

Main Article

Mr B Mettias takes responsibility for the integrity of the content of the paper

This paper was presented at the Midlands Institute of Otorhinolaryngology Winter Meeting, 17 January 2020, Cosford, UK.

Cite this article: Mettias B, Charlton A, Ashokkumar S. Outcome of two-week head and neck cancer pathway for the otolaryngology department in a tertiary centre. *J Laryngol Otol* 2021;**135**:869–873. <https://doi.org/10.1017/S0022215121002061>

Accepted: 20 January 2021
First published online: 5 August 2021

Key words:

Head And Neck Cancer; Waiting List; Early Detection Of Cancer; Guideline Adherence

Author for correspondence:

Mr Bassem Mettias, ENT Department, Leicester University Hospitals, Leicester LE1 5WW, UK
E-mail: bassemadel@hotmail.com

Abstract

Background. The two-week-wait head and neck cancer referral pathway was introduced by the Department of Health, and refined through National Institute for Health and Care Excellence guidelines which were updated in 2015.

Methods. A retrospective study was conducted of two-week-wait referrals to out-patient ENT from January to June 2018. The analysis included demographics, referral symptoms according to National Institute for Health and Care Excellence 2015 guidelines, cancer pick-up rates and positive predictive values.

Results. A total of 1107 patients were referred for suspected head and neck cancer over six months, with 6 per cent diagnosed with cancer. Neck lump, persistent hoarseness and throat pain were the most common presenting symptoms. Neck lump had the highest positive predictive value, followed by oral swelling. Oral bleeding and persistent unilateral sore throat showed significant positive predictive values. Investigation for metastatic head and neck cancer of an unknown primary or the involvement of other multidisciplinary teams could hinder the achievement of a 62-day treatment target.

Conclusion. The cancer pick-up rate from two-week-wait referrals is only 1.5 times higher than routine referrals. The 'red flag' symptoms given in the 2015 National Institute for Health and Care Excellence update would benefit from further review.

Introduction

In the year 2000, the Department of Health developed UK National Guidelines for referring suspected head and neck cancer cases. Termed the two-week-wait pathway, in England, this means suspected cancer patients should be seen by a specialist within 14 days of the primary care referral, to aid early detection. The target in England is 93 per cent.¹ The National Institute for Health and Care Excellence (NICE) generated referral guidelines in 2005, which were revised in 2015 and last revised in 2021 without further new changes.² Despite this, the cancer pick-up rate from two-week-wait referrals is not significantly different from non-urgent referrals.^{3,4} Since the introduction of the guidelines, cancer pick-up rates range from 6.2 per cent to 10 per cent.^{3,5}

There is a lack of published data exploring the pathway after the referral.⁶ There is also a paucity of research evaluating the effect of the revision of NICE referral guidelines in 2015 regarding cancer detection rates and compliance of referrals with the guidelines. This study explored these factors in diagnosed cancer patients from the two-week-wait out-patient otolaryngology clinic.

Cancer patients should receive their first definitive treatment within 31 days of the diagnosis,¹ measured from the date when the patient is informed of the diagnosis and a management strategy is agreed, ideally after the multidisciplinary team (MDT) meeting. The patients should start first definitive treatment of their cancer within 62 days of their original referral. The target for these outcomes in England is 85 per cent. This means there are only 31 days for the specialist to diagnose and stage the cancer.^{1,2}

Materials and methods

Analysis was based on existing, anonymised data, and therefore did not require ethics committee approval.

A retrospective audit was conducted for the period from January to June 2018 in a tertiary centre for head and neck surgery. Referral symptoms were analysed for all ENT two-week-wait referral patients, and sensitivity, specificity and positive predictive values were calculated for each symptom. In cases where cancer was diagnosed, the site of primary cancer, time taken to reach a diagnosis and first treatment, and staging and histology of the cancer were reviewed. Statistical analysis was conducted using Microsoft Excel® spreadsheet software for the cancer pick-up rate, compliance with the NICE referral criteria (Table 1) and compliance with the national cancer wait targets. The symptoms of 'sore throat' and

Table 1. NICE 2015 referral criteria guidelines for two-week-wait referral to head and neck specialist clinic

Laryngeal cancer
– Persistent unexplained hoarseness
– Persistent & unexplained neck lump
Oral cancer (when assessed first by a dentist)
– Unexplained ulceration in oral cavity lasting >3 weeks
– Persistent & unexplained neck lump
– Lump on lip or in oral cavity consistent with oral cancer
– A red or red & white patch in oral cavity consistent with erythroplakia or erythroleukoplakia
Thyroid cancer
– Unexplained thyroid lump

NICE = National Institute for Health and Care Excellence

'odynophagia' were applied inconsistently and often overlapped, and so were merged under the refined variable 'sore throat'.

