Ultrasound-guided FNA efficiency in diagnosing of metastatic nodes of oral squamous cell carcinoma: A review

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ARTICLE INFO	ABSTRACT
	Oral cancer comprises a group of neoplasms affecting any fields of the oral cavity, pharyngeal regions and salivary glands. However, this term tends to be used interchangeably with oral squamous cell carcinoma (OSCC), which represents the most common of all oral neoplasms. It is estimated that more than 90% of all oral neoplasms are OSCC. Oral SCC prefers to spread through the lymphatic system than the bloodstream, and in this region tongue tumors have the greatest potential for neck metastases. Primary tumor's histopathologic features like depth of invasion, thickness, growth pattern, differentiation, lymphovascular or vascular invasion have a limited prognostic value for nodal disease. Cervical lymph node status accurate assessment in HNSCC patients is critical issue because of its influences on prognosis and treatment decisions, USgFNAC proved widely accepted not only because of safety and availability in diagnosis but also it is repeatable, minimally invasive and cost-effectiveness. **Keywords:** Squamous cell carcinoma; Hhead and neck cancer; Ultrasound-guided fine needle aspiration cytology; Ultrasound; Sentinel lymph node biopsy.

Introduction

Oral cancer comprises a group of neoplasms affecting any fieldsof the oral cavity, pharyngeal regions and salivary glands. However, this term tends to be used interchangeably with oral squamous cell carcinoma (OSCC), which represents the most frequent of all oral neoplasms. It is estimated that more of 90% of all oral neoplasms are OSCC [1]. It usually occurs after the fifth decade of life, and is more common in men. They account for 5% of all malignancies worldwide and 3% in the United States [2,3]. Some of the proven main risk factors are: tobacco and alcohol consumption, Epstein-Barr virus (EBV) and human papilloma virus (especially 16 and 18) infections, and reverse smoking [4]. Current recommended treatment strategy is surgical resection with or without

chemotherapy and radiation therapy. The 5-year survival rate for oral and pharyngeal cancers is 56%, whereas it is 62% in laryngeal cancers. Two third of these patients present debilitating symptoms that impact their quality of life [5]. The oral cavity is full of lymphatic drainage, and regional nodal metastasis occurs early and constantly in oral SCC [6]. Cervical lymph node status accurate assessment in HNSCC patients is critical issue because of its influences on prognosis and treatment decisions [7]. Oral SCC prefers to spread through the lymphatic system than hematogeneously. In this region tongue tumors have the greatest potential for neck metastases [8,9]. Early diagnosis of neck metastasis is an important prognostic factor. The survival rate of patients with Single ipsilateral or contralateral metastatic node decreases by 50% and it further reduces by 50% if there are bilateral metastatic nodes [10]. Surgical excision is essential to control primary tumor in SCC, recurrence often happens in cervical lymph nodes, which is the most important factor in the long-term prognosis of patients [11,12]. Primary tumor's histopathological features like depth of invasion, thickness, growth pattern, differentiation, lymphovascular or vascular invasion, extent of inflammatory reaction around the tumor, perineural invasion and numbers of biomarkers have a limited prognostic value for nodal disease [13]. According to latest articles, neck dissection (ND) in oral cancer patients with nodal involvement is the most suggested treatment method, but there is not an agreement to treat all patients with a clinically negative neck (cN0) with ND.

Lymph nodes excisional biopsy in cNo patients should be avoided because of potential of local complications (like hematoma, infection, disruption of fascial planes for subsequent neck disscetion), as well as the theoretical risk of neck recurrence [14] Using selective neck dissection as a treatment could have risk of morbidity [15]. For example "shoulder syndrome" has been reported as a iatrogenic injury that occurs in spinal accessory nerve injury [16]. Carlos Moreno-García in 2016 reported 23.7-42% of recurrence in N0 neck [13]. If the "wait and see" policy is provided for cN0 patients occult neck metastasis can occur. The site, stage, and other characteristics of tumor are the risk factors of occult metastasis [15]. By following-up cN0 patients closely with the help of diagnostic techniques, such as ultrasound-guided fine-needle aspiration cytology (USgFNAC), occult metastases can be detected at early stages [16]. Screening of clinically N0 neck with ultrasound, magnetic resonance imaging (MRI), positron emission tomography (PET) or computed tomography

