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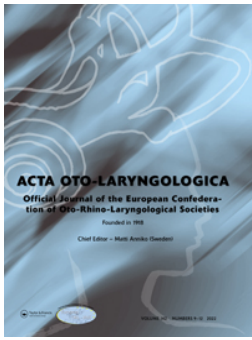
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Complications in lymph node excision in the head and neck area

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ABSTRACT

Background: Although needle biopsy is widely used in work-up of lymphadenopathy, lymph node excision (LNE) is often required especially in lymphoma diagnostics. LNE is an invasive procedure, which carries a potential risk of complications. However, comprehensive studies evaluating the spectrum and occurrence of complications are lacking.

Aims/Objectives: This study addresses the role of preoperative needle biopsies in patients who underwent LNE. Furthermore, surgical complications related to LNE are analyzed.

Materials and methods: Altogether 321 patients, who underwent LNE in two-year period in 2018–19, and fulfilled our study criteria, were included. Patients' data were retrieved from the electronic patient records.

Results: The surgical complication rate was 5.9%. Most of the complications ($n = 16$; 84.2%) were categorized as minor (I–II) according to the Clavien–Dindo scale. The remaining three (15.8%), all hemorrhages, were categorized as major complications and required intervention. Preoperative needle biopsy might have avoided the need for LNE in some patients, which we discuss in this study.

Conclusions and significance: Surgical complications after LNE in the head and neck area are rare and mostly minor. Needle biopsy is often recommended preoperatively to avoid unnecessary operations and to refrain performing LNE for patients with non-lymphatic malignancy.

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KEYWORDS

Lymphadenopathy; open neck biopsy; fine needle aspiration cytology; core needle biopsy

Introduction

Patient's medical history, symptoms, and clinical examination including endoscopies are the cornerstones in diagnostics of cervical lymphadenopathy. Ultrasonography (US) combined with fine needle aspiration biopsy (FNAB), or core needle biopsy (CNB) is widely used in diagnostics and helps to differentiate between benign and malignant etiology [1,2]. As pathological techniques have evolved, FNAB/CNB can even provide reliable and a specific diagnosis. Nevertheless, approximately 5% of CNB [3] and up to 30% of FNAB [4] remain inadequate in the head and neck area. Especially in the work-up of lymphoma, needle biopsies do not often provide sufficient yield to specifically categorize the disease. Thus, National Comprehensive Cancer Network (NCCN) still recommends lymph node excision (LNE) in lymphoma diagnostics [5]. WHO classification of tumors of the hematopoietic and lymphoid tissue is also based on the histologic specimen [6].



LNE is an invasive procedure, which carries a possible risk of complications. In cervical area, accessory nerve injuries have been described in small case series [7,8] but other complications or contributory factors leading to complications have not been assessed before. This study is aimed to

evaluate the role of needle biopsies in patients undergoing LNE. In addition, we addressed the occurrence and the spectrum of complications in cervical LNE.

Material and methods

This retrospective study was conducted at the Department of Otorhinolaryngology – Head and Neck Surgery, Helsinki University Hospital, Helsinki, Finland, a tertiary care center with a referral area of 1.6 million people. Patient data between 1 January 2018, and 31 December 2019 were retrieved from the electronic patient records. We included patients, who were ≥ 16 years old and treated in the operative theatre at our department with an operative code PJD41, which stands for excision of a cervical lymph node. We included all preoperative diagnoses. In total, 321 patients matched the selection criteria and formed the study cohort.

Research ethics committee of Helsinki University Hospital approved the study (DNRO 89/13/03/02 C/2011; 13 Feb 2011) and an institutional permission was granted (HUS/58/2020).

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Table 1. Patient characteristics and preoperative evaluation ($n = 321$).

