

5 succinct/key points

1. There is a considerable burden to outpatient head and neck cancer (HaNC) surveillance, and it is unclear to what extent the current recommendations facilitate the detection of HaNC.
2. Our 100 patient retrospective analysis demonstrated three asymptomatic recurrences (all within the first year of follow up) and 20 symptomatic recurrences (mean time to recurrence of 21.4 months).
3. Seventy-four percent of those patients who recurred did so within the first two years following primary treatment, increasing up to 83% by three years.
4. We believe the value of routine follow up is more apparent within the first two to three years following primary treatment as this is when the rate of recurrence is highest.
5. We anticipate larger trials investigating the efficacy of an initial two years of frequent follow up followed by longer-term patient-led follow up.

Introduction

Surveillance for cancer recurrence is a cornerstone of head and neck cancer management. Current guidelines recommend that following primary treatment, patients are followed up for a minimum of five years involving two monthly appointments in the first two years and a reducing frequency in the latter three, and that each of these appointments include a multi-disciplinary team¹. This amounts to between 18-24 appointments for every head and neck cancer patient. The outpatient burden of this surveillance programme forms a major bulk of the head and neck cancer surgeons' workload: it is unclear to what extent these recommendations facilitate the detection of head and neck cancer recurrences. Systems where patients that are educated regarding symptoms suspicious of a recurrence can institute their own follow up, a so called 'open' appointment system, have been found to be effective². This is explained partly by the observation that recurrences in the absence of symptoms are rare³.

Our institution is a high volume head and neck cancer centre with approximately 200 new patients a year. To analyse patterns of recurrence and follow up practise at our centre we performed a retrospective review of 100 patients that had completed their 5-year follow up. We determined the rates of recurrences in this group and then further analysed each recurrence to determine the site, stage, histology and treatment of the primary tumour, whether the recurrences were symptomatic or asymptomatic, how these recurrences were managed and what the outcomes were.

Methods

The Newcastle upon Tyne Hospitals Head and Neck MDT meeting database from 2012-2015 was searched to identify patients who had a new diagnosis of a Head and Neck Cancer (HaNC). We included all patient with a new diagnosis and extracted the following data from their electronic healthcare records:

1. Cancer histology
2. Cancer location
3. Staging (TNM)
4. Type of treatment received
5. Number of follow-ups
6. Recurrence (if any)

Number of follow-ups was determined by counting the number of clinics that the patient attended under Otolaryngology and/or Maxillofacial Surgery. A follow-up clinic was defined as any clinic following the primary treatment of the patient's cancer that was conducted by a doctor in either specialty. Clinics conducted by speech and language were excluded.

Recurrence was defined as any tumour or metastatic disease picked up following primary treatment. If a recurrence was identified, the following additional data were recorded:

1. Date of recurrence (endoscopically or histologically confirmed)
2. Signs and symptoms of recurrence
3. Time between primary treatment and recurrence (months)
4. Treatment for recurrence

The data were recorded in an Excel Spreadsheet and subsequently analysed. We have produced a mini case series of those patient with asymptomatic recurrences.

Results

Initially 100 patients were identified as having a new diagnosis of head and neck cancer (HaNC). The average number of appointments for this group over the standard 5-year follow-up period was 14.5. Twenty-three patients had a recurrence. Of these, 16/23 had less than 16 follow up appointments. Ten of these recurrences had a T1 primary tumour detected with 12/23 being N0 at primary staging.

The mean time between primary treatment and recurrence was 19.3 months (range = 2 months – 72 months). These recurrences were symptomatic in 20 patients (see Figure 1 – Presenting symptoms) and asymptomatic in 3 patients. Of the patients that were symptomatic (n=20), the most common presenting symptom was pain (n=8) followed by sore throat (n=5).

The mean time between primary treatment and recurrence in symptomatic patients was 21.4 months (range = 2 months – 72 months), and in asymptomatic patients was 5 months (see Figure 2 – Time between primary treatment and recurrence distribution). Seventy-four percent of those patients who recurred (n=17/23) did so within the first two years following primary treatment, increasing to 83% (n=19/23) by three years.

Of the patients who had recurrences, 14/23 had an intervention with curative intention. Ten of these interventions were unsuccessful with a further recurrence (re-recurrence) or death occurring within 3 years. Four of the interventions were successful and curative. There were 17 deaths from disease recurrence.

From the asymptomatic group of patients (n=3) who had recurrence the following mini-case series was created (see Table 1 – Asymptomatic patient case series).

Discussion

Our data demonstrates that in a cohort of 100 patients, only three patients had asymptomatic recurrences. All three of these occurred within the first year of follow up. These patients all had extensive nodal disease at the time of diagnosis and were therefore offered scans and examinations under anaesthetic (EUA) as part of their routine follow up. Two of these patients were offered curative treatment for their recurrences but all three patients died within one year of recurring. Twenty patients had recurrences that were symptomatic with a mean time to recurrence of 21.4 months. The most common symptom was pain followed by sore throat.

