Symptom-based remote assessment in post treatment head and neck cancer surveillance

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Symptom-based remote assessment in post treatment head and neck cancer surveillance: a prospective national study

Abstract

Objectives

To report the incidence of locoregional recurrence in HNC patients under surveillance following treatment undergoing symptom-based remote assessment.

Design

A 16-week multicentre prospective cohort study.

Setting

UK ENT departments.

Participants

HNC patients under surveillance following treatment undergoing symptom-based telephone assessment.

Main outcome measures

Incidence of locoregional recurrent HNC after minimum 6-month follow-up.

Results

Data for 1,078 cases were submitted by 16 centres, with follow-up data completed in 98.9% (n=1,066).

Following telephone consultation, 83.7% of referrals had their face-to-face appointments deferred (n=897/1,072). New symptoms were reported by 11.6% (n=124/1072) at telephone assessment; 72.6% (n=90/124) of this group were called for urgent assessments, of whom 48.9% (n=44/90) came directly for imaging without preceding clinical review.

The sensitivity and specificity for new symptoms as an indicator of cancer recurrence were 35.3% and 89.4%, respectively, with a negative predictive value of 99.7% (p=0.002).

Locoregional cancer identification rates after a minimum of 6 months of further monitoring, when correlated with time since treatment,were: 6.0% (n=14/233) <1 year; 2.1% (n=16/747) between 1 and 5 years; and 4.3% (n=4/92) for those >5 years since treatment.

Conclusions

Telephone assessment, using patient-reported symptoms, to identify recurrent locoregional HNC was widely adopted during the initial peak of the COVID-19 pandemic in the UK. The majority of patients had no face-to-face reviews or investigations. New symptoms were significantly associated with the identification of locoregional recurrent cancers with a high specificity, but a low sensitivity may limit symptom assessment being used as the sole surveillance method.

Key points

1. This is a prospective multicentre study of 1,078 patients in 16 UK centres being followed-up after head and neck cancer treatment who underwent symptom-based telephone assessment, with a minimum subsequent follow-up of 6 months and data completion rate of 98.9%.
2. Following telephone assessment, 48.9% of patients complaining of new symptoms who underwent further assessment were sent directly to an imaging investigation prior to face to face appointment.
3. If symptom free at telephone assessment, 97.7% were still free of locoregional disease after a minimum of 6 months of further monitoring (negative predictive value, p=0.0002).
4. Oropharyngeal and laryngeal cancers represented over two thirds of all surveillance practice (67.9%).
5. Despite a high specificity (89.4%), the sensitivity of new symptoms being linked to further locoregional cancer by 6 months was low (35.3%), potentially limiting its usefulness as the only test for assessing these patients for recurrent disease.

Introduction

Face-to-face appointments are the standard of care after treatment for head and neck cancer (HNC). These encounters allow many of the complex needs of these patients to be met, including the detection of recurrent disease, monitoring for treatment related toxicity, addressing rehabilitation and nutritional needs, and tailored patient support through the survivorship phases.[1] The development of a relationship between this group of patients with the clinical team is fundamental in the holistic approach to their care, which should include psychological support, patient education and addiction counselling.[2] Though guidelines exist for follow-up intervals in post-treatment HNC patients, these are based on expert recommendations and there is a paucity of evidence to support its efficacy.[1,2]

A recent national audit of current UK practice for post-treatment HNC patients showed significantly higher detection rates of disease in patients who had expedited appointments, compared with routine follow-up, suggesting potential benefits from a patient-initiated model.[3]

Since the emergence of COVID-19 in early 2020, a shift towards telemedicine has formed a fundamental part of NHS practice. Minimising person-to-person contact to reduce the spread of infection and preserve resources during the pandemic has influenced many aspects of healthcare,[4,5] including outpatient services in ENT and head and neck surgery.[6] Whilst there was reluctance to perform routine per oral examination or flexible nasendoscopy, the additional risk of attending hospital in person for follow-up seemed excessive, and so a remote model to allow symptom assessment could be justified. In the new patient setting, remote assessment may allow triage directly to imaging investigations for the highest risk patients, and even avoid hospital attendance entirely for the lowest risk for whom clinical examination may add little diagnostic value.[7] This not only increases efficiency and resource management, but may also improve patient compliance and satisfaction by eliminating travel and wait times. Unfortunately, this surveillance cohort does not have a validated risk calculator to support decision making, but national audit data may still be able to provide useful context for the patients being assessed.[3,8]