Clinical findings and outcomes were recorded anonymously. The data were collected from electronic clinic letters, patient information software (Integrated Clinical Environment ('ICE')) and InfoFlex digital health software (for access to MDT meeting information). This was an audit of clinical practice and formal ethical approval was not required.

Results

Demographics

A total of 1107 patients were referred through the two-week-wait pathway, with an average of 184 (standard deviation = 14) monthly referrals. The national target for specialist review within two weeks of referral was met 98.8 per cent of the time, with patients being seen within 6 days on average. History of smoking and alcohol were documented in 74 per cent of specialist letters. Performance status was rarely documented at all.

The male-to-female ratio of referral patients was 2:3. The youngest referral patient was 15 years old, with only 0.8 per cent of referrals from the 15–20 years bracket. Most referrals fell in the age groups 40–60 years and 60–80 years, accounting for 37.4 per cent of referrals each. However, of diagnosed cancer patients, 51 per cent were in the 60–80 years age group, with an average age of 60 years.

Of all referred patients, 66 (6 per cent) were diagnosed with cancer. Thirty-three per cent of the cancer patients were female. The prevalence rates of different head and neck cancers are illustrated in Figure 1. This pie chart shows that the commonest descending order of head and neck cancers were oropharyngeal squamous cell carcinoma (SCC), lymphoma and laryngeal SCC. Meanwhile, the highest primary site were similar for oropharynx and neck nodes (unknown primary and lymphoma). One per cent of head and neck cancer was metastatic disease in Virchow's node from a hepatobiliary primary. The histology of head and neck cancer was SCC in 68 per cent, lymphoma in 20 per cent and adenocarcinoma in 12 per cent. Half of the adenocarcinomas were metastatic lung cancer with neck nodes, while the other half were from the cervical oesophagus.

Compliance with referral criteria

Fifty-two per cent of the referrals were consistent with the NICE 2015 criteria. In the 48 per cent of non-compliant

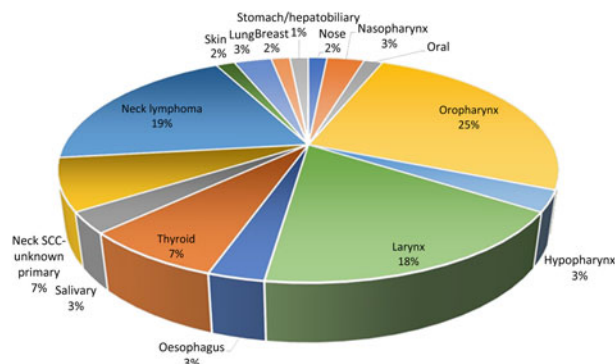


Fig. 1. Incidence of cancer in different head and neck regions. SCC = squamous cell carcinoma

referrals, 38 per cent of cases had isolated globus sensation misinterpreted as sore throat. The remaining referrals represented either inappropriate use of the service or misunderstanding of the episodic history of the patient. The frequencies of all 'red flag' symptoms are illustrated in Table 2 (including original 2005 criteria, which were removed in the 2015 revision), along with the sensitivity, specificity and positive predictive values in relation to cancer.

In those patients diagnosed with cancer, neck lump was the most common presentation. This was followed by persistent hoarseness and sore throat. One patient diagnosed with laryngeal cancer presented with mixed globus sensation, and two other red flag symptoms of persistent unilateral sore throat and voice changes. Neck lump had the highest positive predictive value for cancer (17.4 per cent), followed by oral swelling (10.2 per cent).

The analysis showed remarkable positive predictive values for those criteria removed during the 2015 guideline revision; specifically, 9.7 per cent for otalgia and 4 per cent for sore throat. Oral bleeding – a symptom which is excluded from both the 2005 and 2015 NICE guidance – had a similar positive predictive value (8 per cent) to dysphagia in this study.

The cancer pick-up rate was equal (0.45 per cent) for each symptom of sore throat, dysphagia and oral swelling, while it was 0.34 per cent (two patients) for otalgia. The term 'oral swelling' described asymmetrical tonsillar enlargement or a visible oropharyngeal lesion.