Our findings are in agreement with previous studies that demonstrate that asymptomatic recurrences of head and neck cancer are rare with an asymptomatic recurrences rate of between 1 and 2%^{4,5}. In our cohort of the patients that did have asymptomatic recurrences two patients were offered curative treatment but all three patients died within one year of recurring.. Other authors have demonstrated a similarly poor outcome for these patients ⁶. A cohort of 661 patients with head and

neck cancer with routine follow up showed a recurrence “cure rate” of 1 in 113 patients⁷. In a separate study of 302 patients, 119 patients had recurrences, and salvage treatment was offered in 49 of these. Only 2 patients survived to five years after relapse⁸.

The purpose of a routine follow up programme as opposed to a symptoms based follow up programme can be justified if asymptomatic lesions are i) frequently detected and ii) detection leads to an overall survival advantage. We believe that the value of routine follow up is more apparent within the first two to three years of primary treatment as this is when the rate of recurrence is highest⁹ and also where patient anxieties following cancer treatment are likely at their highest.

Investigating different follow-up protocols a systematic review by Denaro et al recommended that the outpatient surveillance programme should be tailored to each patient and be determined by the HPV status, smoking status, age, and the site and stage of the primary tumour¹⁰. Our case series may anticipate larger trials where it is demonstrated that following two years of frequent appointments, longer term follow up can be either patient led or individually tailored to the specific patient.

References

1. Simo R, Homer J, Clarke P, Mackenzie K, Paleri V, Pracy P, Roland N. Follow-up after treatment for head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology & Otology*. 2016 May;130(S2):S208-11.
2. Flynn CJ, Khaouam N, Gardner S, Higgins K, Enepekides D, Balogh J, MacKenzie R, Singh S, Davidson J, Poon I. The value of periodic follow-up in the detection of recurrences after radical treatment in locally advanced head and neck cancer. *Clinical Oncology*. 2010 Dec 1;22(10):868-73.
3. Agrawal A, desilva BW, Buckley BM, Schuller DE. Role of the physician versus the patient in the detection of recurrent disease following treatment for head and neck cancer. *The Laryngoscope*. 2004 Feb;114(2):232-5.
4. Pagh A, Vedtofte T, Lynggaard CD, Rubek N, Lonka M, Johansen J, Andersen E, Kristensen CA, von Buchwald C, Andersen M, Godballe C. The value of routine follow-up after treatment for head and neck cancer. A national survey from DAHANCA. *Acta Oncologica*. 2013 Feb 1;52(2):277-84.
5. Ritoe SC, Krabbe PF, Kaanders JH, van den Hoogen FJ, Verbeek AL, Marres HA. Value of routine follow-up for patients cured of laryngeal carcinoma. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2004 Sep 15;101(6):1382-9.
6. Zätterström U, Boysen M, Evensen JF. Significance of self-reported symptoms as part of follow-up routines in patients treated for oral squamous cell carcinoma. *Anticancer research*. 2014 Nov 1;34(11):6593-9.
7. Boysen M, Lövdal O, Winther F, Tausjö J. The value of follow-up in patients treated for squamous cell carcinoma of the head and neck. *European journal of cancer*. 1992 Feb 1;28(2-3):426-30.

8. Cooney TR, Poulsen MG. Is routine follow-up useful after combined-modality therapy for advanced head and neck cancer?. Archives of Otolaryngology–Head & Neck Surgery. 1999 Apr 1;125(4):379-82.
9. Beswick DM, Gooding WE, Johnson JT, Branstetter IV BF. Temporal patterns of head and neck squamous cell carcinoma recurrence with positron-emission tomography/computed tomography monitoring. The Laryngoscope. 2012 Jul;122(7):1512-7.
10. Denaro N, Merlano MC, Russi EG. Follow-up in head and neck cancer: do more does it mean do better? A systematic review and our proposal based on our experience. Clinical and experimental otorhinolaryngology. 2016 Dec;9(4):287.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