In consultation with ENT UK (British Association of Otorhinolaryngology - Head and Neck Surgery) and BAHNO (British Association of Head and Neck Oncologists), and through collaboration with INTEGRATE (The UK ENT Trainee Research Network), a National Service Evaluation was rapidly developed and implemented to monitor this unique shift in practice towards telephone assessment.[9]

Objectives

The primary aim of this study was to understand the incidence of locoregional recurrence in HNC patients under post-treatment surveillance undergoing symptom-based remote assessment during the initial peak of COVID-19 in the UK.

Methods

The protocol for this study was published in advance at https://entintegrate.co.uk. This manuscript has been prepared with reference to the STROBE checklist for cohort studies.

Ethical considerations

The Health Research Authority decision tool determined the study design to fall under the remit of service evaluation, and so no ethical approval was required (available at: http://hra-decisiontools.org.uk/research/).

Study design and setting

A national prospective service evaluation was conducted, supported by ENT UK and BAHNO, and delivered using the INTEGRATE network. All UK ENT departments were invited to participate via social media and mailouts from the supporting organisations. Sites could open at any point during the prospective data collection period. Registration as per local governance guidelines was required to participate.

Participants

Patients were eligible for inclusion if they were under surveillance following treatment for HNC in secondary care, and were undergoing telephone consultation as part of routine follow-up. Patients with known residual/recurrent disease were excluded.

Data collection

Cases were identified over a 16-week period, between 23rd March and 13th July 2020. Final submission of data was accepted after a minimum 6-month follow-up period for all patients. To be eligible for inclusion, cases had to have complete demographic and symptom data with no null data points. To facilitate this, a standardised electronic case report form was created using Excel software (Microsoft Corporation, Washington, USA) and made available online (**Supplementary material**).

Two bespoke results, derived from the 2018 INTEGRATE/BAHNO National Audit of Post-Treatment HNC surveillance,[3] were displayed by the tool for each patient, which were based on the patient characteristics and symptom data entered [**figure 1**]. To promote the submission of complete and valid data, these results were only displayed if all relevant fields were completed by the clinician. Firstly, the clinician was presented with the overall rate of cancer diagnosis related to the time since completion of treatment and the presence of new symptoms. Secondly, the tool presented the highest PPV for any relevant symptom that was reported.

Data were held offline at each centre until the follow-up period had passed for all patients, whereupon the patient record was checked by the local team for a diagnosis of cancer at any time since their initial telephone consultation.

The following data were collected: patient demographics; smoking and alcohol history; a symptom inventory comprising 17 locoregional and three general symptoms (based on the HaNC-RC-v2 and United Kingdom National Multidisciplinary Guidelines for Head and Neck Cancer 2016)[8,10] (**supplementary material**); subsequent management, including face-to-face reviews and investigations; clinician and patient preference

for review/investigation; diagnosis of cancer; time since completion of treatment; and the site of the primary cancer for which they were under surveillance.

Clinicians were asked to record if the patient had experienced '*any new symptoms since your last appointment?*'. Only if answered 'yes 'were further symptom questions revealed through conditional formatting.

The Project Management Team (PMT) handled only anonymised data, with all identifiable information removed prior to submission by the local teams. Where missing or ambiguous data were identified by the PMT, a query was raised with the local site to clarify each data point. Where missing data could not be resolved, that record was excluded from relevant analysis.

Data analysis

The primary outcome was the diagnosis of residual/recurrent/new primary locoregional cancer after a minimum of 6 months follow-up. Distant metastases only were not included.

