2013–March 2018). All consecutive cases were identified from a database maintained by the unit. Patients referred to the unit who were found to have cervical adenopathy detected clinically or radiologically were included in the study including those with suspected lung cancer and evidence of bulky mediastinal lymphadenopathy on computerised tomography of the thorax. Both medical records and procedural logs were interrogated for information regarding lymph node features. Final pathology was retrieved from the central pathology laboratory database. Adequacy of samples submitted for pathological assessment was routinely reported as a quality control measure by the examining pathologist. A record of all NUS-guided lymph node samples performed by radiology regardless of indication was obtained from the pathology department. This group of patients was used as a control and adequacy of sampling was compared against samples taken by respiratory physicians.

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Table 1. Baseline characteristics and final diagnosis of 106 patients that underwent neck lymph node sampling by respiratory physicians

Characteristic	Value
Mean age (SD), years	65.2 (16.1)
Males, *n* (%)	55 (51.9)
Mean short lymph node diameter (SD), mm	13.2 (6)
Diagnosis on lymph node sample, *n* (%)	
Lung cancer	69 (65.1)
Cancer other than lung	8 (7.5)
Lymphoma	4 (3.8)
Sarcoidosis	6 (5.7)
Tuberculosis	2 (1.9)
Other benign[1]	8 (7.5)
Inadequate sampling	9 (8.5)

SD, standard deviation. [1] Other benign: normal lymphoid material or evidence of reactive lymphadenopathy.

Procedures

All patients included underwent standardised NUS. Procedures were performed using a linear US probe with a frequency of 5–12 MHz using one of two machines (Zonare Z one ultra machine [Zonare®, California, USA] and Hitachi EUB-7500A machine [Hitachi, Ltd., Tokyo, Japan]). Patients were positioned in a semi-supine position. Initially, the thyroid isthmus was identified and once visualised the probe was moved laterally to identify the carotid artery and internal jugular vein. The probe, oriented horizontally and later vertically, was then moved cranially to assess the lower, middle, and upper cervical chain to the level of the submandibular gland. The probe was then moved caudally along the posterior cervical chain until the supraclavicular fossa was identified and assessed. The procedure was then repeated to fully assess the contralateral neck.

After this initial screening assessment, any visualised lymph nodes were further assessed in detail. Features including size, shape, presence of hilum, necrosis, and blood flow were recorded. The largest accessible suspicious lymph nodes, based on US features [7], were sampled under direct visualisation following informed written consent. The area was cleaned using chlorhexidine wash and 1 or 2% lidocaine was applied intradermally and subcutaneously to provide local anaesthesia. A sterile sheath was applied to the US probe. After sonographic identification of the node, direct sampling using a 22-G needle was performed with real-time US guidance. The first pass was used to make slides and the rest of the material was sent for analysis in formalin pots. If well tolerated and technically feasible, 2–3 core needle biopsies (CNBs) were obtained from lymph nodes using an 18-G SuperCore™ needle (Aragon Medical Devices, Texas, USA).

Outcomes

Diagnostic yield and sampling adequacy are reported for neck lymph node sampling performed by respiratory physicians and radiologists. The pathological diagnosis on lymph node sampling is also reported including the suitability of samples for special tests for molecular and immunotherapy targets in the case of lung cancer.

Statistical Analysis

Minitab-18 (Minitab® Statistical Software, Pennsylvania, USA) was used to conduct the statistical analysis. Categorical variables are reported as frequencies and percentages and associated 95% CI, while continuous variables are reported as mean and standard deviations or median and interquartile range. χ^2 or Fisher exact tests were conducted for categorical variables, as appropriate. A *p* value of <0.05 was considered significant.

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Fig. 1. Bar chart with associated 95% upper CI of adequacy of neck lymph node sampling performed by interventional radiologists (IR) and respiratory physicians (RP). CNB, core needle biopsy; FNA, fine needle aspiration. "Overall" means all procedures combined.
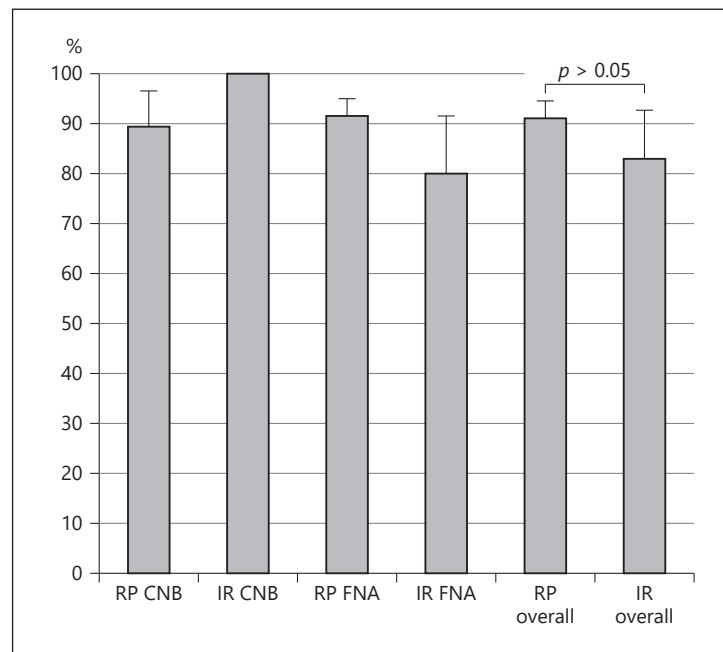
Results

Over a 5-year period, respiratory physicians performed cervical lymph node sampling in 106 consecutive patients compared to 35 consecutive patients by radiology. Respiratory physicians performed NUS in 306 patients and sampled 106 (34%) of those (mean age 65 ± 16 years, 51.9% males, suspected lung cancer in 72.3%) (Table 1). Neck lymph node fine needle aspiration (FNA) and CNB were performed in 38 patients (35.8%) and FNA only in 68 patients (64.2%). A diagnosis was achieved on lymph node sampling in 89/106 cases (84%). The most common diagnosis was lung cancer.