	<i>n</i> (%)
Age, median (range)	55 (16–96)
Sex	
Male	152 (47.4)
Female	169 (52.6)
BMI, median (range)	25.3 (15.4–47.3)
ACE-27	
0	144 (44.9)
1	89 (27.7)
2	61 (19.0)
3	27 (8.4)
Smoking	
Yes	41 (12.8)
No	171 (53.3)
Previous	79 (24.6)
Data not available	30 (9.3)
Previous malignancy	
Yes	94 (29.3)
Lymphoma	52 (16.2)
Other	42 (13.1)
No	227 (70.7)
History of the neck lump	
<2 weeks	18 (5.6)
2–4 weeks	36 (11.2)
>4 weeks–2 months	107 (33.3)
>2 months	154 (48.0)
Data not available	6 (1.9)
Lymphadenopathy	
Single neck node	49 (15.3)
Unilateral neck nodes	127 (39.6)
Bilateral neck nodes	59 (18.4)
Widespread lymphadenopathy	86 (26.8)
Preoperative imaging	
Performed	308 (96.0)
Ultrasound	218 (70.8)
CT	97 (31.4)
MRI	27 (8.8)
PET-CT	21 (6.8)
Not performed	13 (4.2)
Preoperative cytopathological diagnosis	
Performed	192 (59.8)
Reactive changes or benign, not otherwise specified	66 (34.4)
Suspicion of lymphoma	63 (32.8)
Suspicion of malignancy other than lymphoma	22 (11.5)
Inadequate sample	22 (11.5)
Nonspecific/indifferent	15 (7.8)
Granulomatous lesion	1 (0.5)
Necrosis	1 (0.5)
Not performed	129 (40.2)

BMI: body mass index; ACE-27: adult comorbidity evaluation-27; CT: computed tomography; MRI: magnetic resonance imaging; PET-CT: positron emission tomography–computed tomography.

Demographic and clinical data as well as operation-related factors were collected as presented in Tables 1 and 2.

Complications were recorded from patient records and classified using the Clavien-Dindo (CD) scale [9]. We classified surgical and medical complications as perioperative (from surgery until discharge from the hospital) and postoperative (from discharge from the hospital until 30 days after the surgery). We analyzed causes for the surgical complications, and whether any patient- or operation-related factor had influence on the occurrence of a complication. We meticulously reviewed all cases in which any non-lymphoproliferative malignancy was diagnosed after LNE. In these cases, we analyzed the management process and evaluated whether LNE could have been avoided.

All data were manually registered from the electronic hospital charts and transferred to SPSS statistical software.

Table 2. Operation-related factors in 321 patients.

	<i>n</i> (%)
Indication for lymph node excision	
Suspicion of lymphoma	186 (57.9)
Suspicion of lymphoma relapse	52 (16.2)
Unclear lymphadenopathy	69 (21.5)
Suspicion of tuberculosis	14 (4.4)
Neck lymph node level	
I–II	105 (32.4)
III	49 (15.3)
IV	20 (6.2)
V	133 (41.4)
Information not available	15 (4.7)
Anesthesia	
Local	189 (58.9)
General	132 (41.1)
Type of surgery	
Whole lymph node	282 (87.9)
Piece of a lymph node	37 (11.5)
Final histopathological diagnosis	
Lymphoma	172 (53.6)
Other non-lymphoproliferative malignancy	17 (5.3)
Myeloma	6 (1.9)
Reactive changes	71 (22.1)
Granulomatous lesion	35 (10.9)
Other diagnosis*	14 (4.4)
Inadequate sample	3 (0.9)

*Neural tumor ($n = 2$), IgG4 disease ($n = 2$), Kikuch's disease ($n = 2$), Warthin's tumor ($n = 0.1$), vascular malformation ($n = 1$), Rosai-Dorfman's disease ($n = 1$), necrosis ($n = 1$), nodular fasciitis ($n = 1$), lateral branchial cyst ($n = 1$).

Statistical analyses were performed with SPSS software version 25 (IBM, Armonk, NY). We used descriptive statistics to summarize frequencies, proportions, medians, and ranges. Pearson's Chi-square test with asymptotic and exact p values was used when best appropriate to calculate the statistical differences between categorical variables, and independent-samples t -test was used for continuous variables. A two-sided p value of less than .05 was considered statistically significant.

