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Diagnosing oral squamous cell carcinoma: How much imaging do we really need? A review of the current literature

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ABSTRACT

Complementary imaging techniques that round out the clinical examination are fundamentally important in the work-up of patients with oral squamous cell carcinoma (OSCC). Above all, exact determination of primary tumour extent, metastatic spread, and treatment response highly depend on accurate imaging methods. Despite a multitude of recently published reviews, there is still an ongoing debate regarding the best imaging method. In order to update the current literature with the latest evidence, a systematic literature search via Pubmed was performed. In total, 56 studies were enrolled, 4170 patients were analysed, and twenty different imaging methods were evaluated referring to their sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV).

In summary, CT (computed tomography) and MRI (magnetic resonance imaging) currently remain the gold standard for evaluating extension of the primary tumour site. No additional evidence could be obtained for functional imaging methods displaying metastatic spread in the cervical lymph nodes, but was found for distant metastases. Furthermore, functional imaging seems to be beneficial in evaluating treatment response. There is further evidence in the accuracy of the different imaging methods found in this update that could possibly be implemented into the revision of the current guidelines and obtain a clear and coherent approach in the clinical set-up.

1. Introduction

Accounting for 2–4% of all malignancies worldwide, the incidence of head and neck squamous cell carcinoma (HNSCC) is increasing with approximately 650,000 new reported cases annually. Histopathologically, the vast majority of these tumours are squamous cell carcinomas of the oral cavity (OSCC) and oropharynx (OPSCC) ranking as the 8th most frequent tumour in the world (Sadick et al., 2012; Weber et al., 2014; Chai et al., 2015; Schaarschmidt et al., 2016). The main risk factor for developing oral cancer is smoking, showing an up to twenty-fold higher risk of laryngeal cancer. Especially in combination with heavy alcohol consumption, the ethanol may lead to a multiplication effect, most likely by enhancing the penetration of tobacco carcinogens in laryngeal tissue (Talamini et al., 2002; Wolff et al., 2012b). Furthermore, infections with human papilloma virus (HPV) are associated with oropharyngeal carcinogenesis (Kreppel et al., 2013; Krüger et al., 2014). Due to frequent late diagnosis in up to 50% of the cases, the prognosis of HNSCC is generally poor with an overall survival rate of less than 60%, as well as an estimated recurrence rate of 30% (Uribe et al., 2013; Evangelista et al., 2014). Tumour size, infiltration depth, and the occurrence of regional metastases significantly affect the prognosis, whereby the presence of lymph node metastasis is regarded as the single most important predictor of survival (Roh et al., 2007; Sadick et al., 2012; Morandi et al., 2015). In solid tumours such as HNSCC, rapid growth may occur without previous clinical signs. In the process of appropriately staging the primary tumour site, clinical examination must therefore be complemented by precise preoperative imaging (Wolff et al., 2012b; Uribe et al., 2013; Schaarschmidt et al., 2016). Size and location of the primary tumour, assessment of the presence and extent of lymph node metastases, as well as screening for distant metastases are in principal the investigated parameters influencing prognosis and thus treatment selection (de Bree et al., 2009; Mucke et al., 2015; Ren et al., 2015). For primary staging, various imaging techniques such as ortopanthomography (OPG),

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bone scintigraphy, computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET-CT) with or without contrast medium are widely used (Vidiri et al., 2010), but CT and MRI are accepted and recommended as the standard conventional imaging modalities, also stated in the national S3-guidline "Diagnosis and Management of Carcinoma of the Oral Cavity" (Wolff et al., 2012a; Sarrion Perez et al., 2015). However, based on morphologic criteria, the diagnosis of disease activity such as micrometastatic nodes remains challenging in this context (Rohde et al., 2014; Driessen et al., 2015). Therefore, alternative diagnostic tools like the evaluation of tissue metabolism by 18-fluorodeoxyglucose positron emission tomography (FDG-PET) have been proposed and are moreover usable in evaluation of adjuvant therapy, e.g., prediction of recurrence-free patient survival (Dammann et al., 2005; Sadick et al., 2012). As a consequence, controversy exists about the appropriate imaging technique in diagnosis and follow-up of OSCC, among others just recently discussed by Sarrion Perez et al. in their excellent review (Brown and Lewis-Jones, 2001; Sadick et al., 2012; Sarrion Perez et al., 2015). While there is no general coherent approach to the most reliable diagnostic imaging modality to date, the choice of the used imaging modality is often left to the discretion of the radiologist (Kaanders and Hordijk, 2002).

Accordingly, the aim of this article was to review the latest evidence of the recent literature (published < 5 years) in order to determine the diagnostic accuracy of the different imaging tools used for definition of the primary tumour site, screening for lymph node or distant metastases and the evaluation of adjuvant therapy of head and neck squamous cell carcinoma. Therefore, a systematic literature search was performed so as to update and compare data gathered on this subject in recently published studies and reviews.

