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REVIEW ARTICLE

A systematic review of ultrasound-guided FNA of lesions in the head and neck—focusing on operator, sample inadequacy and presence of on-spot cytology service

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ABSTRACT

The objective of this review is to perform a systematic review of ultrasound-guided fine-needle aspiration (FNA) services for head and neck lesions with assessment of inadequacy rates and related variables such as the presence of immediate cytological assessment. A computer-based systematic search of articles in English language was performed using MEDLINE (1950 to date) from National Health Service evidence healthcare database and PubMed. Full texts of all relevant articles were obtained and scrutinized independently by two authors according to the stated inclusion and exclusion criteria. The primary search identified 932 articles, but only 78 met all the study criteria. The overall inadequacy rate was 9.3%, 16 studies had on-site evaluation by a cytopathologist/specialist clinician with a rate of 6.0%. In seven studies, a cytotechnician was available to either assess the sample or prepare the slides with an average inadequacy rate of 11.4%. In 1 study, the assessment was unclear, but the inadequacy rate for the remaining 54 studies, without immediate assessment, was 10.3%. The rate for the cytopathologist/specialist clinicians was significantly different to no on-site assessment but this was not found for assessment by cytotechnicians. The review suggests that the best results are obtained with a cytopathologist-led FNA service, where the pathologist reviews the specimen immediately, in relation to the clinical context, thereby deciding on adequacy and need for further biopsies. A systematic review looking at ultrasound-guided FNA of head and neck lesions has not been published previously.

Fine-needle aspiration (FNA) cytology is well established as an initial investigation for all head and neck lesions subject to it being cost effective, quick to perform, low morbidity, patient acceptability and high diagnostic accuracy.^{1–3} The cost effectiveness and diagnostic accuracy can be increased by using ultrasound guidance and having a cytologist in the clinic to assess the samples, allowing immediate resampling if necessary.^{4–15} The National Institute for Clinical Excellence (NICE) recognizes the importance of FNA in head and neck cancer, and in their document titled “Improving outcomes in head and neck cancers” published in November 2004,¹⁶ they recommend establishment of specialist one-stop clinics for optimum management of all patients with neck lumps. Such clinics are to be structured in a similar way to one-stop breast lump clinics with a cytopathologist present and preferably FNA with ultrasound guidance.

The aim of this article is to perform a systematic review of ultrasound-guided FNA for all head and neck lesions

(thyroid and non-thyroid). A brief search of the literature was performed by the authors to objectively look for reviews looking at the efficacy of ultrasound-guided FNA for head and neck lesions. We found several reviews and comparisons of non-image-guided FNAs of head and neck lesions, image-guided and non-image-guided FNAs of thyroid; however, we could not find any systematic review looking at ultrasound-guided FNA of “head and neck” lesions. To the best of our knowledge, our systematic review is among the first few, specifically assessing inadequacy rates and related variables such as the presence of pathologist on the spot, for ultrasound-guided head and neck lesions.

METHODS AND MATERIALS

Literature search

A computer-based systematic search of articles in English language was performed using MEDLINE (1950 to date) from the National Health Service (NHS) evidence healthcare database and PubMed. Search terms used were “head

