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Editorial

Screening for oral cancers—Which method is most effective?

Oral cancer, an often fatal disease, has the fourth highest incidence of malignancy in males in Taiwan. Oral squamous cell carcinoma (OSCC) accounts for >95% of all oral malignancies. Oral cancer is associated with chronic irritating factors, such as tobacco, smoking, alcohol and betel quid (BQ) use. Cigarette smoking and alcohol drinking are the major risk factors in Western countries, whereas BQ use and smoking are the major factors in the cause of oral cancer in South Asia, Southeast Asia and Taiwan.[1–3] Unfortunately, ~50% of new cases at their first visit to our medical center often present with advanced stages.[4,5] The overall 5-year survival rate of these patients is poor despite recent advances in surgery, radiotherapy and chemotherapy.[5] It is generally accepted that prevention and screening of oral cancer are equally important, and the diagnosis of oral cancer at an early stage allows for less aggressive treatment, improves quality of life and the overall 5-year survival rate.[6] Visual examination of the oral cavity has traditionally been the preferred approach for the detection of oral mucosal abnormalities,[7] including Chang et al's publication in this issue of the Journal of the Chinese Medical Association.[8]

There are other early detection methods that have been developed by many researchers. Use of toluidine blue (TB), an acidophilic dye that stains DNA and RNA, is based on the theory that the content of acidic cellular components in dysplastic tissue is greater than that in nondysplastic tissue. The clinician brushes the dye onto the oral mucosa then examines the oral mucosa for increased cellular staining.[9] Although useful as an adjunct to clinical examination, the specificity of TB staining is limited because cells undergoing inflammatory changes and benign hyperplasia may also retain dye, leading to false-positive results. The overall sensitivity of TB staining ranges from 0.78 to 1.00 and the specificity ranges from 0.31 to 1.00.[10] Oral cytology is another diagnostic technique used to sample oral tissue for histomorphological analysis, which includes cytomorphometry, DNA cytometry and immunocytochemical analysis.[9] The use of oral cytology in the detection of dysplastic lesions shows considerable promise, but has been limited thus far by variable false-positive and false-negative results.[9,10]

The current identification and diagnosis of precancerous and cancerous lesions relies on the histological and cytological examination performed by a pathologist after suspicious tissue is biopsied. Although these methods represent the gold standard for cancer diagnosis, they have several limitations in oral screening. Tissue biopsy is invasive, expensive and often time-consuming. The diagnostic interpretation of the tissue sample has been shown to vary among pathologists, and the pathologic criteria for the identification of precancerous lesions are not well defined.[11] In addition, early precancerous changes are frequently undetectable by conventional visual inspection, leading to missed opportunities for diagnosis. Optical technologies show the potential to provide real-time assessment through a minimally invasive route, eliminating lengthy waiting time and the need for tissue biopsy. Although the benefits of optical technologies are currently limited in clinical practice, the achievement of a highly sensitive and specific optically determined histopathologic diagnosis, an optical biopsy, has the potential to revolutionize medical practice. As the most thoroughly investigated optical techniques for the detection and characterization of oral lesions, autofluorescence spectroscopy and imaging systems are capable of distinguishing normal oral mucosa from cancerous lesions. Research suggests that autofluorescence spectroscopy is exceedingly accurate in distinguishing lesions from healthy oral mucosa (sensitivity 82–100%, specificity 63–100%), although there is a lack of compelling evidence for the discrimination between lesion types.[12] In addition to fluorescence spectroscopy and imaging techniques, several optical diagnostic systems have demonstrated potential for the successful evaluation of the oral cavity. A recent study using a multispectral imaging system (fluorescence, narrow-band imaging and orthogonal polarized reflectance) demonstrated that oral lesion borders change with each imaging modality, suggesting that multimodal imaging can provide important diagnostic information not available through conventional white-light examination or through the use of a single imaging mode alone.[13] Trimodal spectroscopy (fluorescence spectroscopy, elastic scattering spectroscopy and Raman spectroscopy) has been shown to be capable of diagnosing malignant/precancerous tissue with a sensitivity and specificity of 96%.[14] The application of optical coherence tomography (OCT) for the evaluation of oral cavity disease began as early as 1998 when researchers obtained images of the human tooth and oral mucosa.[15] However, the range of specificity and sensitivity of optical biopsy varies widely due to the inhomogeneity of oral cancers and premalignant lesions.

As a noninvasive and traditional technique, oral cavity examination can be done quickly, is without additional diagnostic expense to patients and may be performed by health-care professionals. The evidence regarding oral examination as an

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effective screening technique, however, remains controversial. In a recently published randomized controlled trial with nearly 130,000 participants, investigators concluded that there was insufficient evidence to support or refute the use of oral examination as a screening program. However, this study, done by the Kerala group in India, demonstrated improved survival rates at 9 years among men with tobacco use as a high-risk habit.[7] Although there was no increase in survival for the overall population, this study was the first to clearly support the efficacy of an oral cancer screening program in a high-risk population. In this issue,[8] Chang et al report their evaluation of 13,878 participants, in which the sensitivity and specificity of oral cancer screening were 98.9% and 98.7%, respectively. The relatively high levels of sensitivity and specificity make visual screening superior to other oral examination protocols. Meanwhile, aged males (≥40-years) or a high-risk population (alcohol consumption, BQ chewing and cigarette use) were recommended to receive oral screening periodically. This conclusion is compatible with that of the Indian Kerala group.

Even with remarkable technological advancements made by cancer advocates, researchers, and clinicians, the diagnosis of oral cancer often occurs at a late stage, conferring a dismal prognosis. Importantly, the improvement of patient outcomes is related to the detection and surveillance of cancerous or precancerous lesions at early stages of disease. Although many of these techniques have been implemented in medical settings only recently, they offer scientists highly sought-after methods for the early detection of cancer. Many of the optical diagnostic techniques are still in the research and development stages. In the contemporary era, visual screening still has the highest effectiveness/price (e/p) value.

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