

Dysphagia in head and neck cancer: A review

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Received 1 October 2013; revised 13 November 2013; accepted 26 November 2013

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ABSTRACT

Head and neck cancers are frequently associated with dysphagia. Both pre-treatment and post-treatment etiologies have been described in the literature. The result of dysphagia has been well-documented as causing reductions in both quality-of-life and physical well-being. The goal of this review is to consolidate the current understanding of the relationship between head and neck cancers and dysphagia.

Keywords: Dysphagia; Deglutition; Otolaryngology

1. INTRODUCTION

Dysphagia is a common, yet, understudied phenomenon. It has been well established that dysphagia has an enormous impact on both the overall quality-of-life and health of patients. Patients with head and neck cancers comprise a significant number of those affected by dysphagia. According to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, the most recent age-adjusted incidences of oral/oropharyngeal cancer, laryngeal cancer, esophageal cancer, and thyroid cancer are 10.8, 3.3, 4.25, and 13.21 per 100,000, respectively [1]. These values reflect individuals at risk of developing dysphagia. Furthermore, dysphagia is not only a manifestation of head and neck cancer, but also a complication of cancer treatment. This suggests that dysphagia is a salient issue for a much larger population than previously recognized. The goal of this paper is to consolidate current understanding of the etiology and impact of dysphagia in head and neck cancer patients. Ultimately, our goal is to provide a new baseline understanding from which further innovations in therapy can develop. In order to do this, it is necessary to begin by reviewing normal swallow function.

2. SWALLOW SEQUENCE

Magendie is largely credited with the current, three-

phase description of deglutition [2]. The phases represent a necessary oversimplification of deglutition. In reality, deglutition is a fluid and concerted act with some overlap of the phases. The 3-phase description is, however, helpful for at least two reasons. First, each delineation grossly reflects innervation patterns and the muscles which are predominantly active during a given phase. Second, the subdivisions provide a convenient nomenclature to discuss sites of dysfunction or breakdown in the swallow apparatus. Various investigators have developed alternate deglutition descriptions with some authors preferring a two-phase scheme and still others preferring a four-phase scheme [2-4]. For simplicity's sake, only the three-phase mechanism will be described below.

2.1. Oral Phase

The oral phase marks the initiation of the swallow sequence and is the only truly voluntary portion of the mechanism. The structures involved in this phase include the tongue, hard palate, soft palate, suprahyoid muscles, orbicularis oris muscle and buccinator muscle. The tongue, assisted by the suprahyoid muscles, is responsible for shaping and propelling the bolus posteriorly. The orbicularis oris and buccinator muscles provide closure of the oral orifice to prevent spillage. The soft palate is displaced inferiorly and anteriorly to provide closure of the posterior oral cavity and to widen the nasal airway. Increases in patient age and in bolus viscosity may lengthen the duration of this phase. In healthy individuals, the oral phase lasts 1 to 1.5 seconds at which point the pharyngeal reflex is triggered [2-4].

2.2. Pharyngeal Phase

The pharyngeal phase of swallowing is an involuntary reflex which is physiologically more complex than the oral phase. The pharyngeal phase is unique in that it is the only phase of deglutition during which respiration is momentarily halted to prevent aspiration. The phase is triggered by the glossopharyngeal nerve upon afferent

input from the oropharyngeal mucosa carried by cranial nerves IX and X. The pharyngeal phase is broken down further into a sequence of five events listed below [2-4]:

1) Velopharyngeal closure by the palate to prevent regurgitation of the bolus through the nasal cavity.

2) Retraction of the tongue base to further propel the bolus.

3) Pharyngeal retraction occurs as a peristaltic wave to clear residual contents left behind the bolus.

4) Elevation and closure of the larynx, mediated by the strap muscles, suprahyoid muscles, submental muscles, and laryngeal vocal fold muscles, is directly responsible for airway protection.

5) Opening of the upper esophageal sphincter (UES) allows passage of the bolus into the esophagus and occurs by relaxation of the cricopharyngeus muscle.

The opening of the UES marks the transition from the pharyngeal phase of deglutition to the esophageal phase. The pharyngeal phase typically lasts 1 second in the healthy individual and is the least variable of all the phases [2-5].