Table 1. Summary of review data

Serial number	Study	Performed by	Inadequacy rate (%)	95% confidence interval (%)	On-site cytology	Patients/FNA	Area evaluated
1	Accurso et al ¹⁷	Clinician	22.2	17.8–27.1	Absent	325 patients	Thyroid
2	Accurso et al ¹⁸	Clinician	15.0	12.9–17.3	Absent	1043 patients	Thyroid
3	Addams-Williams et al ¹⁹	Radiologist	11.8	7.9–16.7	Absent	229 patients	Non-thyroid lumps
4	Alexander et al ¹⁹	Clinician	13.0	11.4–14.9	Checked by cytotechnician	1128 patients/1458 FNA	Thyroid
5	Atula et al ²⁰	Radiologist	20.9	13.1–30.7	Absent	91 FNA	Lymph nodes
6	Baatenburg de Jong et al ⁵	Radiologist and clinician	0	0.0–5.2	Absent	76 patients	Lymph nodes
7	Bajaj et al ²¹	Radiologist	1.9	0.7–4.1	Absent	69 patients	Parotid
8	Baloch et al ²²	Radiologist and clinician	1.3	0.0–7.1	Checked by pathologist	282 patients/313 FNA	Thyroid
9	Bellantone et al ²³	Clinician	9.2	4.7–15.9	Absent	119 patients	Thyroid
10	Berker et al ²⁴	Clinician	19.4	16.1–23.1	Absent	426 patients/520 FNA	Thyroid
11	Bhakti et al ²⁵	Clinician	3.6	2.1–5.8	Absent	400 patients	Thyroid
12	Borgemeester et al ²⁶	Radiologist	5.9	2.2–12.5	Absent	126 patients/101 FNA	Lymph nodes
13	Braga et al ²⁷	Endocrinologist	5.7	2.3–11.3	Checked by endocrinologist	124 FNA	Thyroid
14	Brenta et al ²⁸	Clinician	11.3	7.6–15.9	Absent	248 patients	Thyroid
15	Breslin et al ²⁹	Radiologist	2.7	0.1–14.2	Absent	37 patients	Lymph node/thyroid bed
16	Cai et al ³⁰	Cytopathologist	6.4	4.2–9.4	Checked by pathologist	373 patients	Thyroid
17	Can and Peker ¹⁰	Clinician	29.0	22.6–36.0	Absent	136 patients/184 FNA	Thyroid
18	Can ⁴	Clinician	12.5	8.1–18.2	Absent	190 patients	Thyroid
19	Carmeci et al ⁷	Radiologist	7.1	3.3–13.0	Checked by cytotechnologist	127 patients	Thyroid
20	Ceresini et al ³¹	Clinician	0.7	0.1–1.9	Checked by pathologist	307 patients/465 FNA	Thyroid
21	Cesur et al ¹¹	Clinician	21.4	16.8–26.6	Absent	215 patients/285 FNA	Thyroid
22	Chen et al ³²	Clinician	0	0.0–16.1	Absent	21 patients	Parathyroid
23	Cochand-Priollet et al ³³	Radiologist	3.8	1.2–8.6	Absent	132 patients	Thyroid

(Continued)

Table 1. (Continued)

Serial number	Study	Performed by	Inadequacy rate (%)	95% confidence interval (%)	On-site cytology	Patients/FNA	Area evaluated
24	Danese et al ¹²	Radiologist	3.5	3.0–4.1	Absent	4697 patients	Thyroid
25	De Fiori et al ³⁴	Radiologist	13.7	11.3–16.5	Absent	700 patients	Thyroid
26	Ganguly et al ³⁵	Cytopathologist	4.0	2.0–7.1	Checked by pathologist	274 patients	Head and neck
27	Ginat et al ³⁶	N/A	9.5	5.9–14.3	Checked by pathologist	210 patients/211 FNA	Thyroid
28	Hagag et al ³⁷	N/A	20.4	13.2–29.2	Absent	108 patients	Thyroid
29	Hanbidge et al ³⁸	Radiologist	20.3	13.6–28.5	Absent	123 patients	Thyroid
30	Hatada et al ³⁹	Clinician	16.7	8.9–27.3	Checked by cytotechnologist	70 patients/72 FNA	Thyroid
31	Hodder et al ⁴⁰	Radiologist	12.1	3.4–28.2	Absent	33 patients	Lymph nodes
32	Izquierdo et al ⁸	Clinician	7.1	4.1–11.3	Checked by cytotechnologist	219 nodule/225 FNA	Thyroid
33	Kim et al ⁴¹	Radiologist	10.3	7.6–13.5	Absent	121 patients/149 FNA	Thyroid
34	Kim et al ⁴²	Radiologist	18.9	13.7–25.0	Absent	253 patients/438 FNA	Thyroid
35	Kim et al ⁴³	Radiologist	6.0	2.8–11.2	Absent	180 patients/201 FNA	Thyroid
36	Kimoto et al ⁴⁴	Clinician	9.8	6.2–14.6	Absent	169 patients/214 FNA	Thyroid
37	Knappe et al ⁴⁵	Clinician	14.0	9.3–19.9	Cytotechnician preparing slides	56 patients/179 FNA	Lymph nodes
38	Koike et al ⁴⁶	Clinician	4.9	2.8–7.8	Absent	329 patients	Thyroid
39	Kovacevic and Fabijanic ⁴⁷	Radiologist	10.1	4.7–18.3	Absent	68 patients/89FNA	Parotid
40	Kraft et al ⁴⁸	Clinician	32.0	21.7–43.8	Absent	75 patients	Head and neck
41	Leenhardt et al ⁴⁹	Clinician	19.1	15.6–23.1	Absent	450 patients	Thyroid
42	Lieu ⁵⁰	Cytopathologist	2.7	1.2–5.2	Checked by pathologist	298 FNA	Head and neck + thyroid
43	Lohela et al ⁵¹	Radiologist	7.4	0.9–24.3	Checked by radiologist	27 patients	Lymph nodes
44	McIvor et al ⁵²	Clinician	14.9	10.2–20.7	Checked by pathologist	203 patients/195 FNA	Head and neck
45	Mikosch et al ⁵³	Clinician	4.7	3.3–6.6	Absent	718 patients	Thyroid
46	Mikosch et al ⁵⁴	Experienced operator	4.7	3.0–6.8	Absent	538 patients	Thyroid