2. Materials and methods

A Medline literature search was performed via Pubmed using the following key words: medical subject heading (MeSh-) terms "head and neck squamous cell carcinoma" as well as "oral cancer", in combination with "computed tomography", "positron emission tomography", "ultrasound" and "magnetic resonance" tagged in title and/or abstract. Search results were filtered for literature between 01/01/2010 and 10/31/2015 and for the human species. The search was made through October 2015, the latest update was 10/25/2015.

As inclusion criteria, we reviewed all clinical trials, prospective as well as retrospective studies investigating the diagnostic accuracy of conventional staging methods, such as OPT, ultrasound (US), CT and MRI, aside from extended measures like cone beam computed tomography (CBCT), computed tomography perfusion (CTP), single-photon emission computed tomography (SPECT), diffusion weighted MRI (DW-MRI) and whole body FDG-PET, combined with computed tomography (FDG-PET/CT), contrast enhanced computed tomography (FDG-PET/CECT) or magnetic resonance imaging (FDG-PET/MRI) as well as novel tracers like 3-deoxy-3-18F-fluorothymidine (FLT) or L-3-[18F]-fluoro-a-methyl tyrosine (FAMT) in (I) the staging of the primary tumour site with special attention given to a possible bone invasion, (II) the detecting of lymph node metastases inter alia in clinical negative necks plus (III) the evaluation of adjuvant chemoradiotherapy of head and neck squamous cell carcinoma in patients. Investigated parameters were sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) for the respective diagnostic tool. Following search results were excluded: case reports, studies that focused on diagnosis of other tumour types than HNSCC or where the primary tumour was not histopathologically confirmed, besides studies in other than the English language.

3. Results

Overall, the search narrative resulted in 2192 hits on Pubmed. After reading the title and/or abstract, only sixty-four of them fulfilled the above-mentioned inclusion criteria, and full-text was obtained for further analysis. In doing so, seven studies were furthermore excluded for investigating the role of diagnostic imaging; mainly FDG-PET scans, in detecting cancer of unknown primary (CUP) or focused on other histopathologically confirmed tumours than HNSCC. In total, 56 studies published in the last five years were enrolled in this literature review and update. Altogether, 4399 patients were analysed, and twenty different techniques for imaging the above-mentioned topics were evaluated referring to their sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV), as stated in the study. As shown in Table 1, fourteen reports (nine retrospective and five prospective analyses) were identified concerning the characterization of the primary tumour site, 12 of them analysing different imaging modalities that can display a possible bone invasion appropriately. Regarding the detection of lymph node metastases in patients with head and neck squamous cell carcinoma, 35 studies have been obtained, 19 of them prospective and 16 retrospective as summarized in Table 2. Among them, three studies focused on the value of different imaging modalities for distant metastases. Only 11 papers (seven prospective and four retrospective) could be extracted analysing the role of different diagnostic imaging modalities in the evaluation of treatment response after surgical treatment and/or during adjuvant therapy such as chemo or radiation-therapy. For example, showing recurrence in the primary tumour site or distant metastases accurately was presented in Table 3. The paper was grouped by the main investigated parameter examined by the largest sample size in the report if a single study did refer to more than one of these subjects.

4. Discussion

4.1. Imaging methods for staging of the primary tumour site

Precise determination of the spatial expansion of the primary tumour site is crucial for an accurate staging of solid cancer like HNSCC. It significantly alters progression, prognosis as well as therapeutically options if the primary tumour site is known to infiltrate adjacent anatomical structures (Arya et al., 2013). Above all, oral cancer that originates from retromolar trigone, gingiva, hard palate or buccal mucosa is known to invade bone of the maxilla and/or the mandible (Kolk et al., 2014). In this context, the incidence of mandibular invasion ranges in different studies from 12% to 56% (Handschel et al., 2012). Within the scope of a curative surgical intervention, patients with likely infiltration of the mandible will need marginal or segmental mandibulectomy to resect the bone defects. However, histological examination frequently shows no direct bone invasion, yet such interventions are correlated with postoperative complication, morbidity and a reduced quality of life (Kushraj et al., 2011). Therefore, appropriate diagnostic tools besides the clinical examination that can reliably predict a high chance of bone involvement are much in need. As a result, the accuracy of different diagnostic imaging modalities are currently under debate. In the German S3 guideline "Diagnosis and Management of Carcinoma of the Oral Cavity", CT or MRI is recommended for assessing the T-status of the primary tumour site as superior in detecting bone invasion to conventional orthopantomography or CBCT. No evidence has been obtained comparing both imaging modalities, CT and MRI, among each other, but magnetic resonance seems to be beneficial when metal artefacts due to fixed dentures are to be expected. Furthermore, FDG-PET/CT is not