No *a priori* sample size calculation was performed. Categorical variables were compared using the Fisher's exact test, with a two-tailed p value of 0.05 taken as significant. Analysis was performed using R statistical software (R Foundation, Vienna, Austria).

Results will be presented in tables displaying the entire cohort of patients in view of reported symptoms, to show the association of symptoms to further cancer in the context of time since initial presentation and cancer subsite.

Interim report

After 8 weeks, interim data were requested from participating centres and a report was produced to allow rapid feedback of preliminary findings to the UK ENT community. This report was disseminated electronically via an ENTUK mailout on 3rd June 2020 and was hosted online https://entuk.org and https://entintegrate.co.uk (**supplementary material**).

Results

Centres and submissions

Final data were submitted by 16 UK centres who registered to take part (13 in England, 2 in Scotland, 1 in Wales) with 1,078 cases eligible for analysis with complete demographic and symptom data (median 60.5 cases per centre; range 2 to 218; interquartile range (IQR) 8 to 94). A valid outcome from the remote assessment was recorded in 99.4% (n=1,072/1,078) and valid 6-month follow-up was reported in 98.9% (n=1,066/1,078).

The median age for all subjects was 65 (range 19 to 93 years; IQR 56 to 72 years) and 71.9% were male (n=775).

New symptoms and management outcome

Table 1 shows the identification of locoregional cancer for patients reporting new symptoms, further divided by assessment outcome. The overall incidence of newly identified cancer after 6-month minimum follow-up was 3.2% (n=34/1,066).

At the time of telephone assessment, 14.5% (175/1072) patients were given an urgent appointment, with 69.1% (n=121/175) attending directly for a face-to-face clinic appointment and 30.9% (n=54/175) coming straight to an imaging investigation without prior face-to-face clinical review. For the subset of patients reporting new symptoms, the rate of direct to imaging investigations was significantly higher (48.9% vs 11.8%, n=44/90 vs 10/85; p<0.001)

Following telephone consultation, 11.6% (124/1,072) patients reported new symptoms and 83.7% of referrals had their face-to-face appointments deferred (n=897/1,072). There were 34 patients (3.2%) who reported new symptoms and also had their appointments deferred, none of whom developed locoregional recurrence in the subsequent surveillance period. In those being urgently assessed, the incidence of new locoregional disease was significantly higher in those with new symptoms (13.3% vs 1.2%, n=12/90 vs 1/85; p=0.0026).

Overall, the sensitivity and specificity for the association between new symptoms and new locoregional cancer by the end of the 6-month minimum surveillance period were 35.3% and 89.4% (positive predictive value (PPV) 9.8%; negative predictive value (NPV) 97.7%; p=0.0002).

Time since completion of treatment

Locoregional cancer identification rates in the study follow-up period, related to time since completion of treatment, were as follows: 6.0% (n=14/233) within 1 year; 2.1% (n=16/747) between 1 and 5 years; and 4.3% (n=4/92) of those still under follow-up after 5 years (**table 2**). There was a significant association between new symptoms and further cancer for all three cohorts. The lowest specificity was amongst patients more than five years out from treatment (81.8%), highlighting this group as the most at risk of not reporting new symptoms but then developing further cancer during the surveillance period. It should be noted that standard practice in the UK is to follow HNC patients for a period of 5 years, therefore patients in this cohort still under follow up after this time are unlikely to be representative of all patients treated for HNC.

Cancer subsite

Table 3 shows the distribution of head and neck cancers under post-treatment follow-up by anatomical site. The commonest sites were oropharynx (39.7%; n=426) and larynx (28.2%; n=302), comprising 67.9% of all patients. The rates of reporting new symptoms at telephone assessment are also presented, alongside the locoregional cancer identified by the end of the 6-month minimum surveillance period. Associations between these two factors are explored for each primary site. Cancers of the oral cavity (85.7%), larynx (87.4%), hypopharynx (88.7%) and oropharynx (89.2%) had the lowest specificities, highlighting these primary sites as the most at risk of not reporting new symptoms but then developing further cancer during the surveillance period.