(Continued)

Table 1. (Continued)

Serial number	Study	Performed by	Inadequacy rate (%)	95% confidence interval (%)	On-site cytology	Patients/FNA	Area evaluated
47	Mittendorf et al ⁵⁵	Radiologist	22.7	13.3–34.7	Checked by pathologist	66 patients	Thyroid
48	Multanen et al ⁵⁶	Clinician	1.4	0.2–5.0	Absent	143 patients	Thyroid
49	Nabrisi et al ⁵⁷	Clinician	24.6	14.5–37.3	Absent	61 patients	Thyroid
50	Newkirk et al ⁵⁸	Radiologist	10.7	7.0–15.4	Checked by pathologist	234 FNA	Thyroid
51	Ogawa et al ⁵⁹	Clinician	18.0	15.7–20.5	Absent	806 nodules/1012 FNA	Thyroid
52	Robinson and Cozens ¹³	Radiologist	3.4	1.7–6.2	Checked by pathologist	292 patients	Head and neck
53	Robitschek et al ⁶	Surgeon	16.1	8.8–25.9	Checked by cytotechnologist	81 patients	Head and neck
54	Rorive et al ⁶⁰	Radiologist	4.2	3.0–5.7	Checked by pathologist	924 patients	Thyroid
55	Rosen et al ⁶¹	Radiologist	32.2	20.6–45.6	Absent	59 patients	Thyroid
56	Rottey et al ⁶²	Clinician	15.4	4.4–34.9	Absent	26 patients	Lymph nodes
57	Sabel et al ⁶³	Clinician	4.0	0.8–11.1	N/A	76 patients	Thyroid
58	Sahin et al ⁶⁴	Clinician	6.7	4.9–9.0	Absent	612 patients	Thyroid
59	Sahin et al ⁶⁵	Radiologist	4.7	2.9–7.0	Absent	145 + 327 patients	Thyroid
60	Sanchez et al ⁶⁶	Radiologist	20.0	6.8–40.7	Absent	25 patients	Thyroid
61	Schoedel et al ⁶⁷	N/A	8.7	2.4–20.8	Cytotechnologist to prepare slides	46 patients	Thyroid
62	Schueler-Weidekamm et al ⁶⁸	Radiologist	14.3	3.1–36.3	Absent	21 patients	Thyroid
63	Schwartz et al ⁶⁹	Surgeon	9.6	3.9–18.8	Absent	66 patients/73 FNA	Thyroid
64	Seiberling et al ⁷⁰	Clinician	9.6	6.4–13.7	Checked by pathologist	203 patients/271 FNA	Thyroid
65	Siegert et al ⁷¹	Clinician	12.0	7.9–17.2	Absent	208 patients	Head and neck
66	Siewert et al ⁷²	Radiologist	5.6	0.7–18.7	Some checked by pathologist	36 patients	Salivary glands
67	Takashima et al ⁷³	Radiologist	3.7	1.8–6.8	Absent	210 patients/268 FNA	Thyroid
68	Takashima et al ⁷⁴	Radiologist	7.7	3.2–15.2	Absent	70 patients/91 FNA	Lymph nodes