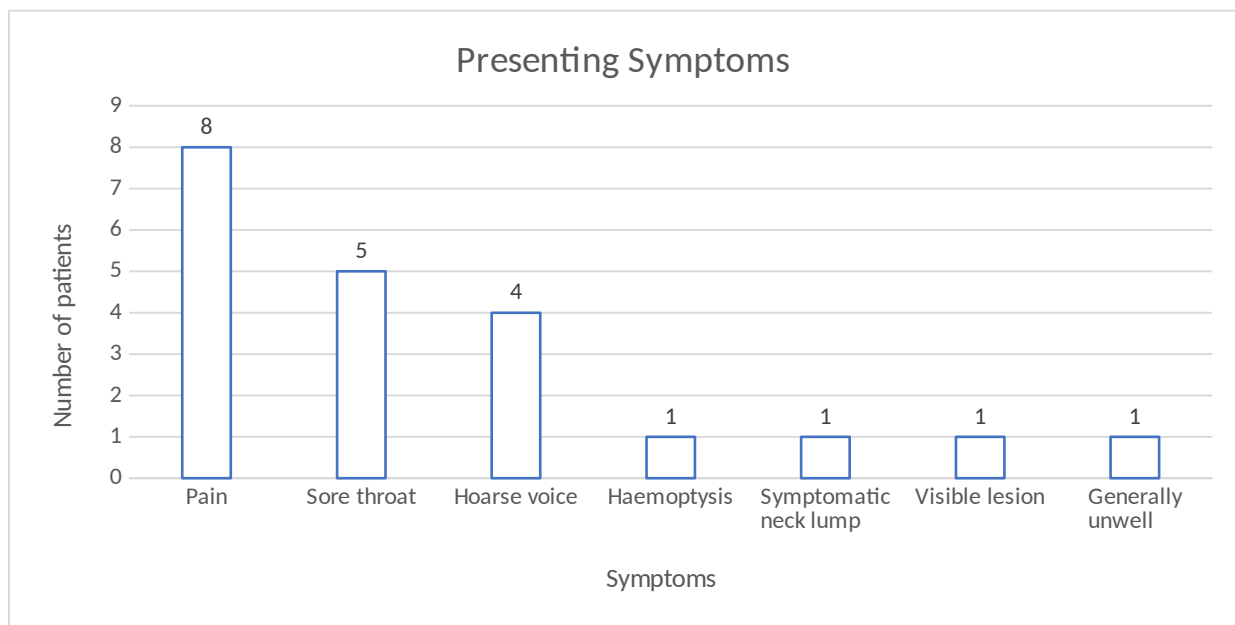


FIGURE 1 – PRESENTING SYMPTOMS

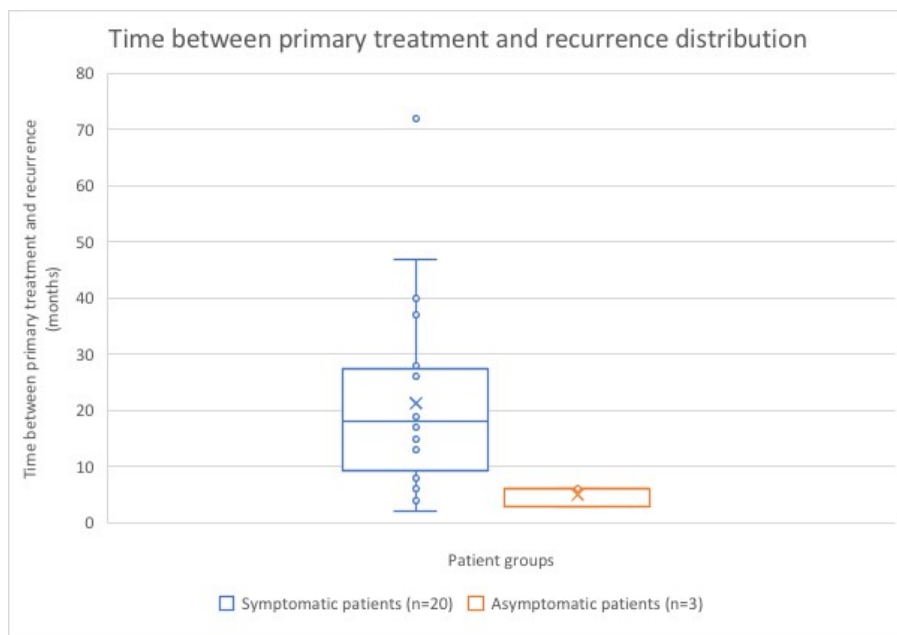


FIGURE 2 - TIME BETWEEN PRIMARY TREATMENT AND RECURRENCE DISTRIBUTION

TABLE 1 – ASYMPTOMATIC PATIENT CASE SERIES

Patient	Age	Primary Staging	Primary Treatment	Time to Recurrence (months)	Method of recurrence detection	Recurrence treatment	Outcome
1	64	T4 N2c M0 Right lateral oropharynx	Chemoradiotherapy	6	Routine follow and CT demonstrated extralaryngeal recurrence and neck node involvement, confirmed with PET-CT and FNA	Patient offered total laryngectomy, partial pharyngectomy, hemithyroidectomy and free flap ALT reconstruction in November 2016. Recurred January 2017 and patient palliated.	Dead from disease
2	46	T4a N2b M0 Right parotid gland	Total right parotidectomy with I-V neck dissection and temporal bone resection (September 2015) followed by adjuvant radiotherapy (December 2015)	3	Routine follow up CT March 2016	Palliative care	Dead from disease
3	64	T1 N0 M0 Pharyngeal wall	TORS and neck dissection	6	Routine follow up endoscopy	Excision of posterior pharyngeal wall tumour (recurrence)	Dead from disease