Oropharyngeal cancer had the largest diversity in presentations (Figure 2), with the commonest being a cervical lymph node at level II (59 per cent).

Timing – compliance with national targets

The average time from tissue diagnosis to the MDT meeting was 14 days. The average time from MDT decision to the beginning of definitive treatment was 21 days. The MDT discussed 105 cancer cases during this six-month period for all head and neck subspecialties (including maxillofacial and thyroid). Sixty-three patients (60 per cent) were referred through the two-week-wait pathway, with 28 referrals (40 per cent) complying with the 62-day target. Forty-two patients (40 per cent) were referred through a routine pathway, with 13 referrals (30 per cent) compliant with the 62-day first definitive treatment target. The chi-square value was 0.86 and the *p*-value was 0.35 (non-significant at *p* < 0.05). The Fisher's exact test value was 0.45, and the *p*-value was not significant at *p* < 0.05.

From ENT two-week-wait referrals, there was 64 per cent and 52 per cent compliance with the 31-day and 62-day targets

Table 2. Relationship between diagnosed cancer cases and presenting symptoms

Parameter	Hoarseness	Oral ulcer	Oral swelling	Dysphagia	Neck lump	Oral bleeding	Otalgia	Sore throat
Year of NICE guidance symptom inclusion	2005 & 2015	2005 & 2015	2005 & 2015	2005 (ENT) & 2015 (GI)	2005 & 2015	N/A	2005	2005
Cases (n (%))	159 (17.8)	10 (1.1)	39 (4.4)	50 (5.6)	209 (23.4)	13 (1.5)	32 (3.5)	108 (12.1)
% cancer cases	1.5	0.1	0.45	0.45	4	0.1	0.34	0.45
Sensitivity (%)	21	2	6	6	55	2	5	6
Specificity (%)	14	1	3	4	17	1	3	10
PPV (%)	8.9	10	10.2	8	17.4	8	9.7	4

NICE = National Institute for Health and Care Excellence; GI = gastrointestinal; N/A = not applicable; PPV = positive predictive value

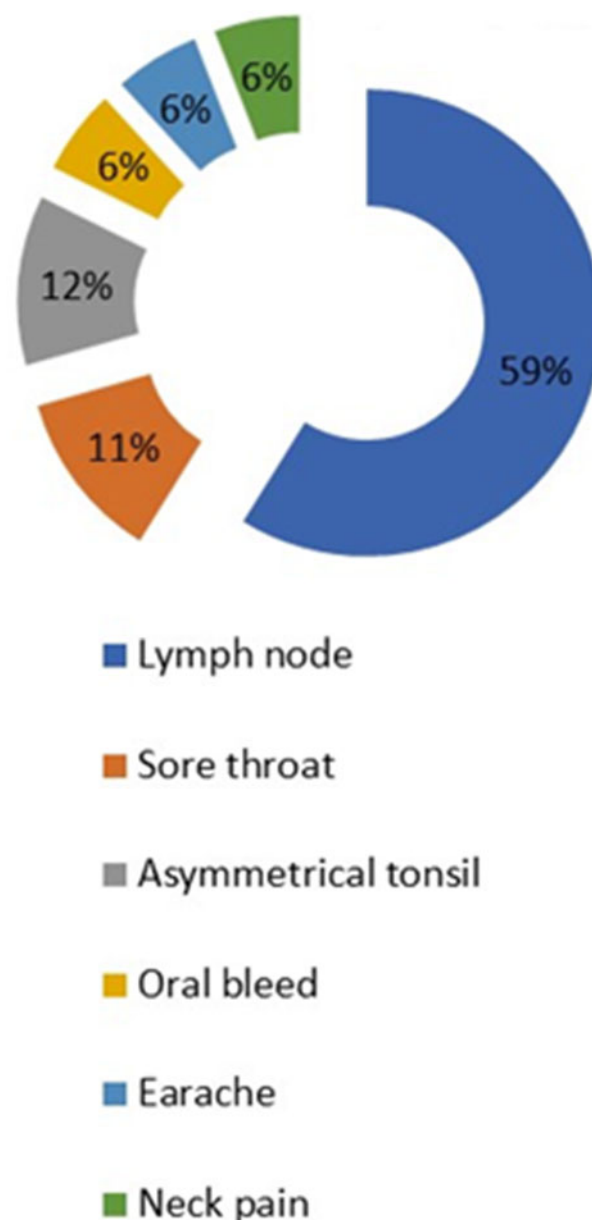


Fig. 2. Oropharyngeal squamous carcinoma presentation symptoms.

for cancer management, respectively. The mean time scales were 32 and 72 days respectively, while the medians were 27 and 67 days respectively. Of the 52 per cent of patients ($n = 33$) where the 62-day treatment target was missed, 55 per cent had a long wait between diagnosis and treatment, while 45 per cent had their lag during the investigations conducted to determine the diagnosis. The 104 days' waiting target was breached in five patients (7.5 per cent).