2.3. Esophageal Phase

The esophageal phase is the final and most variable phase of deglutition, lasting from 8 to 20 seconds in healthy individuals. The primary function of the esophageal phase is to propel the bolus through the lower esophageal sphincter (LES) and into the stomach. This occurs by peristaltic contraction under mixed autonomic and somatic control in the upper one third of the esophagus. Purely autonomic control occurs in the lower two thirds of the esophagus. The esophageal phase is complete once the bolus has passed through the LES [2-4].

3. MEASUREMENT OF DYSPHAGIA

The complexity of the swallow function is what makes its study so difficult. It has been noted that dysphagia has been studied far less than other basic survival functions such as respiration or ambulation [3]. For these reasons, no single measurement modality has provided the variety of data needed to fully characterize dysphagia. Instead, several modalities have been developed to quantify various aspects of swallow function in clinical settings.

3.1. Videofluoroscopy

Videofluoroscopic swallow study (VFSS) has been the gold standard for evaluation of dysphagia since the 1980s [6]. VFSS is performed by radiographically recording the anatomic structures and real-time function of the mouth, pharynx, and esophagus. This occurs while the patient is asked to take a liquid bolus of known viscosity. Radiographic evaluation with a jog-wheel is nec-

essary to identify the site of dysfunction through frame-by-frame analysis of the swallow mechanism [6]. Advances in imaging resolution through the last two decades have significantly enhanced the sensitivity and specificity of VFSS. Image intensifiers in digital imaging systems improve image resolution and thus interpretation accuracy of VFSS data [6].

Interpretation is one drawback of VFSS. Several scales have been developed to objectify the interpretation of VFSS. Reference [7] evaluated the inter-rater reliability of Videofluoroscopic Dysphagia Scale (VDS). The scale consists of 14 items each of which can be classified as a measure of oral, pharyngeal, or esophageal function. Reference [7] found low reliability of all oral phase parameters. Pharyngeal and esophageal parameters demonstrated respectively higher inter-rater reliability, however total score reliability according to intra-class correlation coefficient was only 0.556. To maximize utility, it is imperative that videofluoroscopic data be interpreted under the supervision of a highly experienced provider.

3.2. Manometry

Manometry is the gold standard for the assessment of esophageal muscular contraction. Manometry was developed in the 1950s to record esophageal muscle contraction in patients with dysphagia. Manometry has primarily been used to evaluate patients with gastroesophageal reflux disease, achalasia, and dysphagia following gastric band placement. Concurrent use of videofluoroscopy enhances the ability to detect functional success of bolus transport [8].

The original manometric studies recorded pressures via esophageal electrodes spaced 5 centimeters apart to generate a graph of pressures over time. Over the course of several decades, manometry has progressed from fluid-state transducers, to solid-state transducers, to the most recent, high-resolution manometry. High-resolution manometry uses electrodes spaced only 1 centimeter apart to provide fewer pressure reading gaps between electrodes and thus more accurate pressure readings [8].

Recent literature is controversial regarding the true benefit high-resolution manometry over conventional manometry. Most authors site the lack of a well-established tool for interpreting the sheer volume of pressure signals generated by high-resolution manometry as the greatest drawback in utility [9]. As data interpretation catches up to the advance in technology, manometry will provide even more useful evaluation of dysfunctional esophageal motor segments.

3.3. Endoscopy

Endoscopy provides direct observation of the pharyngeal phase of deglutition as the flexible scope bypasses the

oral cavity. It was developed in the nineteenth century, but has made several recent advances in technology.

Endoscopy can now be used to evaluate sensory function. This technique is known as, flexible endoscopic evaluation of swallowing with sensory testing (FEESST). Its suggested use is as a non-radioactive alternative to the modified barium swallow study. Reference [10] used FEESST to assess laryngopharyngeal sensory threshold (LPST) which refers to the intensity of an air pulse stimulus required to trigger laryngeal adductor reflex. Their study showed a significant correlation between LPST impairment and functional impairment.

Most recently, endoscopy has been developed as a 3D modality. Reference [11] demonstrated that 3D endoscopy provided superior visualization over conventional 2D endoscopy in a case series. While this technology is primarily geared toward surgical use, as familiarity increases and cost decreases, it has the potential to become a diagnostic tool.

