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Management of Head Neck Squamous Cell Cancer From an Unknown Primary: Systematic Reviews and National Audit Outcome Data to Generate National Guidelines

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We take great pleasure in introducing this supplement dedicated to management of head neck squamous cell cancer from an unknown primary (HSCCUP).

The management of HNSCCUP is inherently difficult for several reasons. Firstly, there is a paucity of robust contemporary evidence on the topic. Historic studies predate our understanding of the role of human papillomavirus (HPV) in the head and neck and, with the incidence of HPV related disease rising, management recommendations should necessarily keep abreast of this evolving landscape to be able to offer the greatest certainty of any patient benefit. Secondly, the understanding and definition of what is considered an 'unknown primary' alters during the diagnostic pathway as examination, investigations and biopsies identify disease. As a result, direct interstudy comparisons or meta-analysis are complicated by incongruent cohort definitions and eligibility criteria. Thirdly, true unknown primary disease is not common (3%–5% of all head and neck cancers), and so establishing both a substantial evidence base and reasonable clinical experience regarding its management can be challenging, particularly in the single centre setting.

Despite these limitations, many organisations have produced guidelines covering the management of HNSCCUP, using a variety of methodologies. In considering which methodology to adopt to produce the present guidelines, the editors chose to develop a bespoke multi-stage process for several reasons. Firstly, owing to the paucity of contemporary evidence, consensus opinion will undoubtedly be controversial. Without a robust evidence base, consensus opinion would benefit from being as representative of all stakeholders as possible. This lends itself to as much multicentre national engagement as possible to encourage widespread buy-in to the output. Secondly, by involving as many stakeholders and centres as possible, the resultant guidelines are more likely to be considerate of local resource constraints, and so more likely to be adhered to.

We put in place an ambitious programme of work in consultation with several stakeholder organisations to realise this aim. The methodology for consensus generation was set out ahead of this exercise, and peer reviewed by an expert team to ensure critical feedback and generate stakeholder support [1]. Consultation with a wide array of professional groups The Head and Neck Society | ENT UK, The British Society of Head & Neck Imaging, The Royal College of Radiology | Clinical Oncology section, and The Royal College of Speech and Language Therapists led to focused questions, the answers for which would inform unknown primary management. These led to the format for consensus day, which closely followed the patient journey. The data to inform consensus was generated from systematic reviews, national audits, prospective study [2] and a Delphi exercise. Both national audits were led by INTEGRATE—The UK ENT Trainee Research Network, with input from experts as needed. The practice guidelines arising from this meta-consensus exercise were

published as consensus statements in the sixth edition of the United Kingdom National Multidisciplinary Guidelines [3].

Arain, Madani and Awad [4] offer an evidence-based summary and make recommendations for imaging HNSCCUP, indicating MRI to be an integral part of the cross-sectional imaging, in addition to PET-CT scans. Thomas et al. [5] identify the evidence base for oropharyngeal biopsy in HNSCCUP, while Bowe and Garg [6] inform us that biopsies of non-oropharyngeal sites are not indicated when the imaging and clinical examination is clear. The first national audit on investigations for HNSCCUP [7] captures the national practice for diagnosis of this disease process. Takhar et al. [8] set out the cohort of patients for whom surgery alone will suffice as sole treatment modality, while Iqbal, Jackson and Paterson [9] define the indications for adjuvant radiation therapy to the neck after neck dissection. The second national audit on survival outcomes for HNSCCUP [10] demonstrates the excellent outcomes for HPV positive disease, while cautioning that neck dissection alone might be associated with worse local control, but not overall survival, for patients with HNSCCUP.

The works included in the supplement have helped harmonise practice by offering consensus guidelines, define the outcomes of the current treatment paradigms and will help generate further hypothesis driven studies. Additionally, this process offers a model for generating robust guidelines in rare disease processes.

We are very grateful to all stakeholders and individual participants for generously offering their time and effort, without which this output would not have been possible. We recommend the contents of this supplement to all colleagues involved in the management of HNSCCUP and, to raise awareness, this editorial is jointly published across Clinical Oncology (R Coll Radiol).

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Vinidh Paleri, John Hardman, Tom Roques and Ben O'Leary made substantial contributions to the conception and design of the work, the analysis and interpretation of data for the work, drafted the work, revised it for intellectual content, gave final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

Vinidh Paleri is proctor for Intuitive surgical. John Hardman, Tom Roques and Ben O'Leary declare no relevant COIs.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/coa.14204.

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