(CT) could be helpful in detection of some non-palpable nodal metastases, but their Limited accuracy compromise applying them. According to P Dabirmoghaddam et al in 2014 USgFNAC has a higher sensitivity and specificity to palpation and US alone and has an accuracy of 96%. In palpable metastatic lymph nodes, the sensitivity of USgFNA is often reported from 98% to 100% and 70% in nonpalpable lymph nodes. Adding cytology method increase diagnosis of malignant tumor specificity up to 100%. However, in patients with previous irradiation of the neck false positive findings of FNA have been reported [17]. A meta-analysis assessing all above-mentioned modalities (with the exception of PET CT scan) reported that USgFNAC has the highest diagnostic odds ratio for staging of neck with a pooled sensitivity of 80% and specificity of 98% for it [18]. The other meta-analysis reported PET-CT with few accuracy (specificity & sensitivity) in staging the cN0 patients [19]. Many clinicians still believe in surgery procedure in patient with overt lymph node metastases with or without adjuvant chemotherapy and radiation, But the cost-benefit of this treatment for cN0 patients should be considered [20]. The purpose of this review is evaluating the feasibility and performance of USgFNAC in Diagnosing of Metastatic Nodes of Oral Squamous Cell Carcinoma.

Discussion

-SLNB

The first lymph node in a drain of metastatic tumor cells is the sentinel lymph node, biopsy of this node is an early detective technique to identify the presence of nodal metastasis. Sentinel lymph node biopsy (SLNB) for oral SCC is not yet clearly defined because of the complex nature of head and neck region like various draining lymphatic pathways and high false-positive or negative rate of reports. Studies found SLNB as a valid diagnostic technique that properly stages regional metastases in HNSCC [21,22]. Although operative morbidity is potentially high, SLNB reported as an accurate staging procedure for cN0 patients [23]. A research with huge statically population reported the sensitivity of 93% in SLNB for early stage (T1-T2) oral and oropharyngeal cancers [24]. Also a meta-analysis of 21 studies concluded a 92% sensitivity for SLNB for staging the neck in oral cavity SCC [25]. The SLNB specificity of major studies is over 90%. Chaturvedi et al reported the sensitivity of SLNB (71%) that sound lower in comparison to USgFNAC [25,26]. The results of the two meta-analyses of Bondt et al suggest that efficacy of SLNB and USgFNAC is comparable [18,25].

Although SLNB has high accuracy, but it is not use commonly in most centers because of its time consuming and invasive procedure which requires multidisciplinary expertise [27].

-Ultrasonography (US)

Ultrasonography (US) is a simple method used for detection of noninvasive and soft tissue-related diseases in oral and maxillofacial regions [28]. The ultrasound image reveals the surface structures of computed tomography (CT) and magnetic resonance (MR). US may be clinically applied to assess lymph node-related diseases, salivary gland-related diseases, subcutaneous diseases, and tongue-related diseases [29]. Ultrasound of the neck has been used extensively for cervical metastases in head and neck cancer [30]. Ultrasound has higher sensitivity (96.8%) than palpation (73.3%) for detection of cervical lymph nodes [31]. De Bondt et al meta-analytic study in 2007 reported sensitivity and specificity of 66% and 78% for US. they Also reported that US is the most sensitive imaging technique for neck node staging with a pooled sensitivity of 87% and pooled specificity of 86% respectively [18,19]. according to results of some other research, a higher sensitivity of US has been reported in occult metastasis detection in the clinically negative neck [32-34]. Byers et al reported a sensitivity of 27% and specificity of 71% for the Ultrasound in the clinically negative neck, while To E et al reported a sensitivity of 47%. The result of both last researches declares limited prediction of Ultrasound in evaluating occult metastasis in tongue cancer [35,36].

