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Utility of ultrasound-guided supraclavicular lymph node sampling in lung cancer diagnosis – remodelling the pathway in the era of COVID-19

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ABSTRACT

Introduction: Ultrasound guided sampling (USGS) of supraclavicular lymph nodes (SCLN) is a minimally invasive method for obtaining cytological diagnosis in metastatic lung cancer. Same day USGS service may improve timeliness of investigations, minimise hospital visits and reduce invasive procedures.

Methods: We performed a 3-year retrospective analysis of patients with SCLN amenable to biopsy detected on 2 week-wait (2WW) CT. We identified those who underwent USGS or other procedures, diagnostic yield and their timeliness were determined.

Results: 49 patients (26%) had amenable SCLN, of whom 37 (75.5%) had USGS. USGS alone sufficient for 27 (73%) patients. Diagnostic yield is better for larger nodes (<1cm 62.5% positive; ≥1cm 86.2% positive, 95% CI 0.13 - 0.93, p=0.011). The overall diagnostic yield of USGS SCLN was 81% (30/37, 95% CI 65% to 92%). Although faster to obtain USGS, no statistically significant difference was reached between USGS and other methods (USGS median 15.5 days (IQR 11.2), other pro-

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cedures median 17.5 days (IQR 26.5), Mann-Whitney U p=0.42).

Conclusion: USGS SCLN has potential utility in early lung cancer diagnosis, even in lymph nodes <1cm, and is an underutilized diagnostic investigation. A prospective study of same day 2WW outpatient clinic and USGS procedure is now required to assess its effect on an accelerated diagnostic pathway.

KEY WORDS

ultrasound guided sampling of supraclavicular nodes; lung cancer diagnosis; lung cancer diagnostic pathway

Introduction

Ultrasound guided sampling (USGS) of supraclavicular lymph nodes (SCLN), either with fine needle aspiration (FNA) or core biopsy (CB), is a minimally invasive method for obtaining histocytological diagnosis in the investigation of lung cancer. This modality is recommended in the National Optimal Lung Cancer Pathway, as a "direct-to-biopsy" option for patients where further tests and detailed staging are not needed to guide treatment. USGS is routinely provided by Radiologists, however service capacity can potentially be expanded by training respiratory physicians (1–3). USGS of SCLN could be implemented as a "same day" one stop shop service, expediting diagnosis, saving costs (1), and avoiding risks of bronchoscopy and repeated unnecessary hospital visits, of relevance in the COVID-19 era. The usual coverage of the lower neck in 2 week-wait (2WW) CT scans for suspected lung cancer as per NICE guidelines (4) enables pathological SCLN to be identified early in the investigation pathway. We aim to assess the applicability of USGS in SCLN in a 2WW population, and the potential impact of this technique on length of diagnostic pathway – in terms of the diagnostic yield and time to achieve a diagnosis.

Methodology

A retrospective analysis was undertaken of all referrals to the lung cancer diagnostic pathway from January 2017 to December 2019 at Oxford University Hospitals NHS Foundation Trust. Patients with CT evidence of SCLN amenable to sampling were identified and cases were reviewed by a senior Radiologist. Cases were included where at least N2 mediastinal lymphadenopathy was identified on the 2WW CT with adequate lower neck coverage, on the basis that pathological SCLN are more likely to be seen in the presence of enlarged mediastinal lymph nodes (1,5). Cases with solely N0 and N1 suspected disease on CT were excluded. M status was disregarded as diagnostic sampling from any easily identified lymph node or metastasis would be sufficient to proceed with treatment planning.

Pathological SCLN was defined as a single lymph node or cluster of lymph nodes measuring ≥0.5cm on short axis on CT, or with an irregular or lobulated contour. Whether identified neck nodes were amenable to percutaneous sampling was assessed on the basis of CT features such as surrounding vessels.