4. HEAD & NECK CANCER CAUSES OF DYSPHAGIA

4.1. Oral Cancer

Oral cancer is the most common site of head and neck cancers, accounting for approximately 30% of all cases [1]. According to NCI data collected through the SEER program, the age-adjusted incidence of oral cancer is 10.8 per 100,000 people [1]. Half of these cases are diagnosed in individuals between the age of 35 and 64. The median age at diagnosis was 62 years-old. The vast majority of oral cancer is squamous cell (greater than 80%). Other causes include adenocarcinoma, verrucous carcinoma, lymphoma, and Kaposi's sarcoma [1].

Dysphagia related to oral cancer is more commonly a post-treatment than pre-treatment phenomenon, especially when compared to laryngeal and hypopharyngeal cancer sites [12]. Reference [12] showed that among patients with stage III-IV oral and oropharyngeal cancer, 6% suffered pre-treatment dysphagia compared with 68% who suffered post-treatment dysphagia. A similar study [13] reported significantly different rates of pre-treatment swallow dysfunction between tumor sites. Patients with oral and oropharyngeal cancer had aspiration rates of 14% and 30% respectively, while 67% of patients with laryngeal cancer and 80% with hypopharyngeal cancer had problems with aspiration [13].

Pre-treatment mechanisms of dysphagia in oral cancer include mechanical obstruction, muscle weakness, and neural invasion. Reference [14] found dysphagia to be present in 28.2% of patients with at least stage T2 oral cancer. Adenoid cystic carcinoma of the base of the tongue has been reported as a rare cause of dysphagia [15]. The paucity of literature regarding pre-treatment

dysphagia makes it difficult to ascertain the most common mechanism responsible for pre-treatment dysphagia.

Post-treatment dysphagia in oral cancer is being studied extensively. Causes can be broadly categorized as post-surgical effects or chemoradiation effects. Surgical mechanisms include large resection defects and nerve damage. Reference [16] recognized a need to quantify functional outcomes following glossectomy. In an effort to achieve this, they found that patients with tongue strength greater than 30 kPa post-glossectomy had significantly better functional outcomes. Chemoradiation mechanisms include tissue fibrosis, sensory and motor denervation, and xerostomia [16]. Post-treatment dysphagia related to chemoradiation will be discussed later as a phenomenon common to treatment of all types of head and neck cancer.

4.2. Esophageal Cancer

The age-adjusted incidence of esophageal cancers was most recently estimated to be 4.4 per 100,000 men and women per year. The median age at diagnosis was reported to be 67 years of age [1]. Rates of esophageal cancer vary greatly by international region, likely reflecting significant differences in known risk factors. Worldwide, the rate of esophageal cancer is increasing [17].

In the United States, a reduction in tobacco smoking has been followed by a reduction in the rate of squamous cell carcinoma (SCC), while increased rates of obesity and reflux disease have been associated with a rise in adenocarcinoma [18]. Together, SCC and adenocarcinoma account for more than 90% of all esophageal cancer cases [19]. The remaining cases have been reported to be lymphoma, more commonly non-Hodgkin's type, MALT, melanoma, carcinoid, and leiomyosarcoma [20].

Dysphagia is a common pre-treatment manifestation of esophageal cancers. Many cases are not diagnosed until the tumor burden is large enough to cause lumen obstruction [21]. Late stage disease requires treatment by esophagectomy with the use of neoadjuvant therapy being decided on individual case basis. The surgical management of esophageal cancer has seen a shift toward minimally invasive techniques [22]. Reference [23] found no difference in survival between open versus minimally invasive esophagectomy. These findings were consistent with those of other investigators [24]. Unfortunately, prognosis remains poor despite advances in surgical technique and adjuvant therapies. Such poor survival has resulted in little conclusion regarding how to improve dysphagia associated with esophageal cancer.

4.3. Laryngeal Cancer

The age-adjusted incidence of laryngeal cancer is 3.4 per

100,000 men and women per year with a median age at diagnosis of 67 years [1]. Laryngeal cancer has garnered more attention as Human Papilloma Virus (HPV) has emerged as a significant risk factor [25].

