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Changing rates of synchronous upper aerodigestive tract malignancy in head and neck cancer- why are we still using panendoscopy?

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Running title: Panendoscopy in synchronous primary cancer

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Abstract

Objectives

Head and neck cancer (HNC) has a 5% incidence of synchronous primary cancer (SPC). SPCs are commonly detected with imaging and flexible nasoendoscopy (FNE). Routine panendoscopy is still being used to screen for SPCs. The aim was to establish the method of detection of SPC.

Methods

A retrospective cohort study of newly diagnosed HNC patients with an SPC, presented at the West of Scotland MDT from December 2020- August 2022. This study is Level 3 evidence.

Results

2325 patients were presented to the MDT with HNC and 54 (2.3%) had SPC. 63.8% (30) patients had a panendoscopy. All patients with comprehensive outpatient assessment had their SPC detected on examination or imaging, without the need for panendoscopy.

Conclusion

Panendoscopy did not detect any new SPC in patients assessed with FNE and imaging. With modern high resolution imaging and fibreoptics, panendoscopy does not play a role in the detection of SPCs.

Key words: head and neck surgery; cancer; diagnosis; pathology; endoscopy

Introduction

In head and neck cancer (HNC) there is a 5% incidence of synchronous primary cancer (SPC) in the upper aerodigestive tract (UADT)[1,2,3]. These most commonly occur in the head and neck, lungs and oesophagus[4,5]. Traditionally in the work up of HNC, patients would have a panendoscopy including laryngoscopy, oesophagoscopy and bronchoscopy, to screen patients for a UADT SPC[6]. Cross sectional computed tomography (CT) imaging of the thorax, has become routine practice in staging patients with HNC[7]. In recent years, bronchoscopy has largely been excluded, given the high sensitivity of computed tomography (CT) scanning for detecting lower respiratory tract malignancy[4]. Outpatient (OP) flexible nasoendoscopy (FNE) with or without narrow band imaging (NBI) is used in the evaluation of the UADT. NBI uses a green light filter to narrow the bandwidth of the light delivered from the endoscope. This wavelength is absorbed by haemoglobin and results in an enhancement of blood vessels and can demonstrate abnormal neo-vascularisation which may indicate malignancy[8]. NBI used in the OP clinic setting, has a high sensitivity (97%) and specificity (92.5%) for detecting laryngeal malignancy[8].

The primary outcome of this paper was to assess the rate and method of detection for UADT SPC in HNC and the ongoing use of panendoscopy.

Method

Local Caldicott application was submitted and approved. Research ethics were not required following consultation using the online tool from the NHS health research authority and Medical Research council website[9]. Patients were identified retrospectively through the Regional West of Scotland Head and Neck Multidisciplinary Team (MDT) Meeting. Information was gathered on the patients using electronic records. A database of all new

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patients, presented at the MDT between April 2020 and August 2022, was used. Patients were included if they had synchronous primary malignancies of the UADT at the time of diagnosis of HNC. Patients who had their head and neck primary identified during investigations for another primary cancer were excluded.

Results

2325 new patients were presented at the MDT between April 2020 and August 2022. 54 patients had synchronous UADT malignancies identified at the time of diagnosis. This resulted in a 2.3% rate of synchronous UADT primary malignancy. Of these patients, 47 had their original cancer originating in the head and neck. The remaining 6 patients had an original diagnosis of lung or lower oesophageal malignancies, and their HNC was identified during further investigations. To assess the SPC assessment in the HNC pathway, these 6 patients were excluded from the analysis.

Table 1 demonstrates patient and cancer demographics. The majority of primary malignancies were identified in the oral cavity and oropharynx, 13 (27.7%) and 12 (25.5%) respectively. The most common sites of UADT synchronous primary malignancy was the lung (57.4%) and oesophagus (23.4%). Data were gathered about the OP clinical assessment, the use of FNE and imaging modality (Table 1). 100% (47) of patients had CT neck and thorax and 66% (31) had FNE at OP assessment. 30 (63.8%) patients had a panendoscopy. One patient had an upper oesophageal malignancy and a second synchronous oesophageal malignancy, both of which were identified during oesophago-gastro-duodenoscopy (OGD). This patient was excluded from pathway analysis.

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SPC pathway analysis

Comprehensive OP HNC assessment was defined as clinical examination including FNE, imaging of the primary site, using CT or magnetic resonance imaging (MRI), and CT of the thorax. Method of SPC identification was compared for patients with comprehensive and incomplete OP HNC assessment (Table 2). In all patients with incomplete HNC assessment, FNE was not performed or documented. Overall, 97.9% (46) of the UADT synchronous primaries were identified through OP clinical examination or imaging. Only one (2.1%) patient, in the incomplete OP assessment group, had their synchronous primary identified during a GA examination under anaesthetic. This patient had a left oropharyngeal malignancy identified in palatine tonsil at outpatient clinic. They did not have flexible nasoendoscopy and went on to have an examination under anaesthetic (EUA). The operative findings upstaged this tumour, which extended from the palatine tonsil to the epiglottis. A synchronous right tongue base malignancy was also identified during the EUA and this was classified as a synchronous primary at the MDT. Of the total 2325 patients in this study, this was the only patient with a SPC identified through GA examination (<0.001%).