The first diagnostic modality used (USGS of SCLNs, endobronchial ultrasound (EBUS) or CT guided biopsy (CTGBx) of a lung lesion) was identified from the electronic patient record. Time from initial CT scan until positive diagnostic biopsy was recorded for all modalities, and overall diagnostic yield was determined. A further analysis looked at the proportion of eligible patients who underwent USGS over time. We defined the term 'actionable histocytology' as attainment of sufficient tissue for pathological diagnosis, immunohistochemistry and molecular studies, enabling patients to proceed to definitive oncological treatment. This term was separated out from 'positive' cytology alone to ensure that the required definitive diagnostic biopsy was well-defined in terms that influenced patient care. Those patients who did not have positive diagnostic biopsy results (i.e. no 'actionable histocytology') proceeded to have other diagnostic tests and this is elaborated in the results section and in the supplementary flowchart.

Data analysis was performed using IBM SPSS (1.0.0.1461). Chi squared test was used to analyse change in frequency of use of USGS in discrete time periods. Independent t-test was used to assess continuous variables.

Results

A total of 186 patients with suspected N2 or N3 lym-

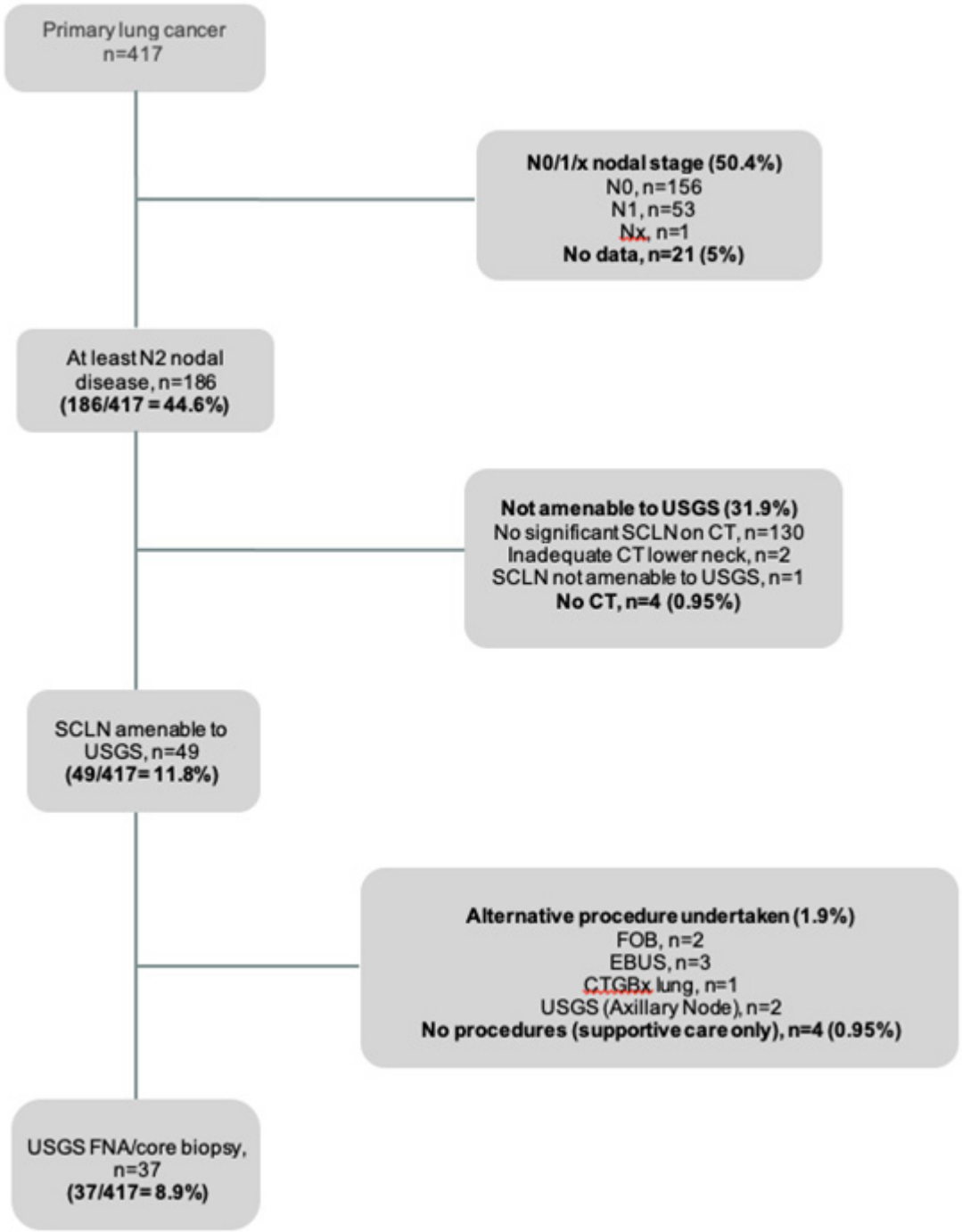

Figure 1: *Flowchart of screened cases and diagnostic procedures undertaken*

phadenopathy on CT were identified. Figure 1 illustrates screened cases and diagnostic procedures undertaken. On radiologist CT review, 49 cases (26%) had SCLN amenable to USGS, of whom 37 (75.5%) had USGS: 21 (56.8%) underwent FNA and 16 (43.2%) underwent CB.

Relationship between supraclavicular node size and diagnostic yield of USGS SCLN There was a significant difference in diagnostic yield (i.e. cytological diagnosis only) according to lymph node size; (<1cm 62.5%; ≥1cm 86.2%, 95% CI for the difference 0.13 to 0.93, p=0.011). The overall diagnostic yield of USGS SCLN was 81% (30/37, 95% CI 65% to 92%), including a single true negative case (SCLN negative, final diagnosis localised lung carcinoid). Sensitivity of USGS was 87.8% (95% CI 71.8% to 96%), including 4