Results

Table 1 presents baseline demographics of the study cohort of 321 patients. Of all patients, 94 (29.3%) had a history of previous malignancy, and in 52 of them (55%) it was lymphoma. Of 321 patients, 308 (96.0%) underwent preoperative radiology, most commonly US ($n = 218$; 70.8%). In 192 (88.1%) of patients Us was combined with FNAB/CNB. Among the 192 patients the cytopathological sample yielded reactive or otherwise benign finding on 66 (34.4%) patients, and suspicion of lymphoma in 63 (32.8%) patients. In 129 patients (40.2%), no needle biopsy was utilized.

Table 2 shows the operation-related factors. The most frequent indication for LNE was suspicion of lymphoma or lymphoma relapse ($n = 238$; 74.1%), followed by unclear lymphadenopathy in 69 (21.5%) patients. Only a piece of a lymph node was removed in 37 (11.5%) patients due to its attachment to surrounding tissue, large size, or challenging location of the lymph node. The procedure was performed under local anesthesia in most patients ($n = 189$; 58.9%).

All complications were retrospectively evaluated using the CD classification. The complication rate was 5.9% with 19 surgical complications in 19 patients. Of these, two (0.6%) occurred perioperatively and 17 (5.3%)

Table 3. Complication-related factors in cohort of 321 patients.

Complication	Yes (%)	No (%)	<i>p</i> -value
Sex			.999
Male	9 (5.9)	143 (94.1)	
Female	10 (5.9)	159 (94.1)	
BMI			.920
<20	1 (5.0)	19 (95)	
20–25	7 (6.8)	96 (93.2)	
>25–30	5 (5.5)	86 (94.5)	
>30	2 (4.1)	47 (95.9)	
Neck level			.407
I–II	9 (8.7)	95 (91.3)	
III	1 (2.0)	48 (98.0)	
IV	0	20 (100.0)	
V or supraclavicular	8 (6.0)	125 (94.0)	
Information not available	1 (6.7)	14 (93.3)	
Surgeon			.417
Resident	12 (7.5)	148 (92.5)	
ENT specialist	2 (3.1)	63 (96.9)	
Specialist in ENT – head and neck surgery	5 (5.2)	91 (94.8)	
Anesthesia			.568
Local	10 (5.3)	179 (94.7)	
General	9 (6.8)	123 (93.2)	
Length of the operation			.089
<20 min	1 (4.2)	23 (95.8)	
20–40 min	5 (3.4)	141 (96.6)	
41–60 min	5 (5.8)	81 (94.2)	
>60 min	8 (12.3)	57 (87.7)	

BMI: body mass index; ENT: ear, nose, and throat.

postoperatively. Medical complications, such as pneumonia or thromboembolic complications, were not recorded. Most ($n = 16$; 84.2%) of the complications were minor (CD I–II). Two nerve complications occurred. One accessory nerve palsy appeared immediately after the procedure and required physiotherapeutic rehabilitation without any greater deficiency later (CD II). Another patient had a palsy of the marginal branch of the facial nerve, which was recorded one week postoperatively on a follow-up call, and that resolved on its own within weeks (CD I). The rest 14 other minor complications were mainly associated with wound healing: local swelling ($n = 5$), local infection ($n = 4$), local bleeding ($n = 2$), stitch protrusion ($n = 2$), and pain ($n = 1$). All three (15.8%) major complications were due to local bleeding and required intervention. One of them was treated under general anesthesia one day after the initial surgery (CD IIIb), and the other two were treated by puncturing the wound-related hematoma (CD IIIa). Table 3 shows complication-related factors. In this cohort, no clear correlations were found. Patient's smoking or comorbidities had no impact on the risk of complications. The experience of the surgeon showed no statistical difference for complications, although experience shortened the duration of the operation.

The final histopathological diagnosis showed lymphoma in 53.6% ($n = 172$) of the samples, and reactive changes presented 22.1% ($n = 71$) of the diagnoses as presented in Table 2. The final histopathological diagnosis was malignant, other than lymphoma or myeloma in 17 (5.3%) patients of all study population (Table 4). Among them, nine had no preoperative FNAB/CNB whereas eight underwent needle biopsy. We further reviewed these eight patients. In three of them, the sample was inadequate. In five, FNAB/CNB already raised suspicion of carcinoma, but LNE was still required for a definite diagnosis. In one patient, melanoma was diagnosed by FNAB but left unnoticed (Table 4, patient

number 11). The patient had the surgical scar removed later after LNE during neck dissection but otherwise LNE had no adverse influence on further management. As concluded in Table 4, LNE was clearly or possibly avoidable in nine patients, which represents 2.8% of the study population.