Fine-needle aspiration (FNA) is a diagnostic method used to investigates masses. Fine-needle aspiration biopsies are very safe, less traumatic and minor surgical procedure with a few complicatios include bruising and soreness. Often excisional biopsy can be avoided by performing a needle aspiration biopsy instead, without hospitalization. FNA avoids the chance of seeding cancer cells in neck and making following treatment of a confirmed malignancy more challenging [35]. In some respects because of small size of sample problematic cells might be missed which could have false negative results [37]. However, FNAC has high efficacy and relative safety and comparing to open biopsy, this is comparatively inexpensive, well tolerated by patients with few complications without needs for general anesthesia [20,38]. In last decade fine needle aspiration cytology has been approved as a gold standard for diagnosing palpable head and neck lesions in the first step [13,39]. Using ultrasound with fine needle aspiration cytology offers the benefit of cytologic analysis of suspicious lymph nodes and the presence of cancer cells and atypical cells in the pathology result of Ultrasound-guided fine-needle aspiration cytology (USgFNAC) was regarded as a positive result; otherwise, the result was considered negative [36]. Which has improved the specificity and overall accuracy of ultrasonography. Lymph nodes cytological analysis has an extremely high specificity that could approve lymph node metastasis presence in patients with HN-SCC [19]. Whereas from the cellular material obtained through USgFNAC, different molecular examination like HPV analysis and tumor DNA sequencing can be achieved [40].

Diagnosing methods like Computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) increase the detection certainty of involved lymph nodes [41,42]. In evaluation of nodal metastasis Ultrasound Guided FNAC is comparable to CT scan and can provide further information about enlarged lymph nodes and can show malignancy in small lymph nodes not found by CT or MRI. Also, clinician can present treatment plan to the cN0 patients before they leave the clinic, which avoids delay [43]. USgFNAC is a rapid and inexpensive procedure without the need of any contrast medium injection [44,45]. Some studies have reported low sensitivity of USgFNAC in clinically negative necks.

The confirmation of high accuracy of USgFNAC was based on 3 meta-analytic studies, 2 of them had included both clinically positive and negative necks [34,46]. It is clear that the larger the size of nodes with metastasis involvement, the more sensitive the USgFNAC technique gets. The third study of this meta-analysis was restricted to USgFNAC in cN0 patients and it reported a lower sensitivity of 48% and specificity of 100%, and overall accuracy of 79% [47]. Some studies also reported low sensitivity of USgFNAC in the estimate of cN0 patients [48,49]. Employing imaging in the neck nodes depends on some factors like the location and clinical extent of the primary tumor. Moreover, costing is also an important factor. USgFNAC can be recommended as a low-priced and most achievable added to the CT scan in the evaluation of neck node metastasis. Currently, the most reliable principle for assessing the nature of a lymph node and lymph node selection for aspiration is its size, measured as the minimal axial diameter. Based on studies, in order to obtain ideal sensitivity lymph nodes with a minimal axial diameter larger than 4mm in level II, and 3mm in other levels of the neck should be selected for ultrasound-guided FNAC. Selection criteria in the head

and neck region can estimate the overall accuracy of USgFNAC [50]. Ultrasound-guided FNAC decreases the risk of occult lymph node metastasis to 21% in the early oral squamous cell carcinoma [27,51]. Provides a plan for surgical intervention in malignant lesions and prevents unnecessary immediate surgery in benign nodules [52]. The limitation of USgFNAC is inaccessibility of paratracheal, retropharyngeal, and mediastinal lymph nodes that cause the main drawbacks of this technique [44,51]. Ultrasound-guided FNAC sensitivity has been reported as high as 73% in patients with a clinically (palpably) negative neck in head and neck squamous cell carcinoma [48]. Most studies identified USgFNA an appropriate technique because of the early availability of results, effortlessness, least trauma or injury, the low rate of complications and not needing heavy sedation or general anesthesia. USgFNA of the head and neck region is a well-accepted technique that has high specificity [53].

Conclusion

USgFNAC is an acceptable method that will be preferred in neck masses diagnosis especially in malignant lesions and it is widely accepted not only because of safety and availability in diagnosis but also it is repeatable, minimally invasive, non-ionizing and cost-effective [44,45]. Furthermore, USgFNAC is a reliable diagnosing method that enhances clinical researchers to collaborate with surgeons and also open the knowledge boundaries to optimistic studies on modifying the diagnosing method for earlier and exact treatment for SCC.

Conflict of Interest

There is no conflict of interest to declare.

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