Seventeen per cent of patients with diagnosed head and neck cancer ($n = 11$) died during this period. All mortality cases had advanced disease on presentation, except one with human papillomavirus positive, early oropharyngeal cancer, which progressed despite chemoradiation treatment.

Discussion

Epidemiology

Head and neck cancer is the 15th most common cause of cancer death in the UK, accounting for 2 per cent of all cancer deaths in 2017. However, over the last decade, head and

neck cancer mortality rates have increased by around 14 per cent in the UK.¹

Referral symptoms

Tikka *et al.* showed the commonest referral symptoms compliant with NICE guidelines were neck lump and hoarseness, with frequencies of 22.5 per cent and 20.2 per cent respectively, and positive predictive values of 17 per cent and 7.8 per cent respectively.⁵ McKie *et al.* reported a slightly higher frequency for oral swelling (20 per cent) than for neck lump (19 per cent) and hoarseness (7 per cent); their study patients were from the maxillofacial surgery department, which one would expect to attract more referrals with oral cavity pathology than laryngeal pathology.³ Our study showed a similar positive predictive value for dysphagia (8 per cent) as in McKie and colleagues' study (7.8 per cent), whereas Tikka and colleagues' cohort study reported a much higher value (18.2 per cent).^{3,5}

Neck lump in our study had the highest positive predictive value for cancer (17.4 per cent), followed by oral swelling (10.2 per cent). A recent retrospective study conducted in London also found the highest positive predictive values for oral swelling and neck lump. The most frequent reasons for referral were persistent hoarseness, neck lump, and unexplained throat discomfort or pain;⁷ these were also the most common reasons for referral in our study, but with a different order of frequency.

In this study, patients were risk-stratified after their first visit; those who were neither discharged nor scheduled for biopsy were classified as medium risk.⁷ Of this group, 32 per cent were diagnosed with cancer, suggesting that they should remain on the two-week-wait pathway. The classification seemed more of academic value.

Tikka *et al.* showed similar figures for commonest presentations in a recent cohort study.⁸ They emphasised the high predictive value of combining symptoms in the form of a risk calculator. They included unintentional weight loss and sore throat in an updated risk calculator.⁸ Their findings are consistent with our study, though we have not evaluated weight loss, as it is a non-specific symptom associated with a wide range of diseases other than head and neck cancer.

Assessment of 2015 referral criteria update

Most primary care providers use a tick box form displaying the NICE 2015 criteria, for direct referral of suspicious cases to secondary care.⁹ Several studies have shown the cancer pick-up rate to be similar for two-week-wait referrals and routine referrals,^{3,10} which is supported by our finding of no significant difference between the two.

In the 2015 update, NICE removed the following criteria: persistent sore throat, unexplained tooth mobility not associated with periodontal disease for more than three weeks, unilateral unexplained pain in the head and neck area for more than four weeks, and unexplained persistent otalgia with normal otoscopy findings. Furthermore, a duration was not specified for the symptom of persistent hoarseness. Difficulty swallowing for three weeks was moved to the gastrointestinal two-week-wait referral criteria.² Patients with 'high' dysphagia may have hypopharyngeal malignancy, which can be missed during flexible oesophagoscopy or can delay diagnosis if not initially referred to ENT.⁴

The positive predictive values reported in a cohort study were 5.9 per cent and 18.8 per cent for unexplained persistent sore throat and odynophagia respectively.⁵ The authors

advocate that the revised NICE 2015 referral criteria can miss 3 per cent of early head and neck cancer diagnoses. Our study demonstrated similar significant positive predictive values for sore throat (4 per cent) and otalgia (9.7 per cent). A recent study also agreed with the high positive predictive value for persistent sore throat (9.5 per cent).¹¹ The authors stated the need to refine the NICE criteria in the next update.¹¹ A recent study conducted in London showed a decrease in cancer detection rate, from 10 per cent to 3.76 per cent, with implementation of the 2015 NICE update; this could point to missing cases that are later diagnosed during routine referral.⁷ However, the authors did not compare cancer pick-up rate with routine referrals. They also recommended a review of the referral scheme in the current guidelines.⁷ Tikka and colleagues' study from Scotland showed a similar failure of the NICE 2015 guidelines to improve the early detection rate in the UK.⁸