Discussion

To our knowledge, we present the first comprehensive study on complications in cervical LNE. Our study shows the overall surgical complication rate in LNE to be low, and mostly minor according to the CD classification. We reviewed all 321 LNEs performed in our tertiary care center during a two-year period.

Suspicion of lymphoma or lymphoma relapse were among the most common indications for LNE in the present study. LNE has long been the gold standard in lymphoma diagnostics [6], although a review by Frederiksen et al. showed that FNAB/CNB provided a definitive diagnosis in 65–75% of the lymphoma cases [10]. Thus, it seems reasonable to assume that for some patients in our cohort, CNB alone might have been sufficient for lymphoma diagnosis, although we cannot provide solid data. Over the last couple of years, we have changed the protocol to take primarily CNB instead of FNAB when technically possible from head and neck lesions, and we believe this will reduce the need for LNE in the future. However, since FNAB/CNB fail to yield a definite diagnosis for lymphoma in a quarter of patients, LNE remains indefinitely the recommended diagnostic method in this disease entity [10–14].

In our cohort, FNAB/CNB did not precede LNE in 40% of patients. The literature emphasizes cytological sampling prior to LNE and diagnostic US should include simultaneous FNAB/CNB when assessing pathological lymph nodes. However, in 8% of our patients, a concomitant FNAB/CNB was not taken. FNAB/CNB was mainly opted out in patients with a high probability of lymphoma, based on clinical history and imaging findings, or when lymphoma relapse was suspected. In these cases, LNE instead of needle biopsy might even expedite further treatment. Our retrospective evaluation showed that LNE might have been avoided in some patients.

Current data on complications associated with LNE in head and neck area are limited, and studies focus on nerve injuries in small case series [8]. Our data revealed two partial nerve injuries, where a resident was the operative surgeon assisted by a senior. In our department, a resident is allowed to perform LNE independently, but a senior is always ready to help upon request, which we have found to be good practice. However, the degree of difficulty of surgery should be carefully assessed preoperatively, and depending on the experience of the resident, the more challenging cases are performed by senior surgeons. Even though most of the complications observed in the present study were minor and related to normal wound healing, they are significant when considering consumption of health care resources. Additional hospital visits and prolonged sick leaves increase costs of treatment. In addition, the form of anesthesia has a

Table 4. Patients with non-lymphoproliferative malignancy as a final diagnosis.

Patient	History of previous malignancy	Preoperative imaging	Preoperative cytological diagnosis of the neck node	Type of needle biopsy	Location of LNE	Final histopathology	Site of the primary	Avoidability of LNE
1	Prostate cancer	Neck US	Not taken		Supraclavicular fossa	Adenocarcinoma	Unknown primary	Possibly
2	No	Neck US, full-body CT	Not taken, unreachable location		Supraclavicular fossa	Microcellular carcinoma	Lung	No
3	No	Neck US, full-body CT	Inadequate sample	CNB	Not available	Microcellular carcinoma	Lung	No
4	Rectum cancer	Full-body CT	Not taken		Supraclavicular fossa	Carcinoma	Prostate	Possibly
5	No	Sinus CT, sinus MRI, full-body CT	Suspicion of rhabdomyosarcoma	FNAC	Supraclavicular fossa	Rhabdomyosarcoma	Sinonasal, maxillary sinus	No
6	Colon cancer	Full-body CT	Not taken		Supraclavicular fossa	Adenocarcinoma	Colon	Possibly
7	Lymphoma	Neck US	Not taken		Neck level II	Rhabdomyosarcoma	Sinonasal, maxillary sinus	Possibly
8	Papillary thyroid cancer	SPECT CT, neck US	Suspicion of papillary thyroid carcinoma	FNAC	Supraclavicular fossa	Papillary thyroid carcinoma	Thyroid gland	No, part of the treatment
9	No	Full-body CT, abdominal MRI	Not taken		Supraclavicular fossa	Adenocarcinoma	Pancreas	Possibly
10	No	Cervical MRI, PET CT	Suspicion of carcinoma	FNAC	Supraclavicular fossa	Adenocarcinoma	Lung	No
11	No	Neck US	Melanoma	FNAC	Neck level II	Melanoma	Sinonasal, maxillary sinus	Yes
12	No	Neck US	Not taken		Supraclavicular fossa	Adenocarcinoma	Colon	Possibly
13	Cervix cancer	Full-body CT	Not taken		Supraclavicular fossa	Adenocarcinoma	Unknown primary	Possibly
14	Pancreatic cancer	Neck US, full-body CT	Inadequate sample	FNAC	Supraclavicular fossa	Adenocarcinoma	Pancreas	No
15	No	Neck US, cervical MRI	Inadequate sample	FNAC	Intraparototic lymph nodes	Melanoma	Unknown primary	No
16	Melanoma	Abdominal CT, MRI and US	Not taken		Supraclavicular fossa	Adenocarcinoma	Prostate	Possibly
17	No	Neck US, cervical MRI	Suspicion of thyroid carcinoma	FNAC	Supraclavicular fossa	Adenocarcinoma	Two primaries simultaneously, thyroid and adenocarcinoma	No

