KEY POINTS

- The COVID-19 pandemic imposed dramatic changes on delivery of medical services, leading to significant reductions in urgent referrals for suspected cancer.

- A resultant surge in patients presenting with advanced disease, potentially in an emergency context, has been anticipated but, until now, no real-world data have been disseminated.

- Herein, we report a dramatic surge in new and newly recurrent HNCs presenting with advanced disease in an emergency context in the period immediately following the COVID-19-induced UK national lockdown.

- HNC MDTs need to prepare for an ongoing influx of such patients, and prompt provision of patient and primary care education, together with expansion of secondary healthcare capacity, is required to minimise adverse outcomes.

- These data are likely to have lasting significance and will help inform practice and healthcare policy during and following any future COVID-19 outbreaks.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic led to the implementation of a nationwide lockdown in the United Kingdom (UK) spanning March-June 2020 as part of national strategy to reduce the potential impact on the National Health Service (NHS). This imposed dramatic changes on delivery of medical services, with a decrease in, or cessation of, most non-COVID-19 NHS services, leading to significant concern regarding collateral effects on other patient groups requiring time-critical access to healthcare. With respect to cancer services, referrals via the 2-week-wait urgent pathway for suspected cancer in England are reported to have decreased by up to 84% during the initial lockdown period(1), with only partial recovery following lockdown-easing(2). Indeed, Cancer Research UK has estimated that approximately 2,300 cancer cases were likely to have gone undiagnosed every week across the UK during the initial lockdown period(3), and data published in June 2020 indicated approximately 10000 "missing" cancer referrals in April 2020 alone(4). Such figures have clear implications for delays in diagnosis and treatment, and, by association, an anticipated surge in patients presenting with advanced disease, potentially in an emergency context. Indeed, numerous studies have suggested this and have modelled lives and life-years lost predicated on these anticipated delays(1, 2, 5). As yet, however, no real-world data has been published on the impact of these delays on cancer presentation patterns.

Specific to head and neck cancer (HNC), significant delays have the propensity to result in patients presenting in an emergency context, typically with issues relating to airway compromise, dysphagia and associated malnutrition, and less commonly exsanguination. Largely this reflects sacrosanct and complex locoregional anatomy, but is compounded by the fact that HNCs typically have a short tumour volume doubling time(6).

The principal aim of this study was to examine whether the COVID-19 pandemic has had a tangible impact on the rates of newly diagnosed HNC, or newly diagnosed recurrent HNC, presenting in an emergency context.

METHODS

Ethical considerations

This study was undertaken in accordance with our institution's Clinical Information and Audit Department regulations and approval. All patient data were kept anonymous and encrypted throughout.

Patients and setting

All patients presenting to our department in an emergency capacity related to a new diagnosis of a HNC, or a new diagnosis of HNC recurrence, over a six-month period following the initial UK nationwide lockdown (June-November 2020 inclusive) were identified prospectively. All such patients presenting over the same time period in the previous three years (2017-2019 inclusive) were identified retrospectively from electronic emergency handover records. Patients presenting as emergencies but with an existing diagnosis of HNC were excluded. Relevant clinical data including demographics, presenting features, underlying diagnosis, and subsequent treatment details were extracted from electronic hospital records.

The total numbers of patients diagnosed with a new, or newly recurrent, HNC through any route, and under the care of our department, over the same time periods were also extracted from our HNC and thyroid multi-disciplinary team (MDT) meeting databases to ascertain the proportion of emergency HNC presentations.

Data analysis

Data were collated in Excel for Mac 2011 (Microsoft, Redmond, US) and analysed using SPSS® version 27 (IBM, New York, US). Chi-squared and Fisher's exact tests were used to examine differences in proportions of HNC-related emergency presentations between years.