Globus sensation as a sole symptom had no association with head and neck cancer.⁵ When globus sensation co-existed with other symptoms such as otalgia or oral bleeding, the risk of head and neck cancer increased by 4 and 5.6 times respectively.⁵ None of these symptoms on their own are an indication for specialist referral according to NICE guidelines;² however, the combination would likely still benefit from referral. The same principle was witnessed in our study: dysphagia had a positive predictive value of 8 per cent, but when combined with sore throat this generated a positive predictive value of 12 per cent.

In light of the above evidence, we recommend a review of the NICE 2015 referral criteria for the addition of oral bleeding, and unexplained persistent unilateral sore throat or earache. The duration of persistent hoarseness also needs to be clarified.

- Head and neck cancer diagnosis from the two-week head and neck referral pathway is very low (6 per cent), only 1.5 times higher than routine referrals
- There is no significant difference between urgent and routine referrals in compliance with the 62-day treatment target for diagnosed cancer patients
- Neck lump is the most common reason for referral with the highest positive predicate value for cancer
- Oropharyngeal cancer is the commonest head and neck malignancy, which has variable presentations
- Investigation for metastatic head and neck cancer of an unknown primary or other multidisciplinary team involvement could delay target treatment
- The 2015 National Institute for Health and Care Excellence update would benefit from further review

Conclusion

The cancer pick-up rate from two-week-wait referrals is only 1.5 times higher than that from routine referrals. Neck lump is the most common reason for referral with the highest positive predicate value for cancer. Oropharyngeal cancer is the commonest head and neck malignancy, which has a wide range of presentations. The red flag symptoms given in the 2015 NICE update would benefit from further review for the inclusion of unilateral sore throat, unilateral otalgia and oral bleeding.

Data availability statement. The data used to support the findings of this study are available from the corresponding author upon request.

Competing interests. None declared

References

- 1 Cancer Research UK. In: <https://www.cancerresearchuk.org/> [4 September 2019]

- 2 NICE. Head and neck cancers - recognition and referral. In: <https://cks.nice.org.uk/head-and-neck-cancers-recognition-and-referral/> [4 September 2019]
- 3 McKie C, Ahmad UA, Fellows S, Meikle D, Stafford FW, Thomson PJ *et al.* The 2-week rule for suspected head and neck cancer in the United Kingdom: referral patterns, diagnostic efficacy of the guidelines and compliance. *Oral Oncol* 2008;**44**:851–6
- 4 Hobson JC, Malla JV, Sinha J, Kay NJ, Ramamurthy L. Outcomes for patients referred urgently with suspected head and neck cancer. *J Laryngol Otol* 2008;**122**:1241–4
- 5 Tikka T, Pracy P, Paleri V. Refining the head and neck cancer referral guidelines: a two-centre analysis of 4715 referrals. *Clin Otolaryngol* 2016;**41**:66–75
- 6 Douglas CM, Carswell V, Montgomery J. Outcomes of urgent suspicion of head and neck cancer referrals in Glasgow. *Ann R Coll Surg Engl* 2019;**101**:103–6
- 7 Gao C, Qin C, Freeman S, Oskooee N, Hughes J. Two week wait referral criteria - heading in the right direction? *J Laryngol Otol* 2019;**133**:704–12
- 8 Tikka T, Kavanagh K, Lowit A, Jiafeng P, Burns H, Nixon IJ *et al.* Head and neck cancer risk calculator (HaNC-RC)—V.2. Adjustments and addition of symptoms and social history factors. *Clin Otolaryngol* 2020;**45**:380–8
- 9 Duvvi SK, Thomas L, Vijayanand S, Reddy KT. Two-week rule for suspected head and neck cancer. A study of compliance and effectiveness. *J Eval Clin Pract* 2006;**12**:591–4
- 10 Pracy P. The 2-week wait head & neck cancer referrals: is this system working? *The Otorhinolaryngologist* 2013;**6**:182–6
- 11 Allam A, Nijim H. Persistent unilateral sore throat: should it be included in the 2-week wait referral criteria by NICE. *Int J Otolaryngol* 2019;**5**:4920514