Discussion

This prospective multicentre cohort study was uniquely placed to investigate a major shift in practice in HNC surveillance, catalysed by the COVID-19 pandemic in the UK. The findings corroborate those of previous retrospective studies, showing symptoms to be an effective method for identifying residual, recurrent or new primary disease in this group of patients, but which may have been confounded by face-to-face clinical examination.[3,11,12]

Nearly three-quarters of the 11.6% of patients who reported new symptoms at telephone assessment were offered an urgent face-to-face appointment or imaging investigation. Additionally, the rate of locoregional recurrence was significantly higher in those who reported new symptoms (9.8%) compared to those who were symptom free at time of telephone assessment (2.3%; p=0.0002, **Table 1**). This association suggests that using patient-reported symptoms as a predictor of disease may be an appropriate initial assessment tool in similar contexts. Current practice relies heavily on scheduled outpatient reviews but it is possible that focusing resources on patients who report new symptoms could lead to earlier identification of locoregional recurrent disease, as well as save resources on potentially superfluous outpatient appointments.

However, caution must be observed, as the relatively low sensitivity of 35.3% indicates a reasonable number of patients are found to have further locoregional disease who may not present with specific symptoms. The high specificity (89.4%) reflects the low incidence of cancer in those patients who did not report new symptoms. These findings were consistent even when stratifying for time since completion of treatment and by cancer subsite, showing agreement across a wide spectrum of patients. A small number of patients (22) were identified to have further cancer during the surveillance period, and this is reflected in the groups with lower specificity. No particular group was identified to be at a markedly higher risk of developing further cancer having reported no new symptoms, as shown by the relatively high specificities (time since treatment: 81.8% - 91.4%, cancer subsite: 85.7%-96.6%). These findings may offer further impetus for adoption of a patient-initiated, symptom-based follow-up model, as previously proposed,[3] but in conjunction with additional elements given the low sensitivity.

Symptom-based remote assessment was not shown to be equally effective in all subgroups investigated in the present study. New symptoms in patients over 5 years since initial treatment did not correlate well with the development of new cancers (specificity 81.8%). It was also observed that the rate of further cancers in this group was higher than for patients 1-5 years post treatment. As such, this cohort is unlikely to be representative of all HNC patients and caution should be observed for remote review, especially for HNC subtypes like laryngeal cancer, which have previously been shown to recur later than oropharyngeal and hypopharyngeal subtypes.[13]

It should be noted that many aspects of the standard of care pathway for post-treatment HNC patients were disrupted by the Covid-19 pandemic. Most notably, the shift to remote consultations precluded any chance of physical examination at the time of assessment. As such, symptoms could not be linked to clinical signs, and incidental examination findings in otherwise asymptomatic patients would never be investigated. Clinicians should be mindful when conducting remote assessments that early post-treatment symptoms can mimic those of residual or recurrent disease, and as such, have a low threshold for investigating patients further.[14]

During this initial period of the COVID-19 pandemic, instrumentation of the upper aerodigestive tract was discouraged over fears of contamination and aerosol generation.[15] This shift in practice was at odds to the current practice of HNC surveillance in the UK, where routine scheduled clinical review including flexible nasendoscopy is gold standard.[10] The PET-NECK trial showed a scheduled FDG-PET CT at 3 months resulted in lower morbidity and costs than routine neck dissections following chemoradiotherapy for head and neck squamous cell carcinoma.[16] Other studies have suggested a role for FDG-PET CT for detection of further

disease at the primary site.[14,17,18] It is possible that wider adoption of scheduled post treatment imaging, used alongside a patient-reported symptom-based model, may facilitate earlier detection of recurrence and be more responsive to patients needs. The PET-NECK-2 trial may go some way towards answering this question, though results are still some way off.[19]

Limitations

The following limitations are acknowledged: the use of only local data may have missed patients who subsequently presented to other units; it is not possible to assert that consecutive patients were included from all centres or submitted by each clinician; local practices may have included pre-screening of suspected HNC appointments to ensure they were suitable for telephone assessment; and the rate of oral cancer was lower than anticipated, reflecting low engagement from oral surgery and maxillofacial specialties.