(Continued)

Table 1. (Continued)

Serial number	Study	Performed by	Inadequacy rate (%)	95% confidence interval (%)	On-site cytology	Patients/FNA	Area evaluated
69	Takes et al ⁷⁵	Radiologist	4.7	1.0–13.1	Some checked by pathologist	64 patients	Lymph nodes
70	Tambouret et al ⁷⁶	Radiologist	15.2	11.3–19.8	Checked by pathologist	251 patients/290 FNA	Thyroid
71	Tseng et al ⁷⁷	Clinician	8.3	3.1–17.3	Absent	72 patients	Parathyroid
72	Tublin et al ⁷⁸	Radiologist	12.2	7.8–17.9	Absent	180 FNA	Thyroid
73	Van den Brekel et al ⁷⁹	N/A	3.2	0.7–9.1	Absent	67 patients/93 FNA	Lymph nodes
74	Van den Brekel et al ⁸⁰	N/A	6.7	2.2–14.9	Absent	53 patients/75 FNA	Lymph nodes
75	Van den Brekel et al ⁸¹	N/A	10.5	4.0–21.5	Absent	54 patients/57 FNA	Lymph nodes
76	Yang et al ⁸²	Radiologist	0.7	0.3–1.4	Checked by pathologist	1135 patients	Thyroid
77	Yerli et al ⁸³	Radiologist	12.0	2.6–31.2	Absent	25 patients	Parotid
78	Yokozawa et al ⁸⁴	Clinician	12.0	10.1–14.2	Absent	1000 patients	Thyroid

FNA, fine-needle aspiration; N/A, not available.

and neck biopsy”, “head and neck ultrasound”, “head and neck ultrasound biopsy”, “head and neck ultrasound aspiration biopsy”, “head and neck needle biopsy”, “head and neck ultrasound guided biopsy”, “head and neck ultrasound guided”, “head and neck guided biopsy”, “head and neck FNA”, “head and neck ultrasound FNA”, “head and neck ultrasound guided FNA”, “head and neck guided FNA”, “head and neck guided aspiration”, “head and neck guided aspiration biopsy”, “head and neck ultrasound guided aspiration biopsy”, “head and neck ultrasound aspiration cytology”, “head and neck ultrasound guided FNA cytology”, “head and neck aspiration cytology”, “head and neck ultrasound guided aspiration biopsy FNA cytology”. A separate search of the Cochrane database was performed looking for reviews and clinical trials.

Abstracts of all relevant articles mentioning inadequacy rate of ultrasound-guided FNA for lesions in the head and neck were selected. Full texts of all relevant articles were obtained and scrutinized independently by two authors.

Inclusion criteria

Certain inclusion criteria were pre-selected, which had to be fulfilled for an article to be considered in our review. The article would have to be in English language and specifically mention the sample inadequacy rate for ultrasound-guided FNA for lesions in the head and neck. To ensure inclusion of data reported from all head and neck lesions, we included articles looking at general head and neck lesions and articles looking specifically at thyroid, parathyroid, neck lymph nodes and non-thyroid neck lumps.

Exclusion criteria

The exclusion criteria included articles not written in English and those that did not specifically mention the sample inadequacy rate for ultrasound-guided FNAs. Obviously irrelevant articles, including articles with incomplete data, articles looking at non-image-guided FNA, CT/MR-guided FNA, complications of FNA, repeat FNA, core biopsies, paediatric head and neck lesions and studies looking at <20 patients ($n < 20$) were excluded. Reviews, case reports, letters to author and comments were also excluded.