US: ultrasound; CT: computed tomography; MRI: magnetic resonance imaging; SPECT: single-photon emission computed tomography; PET: positron emission tomography; CNB: core needle biopsy; FNAC: fine needle aspiration cytology; LNE: lymph node excision.

significant economic effect. LNE under local anesthesia requires usually less time in the operating theater and allows the patient to be discharged more quickly. In the present study, 59% of LNEs were performed under local anesthesia, and we believe that local anesthesia could be favored even more often.

Granulomatous lesions comprised 11% of the histopathological diagnoses. Diagnosis of e.g. tuberculosis might have also been achievable through FNAB/CNB [15], although we do not have definitive data on this. Further, reactive changes were the final histopathological diagnosis in 22% of patients, of whom 30% did not undergo preoperative FNAB/CNB. Due to the retrospective nature of our study design, we can only speculate on the number of cases in this group, where FNAB/CNB might have been sufficient for definitive diagnosis. Especially while suspecting a benign condition, FNAB/CNB should be considered primarily, and even repeatedly in some cases.

Most lymph nodes with a histopathological diagnosis of carcinoma after LNE were excised from the supraclavicular fossa. The histology referred commonly to a metastasis from an intra-abdominal site, which is often the primary site for these metastases [16,17]. LNE can lead to a set of complications in head and neck squamous cell carcinoma (HNSCC), which is the most common type of cancer of the head and neck [18]. The complications can include wound-related problems, distortion of anatomy, or even tumor cell seeding [19], and thus affect future treatment options and increase the need for radiotherapy, which then increases patient's treatment burden as well as affects costs of care [20]. In our series we did not have any HNSCC patients undergoing LNE. All patients at the outpatient clinic undergo comprehensive otorhinolaryngological examination including endoscopy of the upper airways that undoubtedly diminishes the risk for unknown primaries and prevents unnecessary LNEs. Thus, our management protocol seems to work efficiently.

We present an unselected series of LNEs performed in our hospital district where these procedures are centralized into our department. This study has its limitations due to the retrospective design. We did not offer routine follow-up visits and patients were not contacted in search for long-term complications. Therefore, some patients with a minor or long-term complication may be missing from our data. However, patients are always advised to contact our department in case of a problem or concern during their recovery time. If a patient had brought up any wound-related complaints, they were frequently asked for a visit.

Conclusions

Utilizing needle biopsies in conjunction with US and favoring CNB, when possible, might obviate LNE in some patients. Still, in selected cases, it might seem reasonable to proceed directly with LNE and thus even expedite diagnostics and further treatment. LNE in the head and neck area carries a low risk of complications, which are mostly minor and often related to normal wound healing process.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The datasets generated during and/or analyzed during the current study are not publicly available due to the sample size. Data are available from corresponding author on reasonable request.

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