Finally, asking about 'any new symptoms since your last appointment 'may have been interpreted differently by individual clinicians. For example, the recurrence of a symptom from the primary disease presentation, or a worsening of an already prevalent symptom, may not have been interpreted as truly 'new', influencing the recording.

Conclusion

Telephone assessment, using patient-reported symptoms, to identify new locoregional disease in post-treatment HNC patients was widely adopted during the initial peak of the COVID-19 pandemic in the UK. The majority of patients had no face-to-face reviews or investigations as a result.

New symptoms were significantly associated with the identification of locoregional recurrent cancers with a high specificity, but a low sensitivity may limit symptoms alone being used as the sole surveillance method.

However, patient-reported symptoms, in combination with other surveillance strategies may be acceptable to patients and facilitate a more appropriate use of healthcare resources.

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***Table 1**: Identification of locoregional recurrence by report of new symptoms and assessment outcome.*

		Further locoregional cancer identified					
		At time of assessment			**By end of 6-month minimum surveillance period**		
	% of all cases	Cancers	Total	%	Cancers	Total	%
New symptoms	**11.6**	**12**	**124**	**9.7**	**12**	**122**	**9.8**
Urgent assessment	72.6	12	90	13.3	12	89	13.5
Non-urgent	27.4	0	34	0.0	0	33	0.0
No new symptoms	**88.4**	**1**	**948**	**0.1**	**22**	**944**	**2.3**
Urgent assessment	9.0	1	85	1.2	2	85	2.4
Non-urgent	91.0	0	863	0.0	20	859	2.3
TOTAL	**100.0**	**13**	**1072**	**1.2**	**34**	**1066**	**3.2**

Table 2: Comparison of the incidence of new symptoms at telephone assessment with the identification of further cancer before the end of the 6-month minimum surveillance period, stratified by time since completion of treatment.

Note: sub-groups with lower specificity are at greater risk of presenting with no symptoms but then developing further cancer.

	Overall		**New symptoms reported at telephone assessment**		**Further locoregional cancer identified by end of 6-month minimum surveillance period**		**Association between new symptoms and further cancer**	**NPV**	**PPV**	**Sens**	**Spec**
Time since completion of treatment	n	%	n	%	n	%	*p*	%	%	%	%
≤1 year	233	21.7	37	15.9	14	6.0	0.0467	95.4	13.9	35.7	85.8
>1 year ≤5 years	747	69.7	68	9.1	16	2.1	0.0471	98.2	6.0	25.0	91.4
>5 years	92	8.6	19	20.7	4	4.3	0.0267	98.6	15.8	75.0	81.8
TOTAL	1072	100	124	11.6	34	3.2	0.0002	97.7	9.8	35.3	89.4

Table 3: Comparison of the incidence of new symptoms at telephone assessment with the identification of further cancer before the end of the 6-month minimum surveillance period, stratified by site of primary cancer.

Note: sub-groups with lower specificity are at greater risk of presenting with no symptoms but then developing further cancer.