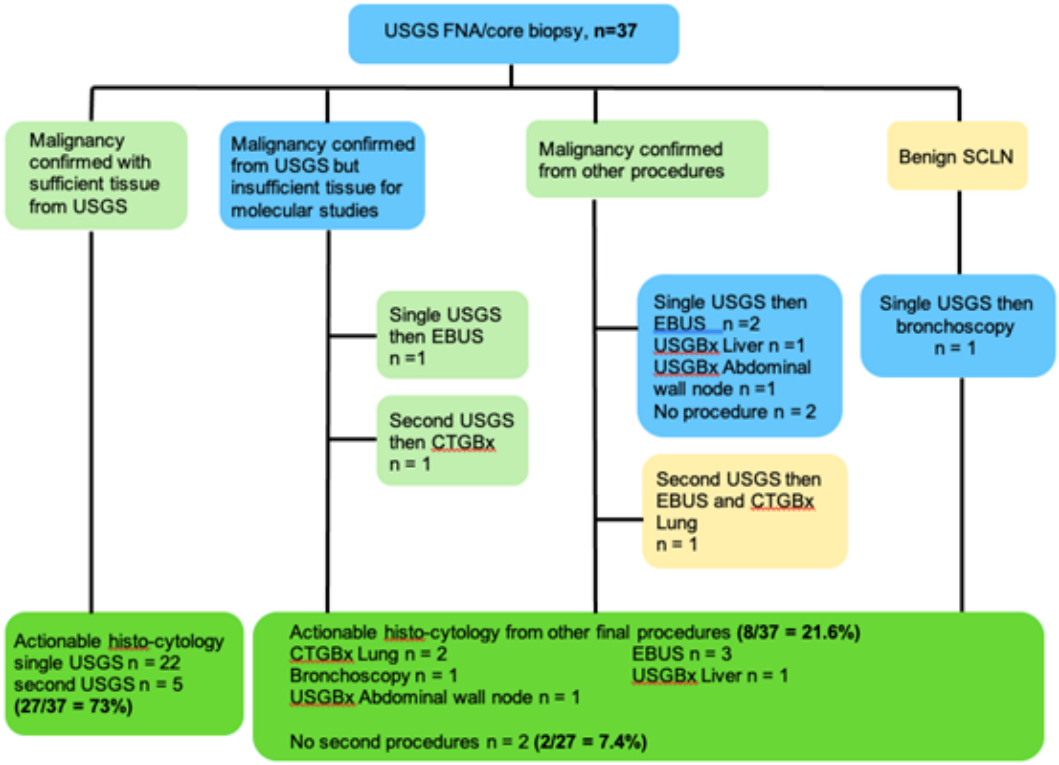

Figure 2: *Flowchart of final diagnostic pathway of USGS patients leading to actionable histo-cytology*

Table 1. Patients who had non-USGS as the first diagnostic test

Year	EBUS	Bronchoscopy	US axillary node biopsy	CT guided lung biopsy	No investigations
2017	3	-	1	-	1
2018	1	-	-	-	-
2019	2	2	1	1	3

false negative cases staged as N3 by lung multidisciplinary team.

Actionable histocytology from USGS and other procedures

Figure 2 illustrates the final pathway of 37 patients who had USGS including the need for other procedures leading to actionable histocytology. From USGS alone, 27/37 (73%) patients had sufficient samples for final actionable histocytology. Two patients had malignancy confirmed on USGS but needed EBUS and CTGBx to obtain further tissue. One case's SCLN was benign. 19% (7/37) with non-diagnostic USGS proceeded to other tests. Two patients did not have repeat investigation due to loss to follow up and considered unfit for further investigation.

Proportion of eligible patients who underwent USGS

The proportion of eligible patients who underwent sampling changed over time (1st year 86%, 2nd year 100%, 3rd year 76%, c2 2df=8.3, p=0.02). We think the proportion of patients dropped in the 3rd analysed year as other routes of diagnostic investigations were favoured.

