Conundrums in Keratinocyte Cancer

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Cutaneous squamous cell carcinoma (CSCC) is a highly prevalent cancer which traditionally has been grouped together with basal cell carcinoma (BCC) and collectively referred to as nonmelanoma or keratinocyte cancer. Together these malignancies account for approximately 12000 invasive cancers per annum in Ireland; totalling >25% of invasive cancers. Keratinocyte skin cancer share many common risk factors for development but may exhibit very different biologic behaviours.

Keratinocyte cancers are largely considered to have low metastatic potential. This is true for most BCCs but belies the significant morbidity which may accompany frequent and mutilating surgery in a largely elderly cohort at the sensitive cosmetic and functional anatomical sites which are most frequently involved by keratinocyte cancer. The National Cancer Comprehensive Network (NCCN) distress thermometer (DT) is a screening tool for measuring distress in cancer patients. It consists of a visual thermometer where patients mark their level of distress on a Likert type scale (0-10) and a 26 item questionnaire about practical, family, emotional, spiritual and physical problems and is recommended for use at every cancer visit by the NCCN. NCCN practice guidelines recommend that a DT score of ≥ 4 indicates moderate to severe distress. Work from our group presented at the World Congress of Melanoma and European Association of Dermato-Oncology 2021 demonstrates that 60% of patients attending our skin cancer services at the St Vincent's Strategic Skin Cancer Network exhibit distress, with 25% indicating a DT score ≥ 4. Documenting distress allows us to advocate for and plan to provide appropriate support services for affected individuals in this patient population. The recent addition of a temporary keratinocyte cancer clinical nurse specialist has been an invaluable support to our patient cohort.

Almost twice the number of patients die of cSCC each year than die from melanoma. Nodal metastases from cSCC is in the region of 5%. Early identification of those tumours which are likely to progress is essential to the stratification of patients who might benefit from baseline or interval radiological imaging, nodal staging, comprehensive margin management and early adjuvant therapy. At present there are a number of unanswered questions regarding cSCC.

The 2018 WHO Classification identifies multiple high-risk prognostic features including tumour size, depth of invasion, site (ear, lip, dorsal hand, central face), differentiation and perineural invasion. CSCC-associated desmoplasia, defined as fine branching tumour cells at the periphery with a surrounding desmoplastic stromal reaction, is a further independent factor in recurrence and metastasis. A recent German cohort study showed that desmoplastic CSCC occurred exclusively in the setting of perineural invasion. Work from our group which will be presented at the British Association of Dermatologist Annual Meeting in July of this year supports this finding and demonstrates a worse prognosis in patients with cSCC with both desmoplasia and perineural invasion than in tumours without these features.

Traditional staging systems failed to accurately predict those tumours which were likely to progress with the majority of cSCC deaths occurring in the T1/T2 groups under American Joint Committee on Cancer 7th edition (AJCC 7). While AJCC8 represents a major improvement in prognostic accuracy the outcomes for those tumours in the T2 and T3 groups are not sufficiently different to allow for easy identification of those patients who might benefit from further staging investigations or follow up. Two further staging systems are in common use. The Brigham and Women's Hospital (BWH)Tumour Staging System for Cutaneous Squamous Cell Carcinoma which was introduced in 2014 has demonstrated superior prognostic accuracy than AJCC8. BWH T2b/T3 tumours define a high risk group requiring further study for optimal management. The BWH system has not been validated in a European population and consequently the most recent British Association of Dermatologists Guidelines for the management of cSCC published in November 2020, arguably the most highly regarded guidelines in the field were based on neither of the above staging systems but instead on the International Union Against Cancer (UICC) staging. Ongoing audit of the cSCC cohort identified via the dedicated SVHG cSCC multidisciplinary team meeting and database has not as yet demonstrated a significant difference between these staging systems in an Irish population.

Regardless of staging system used is clear that early detection and treatment is essential to ensuring good outcomes in patients with cSCC. The National cancer Control Programme (NCCP) provides support to rapid access (RAC) pigmented lesion services at 17 sites distributed nationally. This network provides timely specialist and multidisciplinary care to patients referred with possible melanoma. From July 2020, in an attempt to reduce the treatment burden for patients during the COVID-19 pandemic, dermatology and plastic surgery at SVHG skin cancer network began providing same day surgery and interdisciplinary review for keratinocyte cancers in a similar model to pigmented lesion RACs. This new pathway reduced the average time to treatment completion for patients with keratinocyte cancers from 150 to 35 days. Similarly the new pathway reduced the treatment burden on patients from an average of 7 to 5 total healthcare encounter days, which includes all surgeries, virtual and in person outpatient appointments. We would advocate for a national RAC model for keratinocyte cancer similar to the highly successful pigmented lesion pathway. We are thrilled that our model of keratinocyte cancer care has been shortlisted for a HSE National Healthcare award. In anticipation of the outcome of the National healthcare awards a 'Triple win' for us has been the opportunity to reduce carbon emissions through our same day surgery model. The total carbon savings resultant from same day surgery from July to December 2020 was 2.93 tonnes CO_2e, equating to a total carbon saving of 55%; 0.013 tonnes per patient.

Although many questions remain unanswered in the management of keratinocyte cancer we look forward to providing ongoing early, effective and person-centred care for our patients.