Fisher exact test was used to determine statistical significance comparing comprehensive and incomplete HNC assessment, but this was not significant (0.36).

Discussion

Primary outcome

There was a 2.3% rate of synchronous UADT primary malignancy in this retrospective cohort study of 2325 patients, lower than previous reported rates of synchronous primary malignancy in the UADT[10]. Coca-Pelaz et al[10] carried out a systematic review to investigate the rate of second primary malignancy in HNC. This review included 61 articles published

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between 1979 and 2019, and results found a mean incidence of 5.3% synchronous primary tumour. Over this 40 year period, the aetiology of HNC has changed and this is shown in the lower rates of SPC in this article's study population from 2020 to 2022. In this cohort, over half (25, 53.2%) of the patients' initial primary malignancy originated in the oral cavity or oropharynx. Rates of SPC have declined in this population, likely secondary to the rise in human papillomavirus (HPV) related cancers[11]. Slaughter et al[12] introduced the concept of 'field cancerisation', that suggested a regional carcinogenic exposure to the mucosa of the UADT increases the risk of multiple malignancies within this area. Traditionally, in the UADT carcinogenesis have been associated with smoking and alcohol[1]. Our results suggest the risk of SPC has decreased, as the HPV-related HNC has risen.

Comprehensive OP HNC assessment

The authors have defined comprehensive OP HNC assessment as OP clinical examination with flexible nasoendoscopy and imaging. Fleming et al[13] compared the use of outpatient flexible endoscopy with rigid endoscopy under general anaesthesia (GA) in patients with HNC. For the patients with OP flexible nasoendoscopy performed, there were no new malignancies identified on GA examination. In HPV-related oropharyngeal malignancy, SPCs are most likely to occur in the head and neck, rather than other areas of the UADT[11]. The authors have found these mucosal surfaces are more amenable for outpatient examination, than the lung and oesophagus, through headlight inspection of the oral cavity and FNE. The results of this study demonstrate that comprehensive OP HNC assessment was effective in detecting all UADT SPCs, including those in the head and neck region. The only patient who had a new SPC identified at GA, did not have FNE used at OP assessment. This SPC was located in the tongue base, which is challenging to exam in the OP setting without

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the use of endoscopy. In all patients who had FNE and CT examination, the SPC was identified without the need for GA endoscopy.

Imaging for SPCs

CT of the neck and thorax was performed in all patients. At the authors' institution, this is the preferred method of staging and imaging assessment for SPC during initial work. In oropharyngeal malignancy, UK guidance recommends that MRI can improve staging and soft tissue assessment[14]. MRI may also provide superior cross-sectional assessment for SPCs in the head and neck region. Due to availability of MRI, this imaging modality is not routinely used in initial assessment at our institution, but is used when clinically indicated, such as streak artefact created by dental amalgam. In patients with suspected SPC detected on initial imaging, Positron Emission Tomography (PET)-CT can be used to further delineate the aetiology and metabolic activity of the suspicious lesion. However, it is not routinely used for screening patients for SPCs at initial work up.

The role of panendoscopy

In this cohort, 63.8% (30) patients had a panendoscopy, or examination under GA. When indicated, panendoscopy has an important role, in the diagnosis and assessment of HNC. EUA can provide valuable information in the assessment of tumours, and aid in biopsy and planning for surgical resection. However, the authors would propose that there is a limited role of panendoscopy in the routine screening of HNC patients for UADT SPC, if they have had a comprehensive OP HNC assessment. The results of this study found 100% (30) of patients with comprehensive HNC assessment had their SPC identified. Of the 2325 patients

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in this study <0.001% (1) of patients had a synchronous primary identified through GA examination.

For diagnostic purposes, some lesions will not be amenable to biopsy under LA and require a GA to gain tissue diagnosis. In particular, sites like the glottis and subglottis can be challenging to biopsy in the OP setting. For sites that are easier to access at OP clinic, including the oral cavity and oropharynx, representative biopsies can be taken under LA. The results of this study found, despite the majority of primary malignancies originating from the oral cavity or oropharynx, 63.8% of patients had a panendoscopy. This high rate of GA endoscopy in tumours that are potentially accessible in clinic, suggests the rate of panendoscopy may be reduced if clinic based LA biopsy is utilised.

