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The prognostic impact of micrometastases and isolated tumor cells in early oral squamous cell carcinoma

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Dear editor,

With great interest we read the discussion on the impact of micrometastases and isolated tumor cells (ITC) in patients with early-stage (cT1-2N0) oral squamous cell carcinoma (OSCC). Subash et al. [1] mentioned that the impact of micrometastases and ITC has not been established till now and that for studies looking at the role of sentinel lymph node biopsy (SLNB) in early OSCC, this may behold an unexplored arena [1]. However, there are studies which report on the impact of the largest size of metastases in the neck.

Metastasis can be classified as isolated tumor cells (ITC) (size ≤ 0.2 mm), micrometastasis (size > 0.2 mm and ≤ 2 mm) and macrometastasis (size > 2 mm), although additionally, for ITC more specific histopathological characteristics have been described: no contact with vessel or lymph sinus wall, no extravasation, no extravascular stromal reaction and no extravascular tumor cell proliferation. Step serial sectioning and immunohistochemistry of cervical lymph nodes allow for the identification of ITC and micrometastases. This approach is impractical for all lymph nodes in an elective neck dissection (END) specimen. Routine histopathological examination of an END may miss micrometastases in up to 15% [2].

Several studies demonstrated that even small tumor deposits, i.e. ITC and micrometastasis, detectable by the extensive histopathologic workup according the SLNB protocol, have a significant impact on tumor control and survival in early OSCC. Some of these studies showed also a difference between ITC, micrometastasis and macrometastasis.

Brogie et al. reported in 2013 on a different overall survival (OS) and disease-specific survival (DSS) at 3 years for sentinel lymph node (SLN)-negative and SLN-positive patients of 98% and 71%, and 95% and 76%, respectively. Analyzing the impact of different sizes of metastasis on survival, significantly higher adjusted hazard ratios in OS and DSS for micrometastases and macrometastases were found; whereas, ITC was not a significant determinant for survival [3]. In the European multicenter SENT trial of 415 early OSCC patients who underwent SLNB, a significant difference was found for OS between SLN-negative and SLN-positive patients and between ITC, micrometastasis and macrometastasis positive SLN patients [4]. The results of these and other studies underline the clinical importance of reporting and detecting ITC and micrometastasis in early OSCC patients.

Although similar sensitivity and negative predictive value to detect occult metastases and equivalent survival rates with reduced morbidity, costs and length of hospital stay and increased quality of life have been reported for SLNB as compared to END in early OSCC [5], SLNB for these tumors remains rarely used in many countries. For those who do not want to refrain from doing END in early OSCC patients, SLNB-assisted END (with step serial sectioning and immunohistochemistry of SLN(s) only and routine histopathological examination of the remaining lymph nodes in the END specimen) may be an option to improve staging of the neck and improve prognostication in those patients.

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Compliance with ethical standards

Conflict of interest No conflict of interest amongst authors and all authors have contributed towards the article. There are no financial affiliations, and the authors have nothing to disclose.

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