During the study period, the radiology department performed 35 NUS-guided lymph node sampling procedures with a final diagnosis of malignancy in 10/35 cases (28.6%). CNB was performed in 5 patients (14.3%) and FNA in 30 patients (85.7%). There was no difference in the mean short diameter of lymph nodes sampled by radiologists and respiratory physicians (11.75 ± 5.7 vs. 13.2 ± 6 mm [$p = 0.203$]). There was also no significant difference in the adequacy of sampling in the two groups. The overall adequacy rate for respiratory physicians was 91.5% (95% CI 84.5–96%) compared to 82.9% (95% CI 66.4–93.4%) for radiologists ($p = 0.2$). Results are displayed in Figure 1. No significant complications were reported in either group.

Other Procedures and Further Pathological Testing

Among patients assessed by respiratory physicians, neck lymph node sampling was the only procedure performed to obtain tissue in 48 cases (45.3%). The most commonly performed other procedure was EBUS in 26 patients (24.5%). Excisional lymph node biopsy was performed in 8 cases (Table 2).

Among 76 patients with suspected malignancy on cytological examination there was sufficient material for immunohistochemistry staining in 73 patients (96.1%). Further testing for molecular analysis or programmed death ligand 1 (PDL 1) was requested in 18 samples and was possible in 17 (94.4%). In 1 case the percentage of tumour cells in the sample was <10% and therefore a polymerase chain reaction test for mutations was not possible. PDL 1 was requested in 3 cases and samples were adequate for testing in all of those.

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Table 2. Breakdown of results of excisional lymph node biopsy performed in 8 cases

Diagnosis on needle sampling	Excisional biopsy result
Inadequate	NHL
SCLC and granulomatous inflammation	NHL
Adenocarcinoma	Adenocarcinoma
Reactive lymphadenopathy	Low-grade B-cell lymphoma
NHL	NHL
Reactive lymphadenopathy	Castleman lymphadenopathy
NHL	NHL
NHL	NHL

SCLC, small cell lung cancer; NHL, non-Hodgkin's lymphoma.

Discussion

In this paper we report our results of NUS-guided sampling of adenopathy led by respiratory physicians. Our results demonstrate that this can be performed with a high level of adequacy and safety by respiratory physicians trained in this procedure. Our sampling inadequacy rate (8.5%) was comparable to results from a previous systematic review of US-guided sampling of neck lesions, where the inadequacy rate was 9.6% for radiologists and 11% for clinicians without rapid on-site evaluation (ROSE) [8]. Importantly, in 14/15 (93.3%) cases confirmed as a primary lung adenocarcinoma, further mutational analysis was possible in 93.3% of samples. This demonstrates that adequate material is available in these cases for additional testing which is becoming increasingly important in the modern oncological management of this patient population consistent with a previous study where molecular analysis was possible in 85% of the cases [9].

Incorporating NUS done by respiratory physicians as a point-of-care diagnostic test in the suspected lung cancer clinic and respiratory procedural environment has a significant impact on the patient pathway. This safe, quick procedure provides early confirmation of cancer type and stage, whilst potentially preventing more invasive and expensive diagnostic and staging investigations. Such an impact, explored in diagnostic algorithms, may also have a positive effect on not only individual patient pathway time, but the wider patient cohort flow undergoing investigation by freeing interventional radiology and EBUS lists with likely cost benefits. We believe that this hypothesis is worth further assessment in a prospective study in lung cancer patients.

US as performed by non-radiologists has become increasingly common over the last decade. Adequate training guidance in NUS for the use in this setting has historically been an area of uncertainty. However, the Royal College of Radiologists (RCR) in the UK now have published guidelines for procedures performed by non-radiologists [10]. The guidelines recommend experience in NUS for level 2 training in pleural US, acknowledging the potential benefits of such a skill for respiratory physicians. An inadequate sampling rate of <15% was recommended for level 2 training in head and neck US – a metric achieved in our practice. However, for further advancement of NUS as a skill for respiratory physicians, we propose that separate tailored guidelines and training recommendations should be developed.

This study has a few inherent limitations. Firstly, this is a retrospective cohort and most cases were identified with adenopathy either by careful clinical examination or radiological assessment of the neck; however, the indications for neck imaging in the first place were heterogeneous, introducing an element of selection bias which might be associated with a higher diagnostic yield. In addition, all procedures were performed by 1 of 4 chest physicians with varying degrees of experience in NUS and sampling including core biopsy of neck nodes.

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It is unclear how much experience is required to achieve a high level of sampling adequacy. Further prospective studies should be undertaken to elucidate the role of training respiratory physicians in NUS-guided lymph node sampling.

Conclusion

This study demonstrates that NUS can be performed by respiratory physicians with accuracy in patients with identified adenopathy by clinical examination or imaging of the neck. Subsequent sampling of nodes under direct sonographic guidance was associated with a high level of accuracy and diagnostic yield. Guidelines need to be developed to allow training of respiratory physicians, particularly those with a special interest in lung cancer diagnosis and management.

Statement of Ethics

This study was performed in accordance with the Declaration of Helsinki. This human study was approved by Galway University Hospital Research Ethics Committee – approval: C.A. 2024.

Disclosure Statement

The authors declare no competing interests.

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