Lung malignancy was the most common synchronous primary and 100% of these were detected through CT. Rigid bronchoscopy has fallen out of use and is no longer routinely included in panendoscopy. CT has a high sensitivity for detecting lung cancer[15] and is the gold-standard method of imaging recommended by NICE for diagnosing lung cancer[16]. In this study, synchronous oesophageal malignancies were identified through CT or OGD. Use of rigid oesophagoscopy under GA has traditionally been used to screen for upper oesophageal or pharyngeal malignancies. This procedure can carries an added risk of oesophageal perforation, and in our cohort of patients did not detect any new cancers. If a patient is symptomatic, or a suspicious area has been highlighted in imaging, rigid oeosphagoscopy can be used for further assessment.

Outpatient diagnostic HNC pathway

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HNC pathway times are increasing and represent some of the longest delays in commencing treatment across all cancers[16,17]. Limited outpatient clinics, imaging capacity and access to theatres cannot accommodate the growing number of urgent suspected HNC referrals. In 2020, 9% of all urgent suspected referrals were for HNC. NHS England have introduced a faster diagnosis standard (FDS) that outlines a 28 day best practice pathway from referral to diagnosis[18]. This was in response to poor adherence to cancer pathway targets, with only 61% of HNC patients meeting their 62 day target from referral to treatment between 2018 and 2020[17]. The FDS includes LA biopsy at a one-stop clinic, and only advises EUA/panendoscopy/GA biopsy if required. LA pathways have been found to reduce HNC pathways, in comparison to those patients requiring a GA[19]. In Scotland, the Optimal Diagnostic Pathway also promotes the use of LA pathway and recommends only utilising GA if required[20].

A national survey was carried out to understand the current practice in the UK for investigating HNC and the use of outpatient local anaesthetic biopsy. Only 48% of respondents to the survey reported that they would use oral forceps and channelled endoscopy under LA in outpatients. Respondents were asked about disadvantages of LA biopsy, and 19% reported they were concerned about missing a SPC [21]. Despite national recommendations and growing evidence for the safety and efficacy of outpatient LA biopsy[22], there is a hesitation to move towards an OP diagnostic HNC pathway. Ongoing concern for missing a SPC may contribute to the high rates of panendoscopy in HNC investigation.

Conclusion

With the changing aetiology of HNC, the rate of SPC has decreased. This cohort study has found comprehensive OP HNC assessment, with flexible nasoendoscopy and imaging, is effective in the detection of UADT SPCs. Wider use of local anaesthetic diagnostic pathways may improve cancer waiting times, while reducing the requirement for theatre space and a general anaesthetic.

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Table 1. Demographics of patients with synchronous UADT primary identified during head and neck cancer pathway

Demographics		**Number of patients (n= 47)**
Age (mean, SD)		70 (9.1)
Smoker	*Yes*	26 (55.3)
	No	2 (4.3)
	Ex-smoker	19 (40.4)
FNE	*Yes*	31 (66.0)
	No	16 (34.0)
CT neck/thorax	*Yes*	47 (100.0)
	No	0
Panendoscopy	*Yes*	30 (63.8)
	No	17 (36.2)
Primary HNC	*Oral*	13 (27.7)
	Oropharynx	12 (25.5)
	Pharynx	1 (2.1)
	Hypopharynx	5 (10.6)
	Glottis	9 (19.1)

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	Supraglottis	4 (8.5)
	Subglottis	2 (4.3)
	Oesophageal	1 (2.1)
T staging	*T1*	13 (27.7)
	T2	13 (27.7)
	T3	12 (25.5)
	T4	9 (19.1)
N staging	*N0*	29 (61.7)
	N1	9 (19.1)
	N2	9 (19.1)
MDT outcome	*Curative*	30 (63.8)
	Palliative	17 (36.2)
Synchronous primary site	*Lung*	27 (57.4)
	Oesophagus	11 (23.4)
	Oral	1 (2.1)
	Oropharynx	7 (14.9)
	Larynx	1 (2.1)
Method of synchronous detection	*Outpatient clinic exam*	3 (6.3)
	CT	42 (89.4)

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Examination under anaesthetic	1 (2.1)
OGD	1 (2.1)

Table 2. Methods of detection for synchronous primary

Investigations	**Number of SPCs diagnosed without GA**	**Number of SPCs diagnosed with GA**
Comprehensive HNC assessment	29 (63.0%)	0
Incomplete HNC OP assessment (imaging only)	16 (34.8%)	1 (2.2%)
P value		0.36

Summary

- In head and neck cancer (HNC) there is a recognised risk of synchronous primary cancer (SPC), due to the common carcinogens involved in these cancers.
- Our cohort of new patients with HNC had a 2.3% rate of SPC.
- 63.8% (30) patients had a panendoscopy.
- All patients who had flexible nasoendoscopy and cross-sectional imaging had their SPC detected without the need for a panendoscopy.
- Panendoscopy does not play a role in screening for SPC in HNC.

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