Time to obtain diagnostic biopsy by investigation method

Time to USGS as the first diagnostic test was faster com-

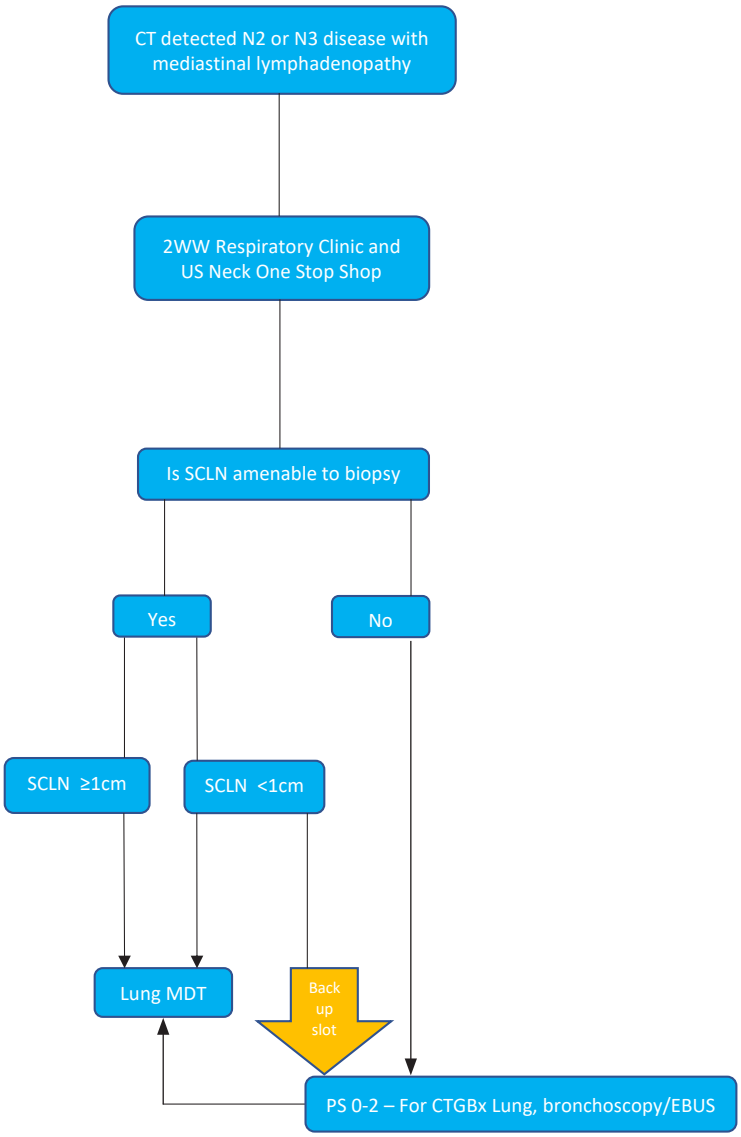

Figure 3: *Proposed direct to biopsy pathway for patients with amenable SCLN in metastatic lung cancer detected on 2ww CT Chest with lower neck coverage.*

pared with other (e.g. bronchoscopy, CTGBx) first diagnostic test, but this did not reach statistical significance (USGS median 15.5 days (IQR 11.2), other test median 17.5 days (IQR 26.5), Mann-Whitney U p=0.42).

Complications

There is no reported immediate significant complication for patients in our study who underwent USGS, apart from minor superficial bleeding. All patients were monitored routinely post sampling for 30 minutes prior to discharge.

Discussion

Our study shows a significant proportion of patients have suitable neck lymphadenopathy for sampling, however 25% of patients underwent bronchoscopy or CTGBx as the first diagnostic procedure. In our cohort, approximately 25% of patients with mediastinal lymphadenopathy had amenable SCLN for USGS, and the overall diagnostic yield was high (81%). This diagnostic yield is comparable to the existing literature. A Dutch study (6) showed a diagnostic accuracy of 90% for USGS core biopsy of SCLNs. A further study (2) demonstrated overall adequacy of 88.6% in USGS by respiratory physicians.

Our data demonstrated a higher proportion of diagnostic yield when SCLN size ≥1cm at 86.2% (25/29). Choe et al. (7) identified a threshold value of SCLN size 0.85cm

for likelihood of positive USGS core biopsy. Based on our findings, we propose that all enlarged SCLN are sampled in patients with CT detected N2 or greater stage, but that a 'back-up' alternative diagnostic procedure is also planned when SCLN measures <1 cm (See Figure 3).

We identified a substantial delay in obtaining USGS in the diagnostic pathway; if this can be timed as a same day procedure with the first outpatient clinic, time to sampling could be shortened to ~9 days for suitable patients. Triage to a ring-fenced USGS slot, either with Radiology or Respiratory, could occur at the time of CT reporting.

There are limitations to this study. This was retrospective and is therefore susceptible to selection bias, both in the group in whom lymph node biopsy was undertaken and those in whom a different first biopsy procedure was considered. However, thorough review of the CT scans provides mitigation against significant bias in terms of missing patients with significant enlarged nodes. Secondly, our study was underpowered to assess certain outcomes including diagnostic time. However, even this small sample size demonstrates a clinically important difference in diagnostic time comparing those undergoing USGS and those not (2 days). Larger, prospective studies are required to assess the true reduction in time offered by adopting a USGS strategy where possible.

Conclusions

USGS SCLN has potential utility in early lung cancer diagnosis, even in lymph nodes <1cm, and is underutilized. A robust remodelling of existing lung cancer diagnostic pathways to incorporate USGS for patients with amenable SCLN in an accelerated pathway should now be assessed, and this could be achieved through a prospective study of same day 2WW outpatient clinic and USGS SCLN procedure, either by Respiratory physicians or Radiologists. **R**

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