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Laryngeal preneoplastic lesions and cancer: challenging diagnosis. Qualitative literature review and meta-analysis.

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A B S T R A C T

Background: Multi-step cancerogenesis guides laryngeal cancer onset and it includes a wide variety of pre-cancerous lesions macroscopically challenging to identify and distinguish from initial cancerous foci.
Object: Different modalities of diagnostic techniques of laryngeal epithelial lesions exist and they do not offer a single system to make a differential diagnosis. Hence, this meta-analysis aimed to synthesize the validity of each single diagnostic tool to improve laryngeal patient management.
Methods: A systematic review of literature was led searching for articles mentioning the following terms: larynx, laryngeal precancerous lesions, laryngeal cancer, white light (WL) endoscopy, stroboscopy, contact endoscopy (CE), autofluorescence (AF), ultrasound (US), narrow band imaging (NBI), computed axial tomography (CAT), magnetic resonance imaging (MRI), positron emission tomography (PET), CAT/PET. Then, a quantitative analysis was carried on for paper published after 2005 onward.
Results: The search identified 7215 publications, of which 3616 published after 2005, with a final results of a total of 214 articles stratified and included by our selection criteria. 42 out of 214 articles were selected for quantitative synthesis. 25 out of 41 studies had a good quality score, 16 were fair.
Conclusions: A comprehensive overview of the most recent advances in laryngeal imaging technology combined with all of the information needed to interpret findings and manage patients with voice disorders can be found herein. Our flow-chart allows clinicians in risk-stratify patients and select proper examination modalities to provide appropriate care. Study limitations, together with possible clinical and research implications have been counted.

1. INTRODUCTION

In otolaryngology, hoarseness is the most common laryngeal symptom for which patients seek treatment and may be caused by a diversity of potential disorders. In this setting, visualization of the structure and function of the vocal folds has become an essential component of the clinical voice assessment protocol (Mehta and Hillman, 2008; Deliyski and Hillman, 2010), because the capacity of history and physical examination alone to yield adequate information to get the right diagnosis or even risk-stratify patients is only 5% compared with a 68.3% accuracy following an initial endoscopic laryngeal evaluation (Paul et al., 2013).

Because of the wide range of potential causes for the dysphonia, determining the precise etiology of the laryngeal/voice disorder is necessary to plan treatment. Since malignant transformation rate of premalignant lesions ranges from 6% to 22%, and it increases with the severity of the precancerous nature, their early detection is of paramount importance. In this setting, early detection and preoperative assessment are important to a curative and function-preserving therapy, because the treatment of laryngeal cancer and its precursor lesions has a great impact on important basic functions of daily life such as breathing, verbal communication and swallowing. Furthermore, delayed diagnosis, leading to loco-regional failure, and a high incidence of second primary are the two main reasons for poor outcome.

From these observations, it is obvious that obtaining images of high quality and resolution, revealing the detailed morphology of the glottal structures, is one of the main tasks in laryngeal imaging. Such images are essential in making correct diagnosis and choosing the treatment to gain the best result. Attempts to examine the human larynx date back more than 150 years, in fact, in 1854 Manuel Garcia, a vocal music teacher, examined his own larynx using a dental mirror and a hand mirror, and published his observations in 1855 (Alberti, 1996). Imaging technologies applicable in laryngology developed enormously since then. Nowadays, the diagnostic procedure of laryngeal diseases in clinical practice is rather complex and is based on the evaluation of patient's complaints, history, and data of instrumental as well as histological examinations. During the last two decades a variety of imaging techniques for the examination of the larynx and obtaining objective measurements of voice quality have been developed (Mafee et al., 2005; Uloza et al., 2005).

For instance, the term "laryngeal imaging" typically refers to the endoscopic imaging of vocal fold tissue clinical aspect and vibration via videoendoscopy and videostroboscopy; in addition, evaluation of larynx has improved significantly with the establishment of computed axial tomography (CAT) and magnetic resonance imaging (MRI), as these technologies provide insights into the endoscopically blind areas and reveal the depth of tumor infiltration (Gallivan and Gallivan, 2002). These technologies may be beneficial in staging laryngeal carcinoma and planning the most appropriate surgical procedure (Rumboldt et al., 2006; Hoorweg et al., 2006). Recently, ultrasonography has become useful as well in cases of larger laryngeal lesions and may have some role in screening for unilateral vocal fold pathologies. At the same time, further fine-tuning of the technique may be necessary (Rubin et al., 2004a; Schade et al., 2003).

Despite all of these efforts in achieving the perfect diagnostic tool, nowadays surgeons cannot trust one single imaging technique to plan laryngeal patients management and treatment; in fact, recent articles, published in literature, emphasized the need for further technological, methodological and clinical research on laryngeal imaging, including the development of clinical norms and objective image processing and measurement methods (Deliyski, 2007; Doellinger, 2009; Verikas et al., 2009).

This paper provides a review of the latest advances in laryngeal imaging over the last decade in order to give a comprehensive overview of the most recent progress in laryngeal imaging technology combined with all of the information needed to interpret findings and successfully manage patients with voice disorders.

2. LARYNGEAL DIAGNOSTIC SYSTEMS

In patients with dysphonia, the diagnostic accuracy from history and physical exam, excluding laryngoscopy, is only 5% compared with a 68.3% accuracy following an initial endoscopic laryngeal evaluation (Lichtenstein and Jaffee, 1943). Because of the wide range of potential causes for the dysphonia, determining the precise etiology of the laryngeal/voice disorder is necessary to plan treatment. Since malignant transformation rate of premalignant lesions ranges from 6% to 22%, and it increases with the severity of the precancerous nature, their early detection is of paramount importance. For instance, survival rates are significantly higher for early stage carcinomas, therefore, it is essential to concentrate on the