RESULTS

In June-November 2020 a total of 29 patients were eligible for inclusion, of whom 21 and 8 were diagnosed with a new or newly recurrent HNC respectively, comprising respective proportions of 12.3% (21/171), 19.5% (8/41), and 13.7% (29/212) for new HNCs alone, newly recurrent HNCs alone, and new and newly recurrent HNCs combined diagnosed through any route. These represent significant increases in proportions presenting as emergencies in any of the previous three years ($p<0.001$, $p=0.018$, and $p<0.001$ for new HNCs, newly recurrent HNCs, and combined HNCs respectively), in which figures were as follows: 2019 – 8/198 (4.0%) new HNCs, 3/33 (9.1%) newly

recurrent HNCs, and 11/231 (4.8%) combined; 2018 – 6/190 (3.2%) new, 3/40 (7.5%) newly recurrent HNCs, and 9/230 (3.9%) combined; and 2017 – 8/185 (4.3%) new, 5/66 (7.6%) newly recurrent HNCs, and 13/251 (5.2%) combined (figure 1).

Patient demographics, presenting symptoms, diagnosis, disease stage, and treatment intent are summarised for the study cohort as a whole and by year of presentation in Table 1. Notably, 91.9% (57/62) presented with advanced (T3/T4) primary disease, 41.9% (26/62) went onto receive treatment with palliative intent, and 16.1% (10/62) died during admission.

DISCUSSION

Key findings & comparison with other studies

The principal findings of this study demonstrate emphatically a surge in new or newly recurrent HNCs presenting in an emergency context in the period following the initial UK national lockdown. This not only has important and obvious consequences for patient experience and provision of resources, but also has significant implications for patient outcomes. Evidence from several countries demonstrates that these patient groups experience poorer clinical outcomes compared to patients diagnosed through other routes(7), and the fact that this metric is audited on a national level in England(8) attests to this notion. It seems intuitive to suggest that the reason for this is that emergency presentation is simply a surrogate of advanced disease presentation. However, a previous study examining emergency HNC presentations prior to the COVID-19 pandemic demonstrated that whilst those patients presenting in an emergency context did so exclusively with advanced disease, survival outcomes were considerably less favourable than those for patients with similarly staged disease who presented through other pathways(9), suggesting other factors are also at play. Nevertheless, this only emphasises the importance of channeling efforts to reduce such presentations.

Although, to the best of our knowledge, this represents the first study to specifically examine the impact of COVID-19 on real-world cancer presentation patterns, our findings align with numerous modelling studies reporting an anticipated surge in emergency and advanced disease presentation. Moreover, in such modelling studies several HNC subsites have been identified as cancers that are particularly susceptible to these delays in terms of clinically significant lives and life-years lost(1), broadly consistent with the inference presented here insofar as the observed surge in COVID-

induced HNC emergency presentations has been associated with remarkably poor patient outcomes.

Study strengths and limitations

We recognise that interpretation of the data presented here is limited primarily by the observational nature of the study, with no definitive cause-effect relationship demonstrated. Notwithstanding, and as alluded to above, this study is unique insofar as it represents the first study to date to report on changes to cancer presentation patterns in the wake of the pandemic. Moreover, the magnitude of the increase observed in HNC emergency presentations immediately following the COVID-19-related UK nationwide lockdown is compelling, and is highly unlikely to be attributable to random clustering alone. Indeed, we suggest the observed surge is likely to reflect significant delays in presentation brought about by COVID-19-induced re-purposing of healthcare services, compounded by increased patient anxiety and associated changes in health-seeking behaviours. Furthermore, even following lockdown-easing the shift from face-to-face to remote consultations, both in primary and secondary care, may have presented further barriers to patients accessing appropriate healthcare services in a timely fashion. Although speculative, this is supported by repeated and consistent anecdotal patient accounts.