Data extraction

Full texts of all relevant articles were obtained and scrutinized independently by three authors. All extracted data were transferred to a standardized excel sheet for appropriate statistical analysis. Parameters evaluated were sample inadequacy rate, designation of the person performing the FNA (radiologist, clinician, cytopathologist or a combination), number of passes attempted and the availability of on-spot cytological assessment of the aspirate by either the cytopathologist or cytotechnician.

Statistical analysis

Statistical analysis was performed using R v. 2.15 (<http://www.R-project.org>). Estimates of inadequacy rate from articles were combined using meta-analysis (the metaprop function in the R package meta) to give a combined estimate for the overall inadequacy rate. Comparisons between groups were carried out using meta-regression (metareg function).

Table 2. Inadequacy rate (95% confidence interval) for different operators

Operator	Number	Inadequacy rate (%)
Radiologist with O/S assessment	9	6.9 (3.1–11.9)
Radiologist without O/S assessment	23	9.6 (6.8–12.8)
Clinician with O/S assessment	9	9.1 (4.7–14.7)
Clinician without O/S assessment	27	11.0 (8.4–14.0)
Cytopathologist (with or without radiologist support)	3	4.3 (2.4–6.8)

O/S, on site.

RESULTS

Primary search using MEDLINE from NHS evidence healthcare database and PubMed revealed 932 articles. Obviously irrelevant articles looking at non-head and neck lesions, non-ultrasound-guided FNAs and duplicates were removed. Abstracts of all relevant articles mentioning inadequacy rate of ultrasound-guided FNA for lesions in the head and neck were selected. Full texts of all relevant articles were obtained and scrutinized independently by two of the authors. The articles were evaluated and removed/retained according to pre-selected exclusion/inclusion criteria. We found one randomized control trial on ultrasound-guided FNA of head and neck lesions, two clinical trials on ultrasound-guided FNA of thyroid lesions and 75 other relevant articles, which met all the study criteria, taking the total number of pertinent articles to 78.

There were no Cochrane reviews. Several other reviews were found through Cochrane (10) and PubMed (54), but these were all related to non-image-guided FNA or ultrasound-guided FNA of thyroid nodules. No reviews were found specifically evaluating ultrasound-guided FNA of general head and neck lesions. We found one meta-analysis on diagnostic value of conventional and ultrasound-guided FNA for thyroid nodules, but not on head and neck lesions. Our review differs from those of others since we endeavour to include data reported from all head and neck lesions (thyroid and non-thyroid); specifically focusing on the role of different variables, such as operator designation, the presence of on-site cytopathologist etc., on the inadequacy rate of ultrasound-guided FNAs of all head and neck lesions.

The designation of the person performing the FNA was not convincingly confirmed in seven articles. Of the remaining 71 articles, ultrasound-guided FNA was performed in 32 by radiologists, 36 by clinicians (with the support of a radiologist in 2) and 3 by cytopathologists with/without help from a radiologist.

The overall estimate of sample inadequacy from the meta-analysis of all 78 studies was 9.3%, with a 95% confidence interval (CI) of 7.7–11.0%. The individual studies reported inadequacy rates ranging from 0% to 32%. Table 1 shows the inadequacy rate, with 95% CIs for each study.

Table 2 shows the inadequacy rate categorized by the operator type. Those studies where the FNA was performed by a cytopathologist (with or without help from a radiologist) had a lower error rate than those where FNA was performed by radiologists or clinicians, although this was not statistically significant ($p = 0.11$).

Table 3 shows the inadequacy rate categorized by on-site cytology. Those studies that had immediate cytological assessment by a cytopathologist or specialist clinician had significantly lower inadequacy rates than those where the slides were prepared or assessed by a cytotechnician, or where no immediate cytological assessment was available ($p = 0.01$). The method of assessment used in one article was unclear and could not be classified.