	Overall		**New symptoms reported at telephone assessment**		**Further locoregional cancer identified by end of 6-month minimum surveillance period**		**Association between new symptoms and further cancer**	**NPV**	**PPV**	**Sens**	**Spec**
Site of primary cancer	n	%	n	%	n	%	*p*	%	%	%	%
Oropharynx	426	39.7	51	12.0	8	1.9	0.0008	99.2	10.0	62.5	89.2
Larynx	302	28.2	42	13.9	16	5.3	0.0503	95.8	12.2	31.3	87.4
Thyroid	61	5.7	6	9.8	2	3.3	0.1885	98.2	16.7	50.0	91.5
Hypopharynx	55	5.1	6	10.9	2	3.6	1.0000	95.9	0.0	0.0	88.7
Oral cavity	50	4.7	8	16.0	1	2.0	0.1600	100	12.5	100	85.7
Unknown primary	48	4.5	4	8.3	0	0.0	1.0000	100	0.0	-	91.7
Other	37	3.5	3	8.1	1	2.7	1.0000	97.1	0.0	0.0	91.7
Nasopharynx	30	2.8	1	3.3	1	3.3	1.0000	96.6	0.0	0.0	96.6
Salivary	26	2.4	1	3.8	1	3.8	1.0000	96.0	0.0	0.0	96.0
Nasal cavity	23	2.1	1	4.3	1	4.3	1.0000	95.5	0.0	0.0	95.5
Skin	14	1.3	1	7.1	1	7.1	1.0000	92.3	0.0	0.0	92.3
TOTAL	1072	100	124	11.6	34	3.2	0.0002	97.7	9.8	35.3	89.4

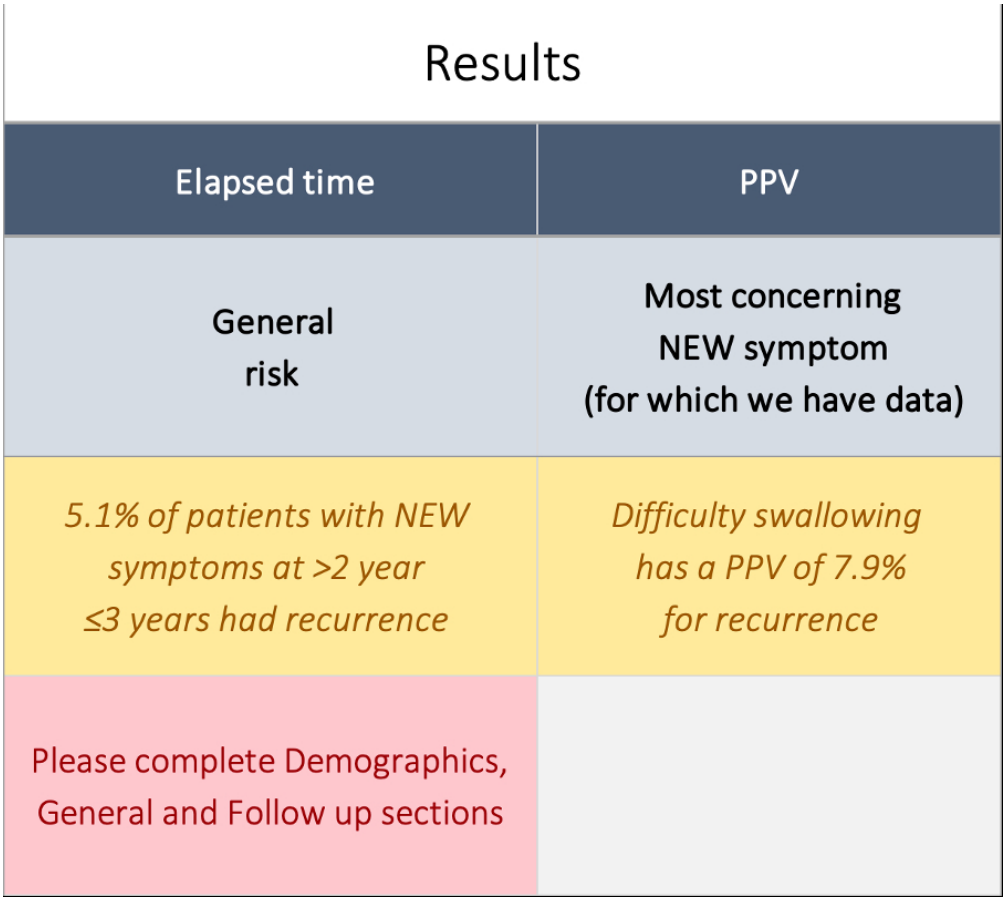

Figure 1. Example of the bespoke results offered to clinicians following completion of relevant data in the Excel Data Tool.

159x142mm (144 x 144 DPI)