A further limitation of this study relates to external validity. The reported changes to HNC presentation patterns are specific to the Cheshire and Merseyside region, which may not extrapolate elsewhere within the UK, or internationally. Indeed, substantial geographical variation has been noted in rates of patient deferment in accessing urgent referral for cancer symptoms(1, 5), which in turn is likely to influence directly any subsequent change in cancer presentation patterns. Future studies investigating such presentation patterns on a national macrodata level will provide interesting insights in this regard.

Clinical applicability

In an era of unprecedented demand placed on healthcare services by the COVID-19 pandemic it is of significant clinical relevance to examine the fallout from this in terms of cancer presentation patterns, given that any disruption is likely to be particularly detrimental to this group of patients. Herein, we have revealed the first real-world data demonstrating a dramatic surge in new and newly recurrent HNCs presenting with advanced disease in an emergency context in the period immediately following the

COVID-19-induced UK national lockdown. This has two major implications for HNC services to mitigate against the risk of adverse patient outcomes: firstly, HNC MDTs need to be proactive in anticipating and preparing for an ongoing influx of HNC patients presenting in this way, which is likely to involve adaptions to both HNC care pathways as well as inpatient facilities and resources; and secondly, prompt provision of patient and primary care education is required, together with expansion of secondary healthcare capacity to address the presentational and diagnostic backlog to minimise any further delays. From a secondary care perspective, this may involve triaging urgent HNC referrals using risk stratification tools, as in currently being examined by the UK ENT Trainee Research Network(10), and/or rationalisation of HNC follow-up regimes to ensure that this additional capacity can be met.

Whilst at the time of writing the UK has passed the first, and indeed is coming out of a second COVID-19 peak, it is evident that Europe is facing a significant third peak and infection rates are likely to continue to fluctuate. Consequently, the data presented here are likely to have lasting significance and will help inform practice and healthcare policy during and following any future COVID-19 outbreaks.

REFERENCES

1. Sud A, Torr B, Jones ME, Broggio J, Scott S, Loveday C, et al. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. Lancet Oncol. 2020;21(8):1035-44.
2. Lai AG, Pasea L, Banerjee A, Hall G, Denaxas S, Chang WH, et al. Estimated impact of the COVID-19 pandemic on cancer services and excess 1-year mortality in people with cancer and multimorbidity: near real-time data on cancer care, cancer deaths and a population-based cohort study. BMJ open. 2020;10(11):e043828.
3. CR-UK. How coronavirus is impacting cancer services in the UK 2020 [Available from: https://scienceblog.cancerresearchuk.org/2020/04/21/how-coronavirus-is-impacting-cancer-services-in-the-uk/.
4. NHS England. Provider-based cancer waiting times for April 2019 2019 [Available from: https://www.england.nhs.uk/statistics/statistical-work- areas/cancer-waiting-times/monthly-prov-cwt/2019-20-monthly- provider-cancer-waiting-times-statistics/provider-based-cancer-waiting-times-for-april-2019-provisional.
5. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol. 2020;21(8):1023-34.
6. Jensen AR, Nellemann HM, Overgaard J. Tumor progression in waiting time for radiotherapy in head and neck cancer. Radiother Oncol. 2007;84(1):5-10.
7. Herbert A, Winters S, McPhail S, Elliss-Brookes L, Lyratzopoulos G, Abel GA. Population trends in emergency cancer diagnoses: The role of changing patient case-mix. Cancer epidemiology. 2019;63:101574.
8. Public Health England. Emergency presentations of cancer: quarterly data 2020 [Available from: https://www.gov.uk/government/statistics/emergency-presentations-of-cancer-quarterly-data.
9. Bannister M, Vallamkondu V, Ah-See KW. Emergency presentations of head and neck cancer: a modern perspective. The Journal of laryngology and otology. 2016;130(6):571-4.
10. ENT-UK. First interim report from the ENT UK INTEGRATE Head and Neck Cancer telephone triage service evaluation 2020 [Available from: https://www.entuk.org/first-interim-report-ent-uk-integrate-head-and-neck-cancer-telephone-triage-service-evaluation.