DISCUSSION

The term head and neck cancer covers a wide range of malignancies and takes into account regional variations, with the incidence of head and neck cancer ranging from 8 to 15/100,000 in England and Wales.¹⁶

FNA for head and neck tumours was first described in 1930s by Martin *et al.*⁸⁵ Over the last half century, clinician-performed palpable FNA has gradually been replaced by ultrasound-guided FNA performed under direct visualization.^{5–13} Palpable FNAs are associated with high inadequacy rates primarily owing to inaccurate needle positioning, the inhomogeneity of lesions and poor aspiration. This leads to a delay in the definitive diagnosis and treatment initiation, which has profound implications for trusts trying to meet national cancer targets. Image guidance for

Table 3. Inadequacy rate (95% confidence interval) with and without on-spot cytological evaluation

Assessment	Number	Inadequacy rate (%)
Immediate cytological assessment by cytopathologist or specialist clinician	16	6.0 (3.5–9.1)
Immediate cytological assessment by cytotechnician	5	11.2 (7.8–15.1)
Immediate slide preparation by a technician only	2	12.7 (8.5–17.4)
No immediate cytological preparation or assessment	54	10.3 (8.3–12.5)

procedure is on the rise, with ultrasound having advantages over CT owing to the lack of ionizing radiation, its dynamic nature and easy manoeuvrability. It also fares better than does MRI since it avoids the complexities of MR compatible equipment, the need for an open access scanner and the use of precious MR scanner time. Ultrasound provides information on the site of origin, characteristics of the lump, accurate delineation of adjacent anatomical structures, helps avoid necrotic and cystic areas and provides the opportunity of sampling impalpable lesions. It has been found to be extremely cost effective for guided head and neck FNA, and this can be further increased by having the samples read by a cytopathologist on the spot to reduce sample inadequacy.^{4,13,22,30,31,50} This provides the cytopathologist with a better correlation of the clinical situation, imaging findings and microscopic appearance. A cytopathologist in the clinic is considered to be the gold standard in the literature.^{1,15,86} Appreciation of the clinical context in which material is being reported is recognized as being essential in avoiding diagnostic errors in FNA assessment.⁸⁷ In most cases, an immediate provisional diagnosis can be given, or if necessary, a repeat aspiration can be performed.^{14,15} This includes taking specimens for other relevant investigations such as immunocytochemistry, which would otherwise have to be performed at another appointment.³

The overall inadequacy rate for head and neck lesions was found to be 9.3% in our systematic review with a range from 0% to 32%. The FNA can be performed by a radiologist, a trained clinician or a cytopathologist. In our review, 36 studies had FNAs performed by clinicians with a sample inadequacy rate of 10.8%; 32 had FNAs performed by radiologists with a sample inadequacy rate of 9.0%; while 3 had FNAs performed by a cytopathologist with the lowest sample inadequacy rate of

4.3% (Table 2). The difference was not statistically significant and probably just reflects the expertise of the particular cytopathologists in this small group of articles.

We found that 16 studies included in the review reported on-site evaluation of the aspirate to check for adequacy by a cytopathologist or a specialist clinician with an average sample inadequacy rate of 6.0%. The sample inadequacy rate for the 54 studies, without the benefit of immediate sample assessment averaged at 10.3% (Table 3), which was a statistically significant difference ($p = 0.02$). In five studies, a cytotechnician was present on-site to check the sample, with an adequacy rate of 11.2%, and in two studies, they just prepared the slides giving an inadequacy rate of 12.7%. Although one study²² has reported that sample adequacy could be checked on-site by a cytotechnician when a pathologist is not available, our data suggest that cytotechnician assessment does not provide any benefit over evaluation in the laboratory ($p = 0.73$).

CONCLUSION

Evidence suggests that delay in diagnosing head and neck cancer has been a major factor in the poorer survival rates in the UK than in some other countries in Europe.¹² This shifts interest towards optimizing the head and neck FNA service in this country. Our review looking at the inadequacy rate and other pertinent variables suggests that the best results are obtained with a one-stop cytopathologist-led FNA service, as recommended by NICE, where the pathologist reviews the specimen immediately, in relation to the clinical context, thereby deciding on adequacy and the need for further biopsies. However, the authors do acknowledge that alternative models for the provision of diagnostic head and neck clinics are possible.⁸⁸

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