Laryngeal cancer may arise in the supraglottis, the glottis, or the sub-glottis. The glottis is the most common site and is more commonly associated with vocal changes than with dysphagia. When dysphagia does occur, it usually manifests itself as an increase in aspiration due to vocal cord or epiglottic dysfunction during the pharyngeal phase of deglutition. In a prospective study of patients with SCC of head and neck, patients whose primary cancer site was located in the larynx suffered the highest rate of aspiration [26].

Patients with HPV develop later stage cancer at an earlier age than their non-HPV counterparts [27]. Recent studies show that the basaloid subtype of laryngeal SCC does confer worse prognosis, and likely greater risk of dysphagia, even after accounting for stage and site [27].

4.4. Thyroid Cancer

The NCI reported age-adjusted incidence of thyroid cancers to be 12.2 per 100,000 women and men. The most common thyroid cancer, by far, is papillary carcinoma, which represents 70% - 85% of cases [1]. Follicular cell carcinoma is the next most common. Medullary thyroid, poorly differentiated, and anaplastic thyroid are far less common. Rare forms of thyroid cancers include squamous cell carcinoma, lymphoma, and sarcoma of the thyroid. Insular thyroid carcinoma is the most recently described form, only being recognized as a unique entity since 1983 [28].

Thyroid disease is a common cause of dysphagia. In a study of patients undergoing thyroidectomy, dysphagia was the most common pre-operative complaint. Thyroid disease causes compressive forces on the swallow apparatus resulting in a progression of worsening symptoms from globus sensation to overt dysphagia [29]. The severity of compressive symptoms directly relates to gland size, owing to direct force by the thyroid gland. The most common causes of thyroid related compressive symptoms are benign goiter, followed by papillary thyroid carcinoma, follicular thyroid carcinoma, and thyroiditis [29].

The presence of more severe compressive symptoms found in patients with smaller gland sizes may be due to underlying disease processes. This suggests that factors in addition to gland size contribute to the development of dysphagia. In particular, invasion and inflammation have been implicated in the development of dysphagia. This notion is supported by disproportionately higher rates of dysphagia reported in patients with lymphocytic thyroiditis than in patients with thyroid carcinoma despite com-

parable gland size [29].

While anaplastic thyroid carcinoma comprises only 1% - 2% of thyroid carcinomas [1], patients commonly present with dysphagia due to rapid growth and distortion of normal anatomy. For this reason, patients presenting with dysphagia as a primary complaint should receive aggressive work-up to rule out malignant etiologies.

5. POST-TREATMENT DYSPHAGIA

Chemoradiation has been an empirically supported mainstay in the treatment of head and neck cancer for over two decades. This practice, combined with earlier age at diagnosis and longer survival has led to a rise in the development of post-treatment dysphagia [30]. Postchemoradiation mechanisms of dysphagia include tissue fibrosis, sensory and motor denervation, and xerostomia [16]. Reference [31] followed 112 patients at 3, 6, and 12 months post-CRT. They found that most patients suffered the greatest functional decline between pre-treatment to 3 months post-treatment. Despite some patient's showing an improvement on objective measures of dysphagia most, patients did not report subjective improvement within the year following CRT [31].

Several modalities to prevent dysphagia and improve functional outcomes following chemoradiation are currently under extensive study. These include use of prophylactic, pre-treatment swallow therapy, use of NG-tube in place of G-tube for feeding during treatment, and use of intensity-modulated radiation therapy (IMRT).

In a meta-analysis, reference [32] found that 5 out of the 6 studies examining prophylactic swallow therapy proved the modality to be beneficial. They noted, however, that neither the cost-benefit ratio nor long term outcomes have been studied.

In general it has been shown that use of NG tube in place of G-tube decreases dysphagia. Maintenance of nutrition through chemoradiation treatment is a difficult task achieved by a diligent multi-disciplinary team. It is thought that use of an NG-tube helps to maintain the strength of motion of muscles involved in the swallow mechanism. Evaluation of patients' appropriateness for NG-tube placement should be done on an individual and multi-discipline basis [32].

Organ-sparing CRT does not spare the structures involved in successful swallow. IMRT is being investigated as a possible alternative to conventional CRT to spare structures critical to successful swallow. Reference [33] demonstrated that IMRT could successfully spare dysphagia/aspiration related structures (DARS), especially the pharyngeal constrictors and the glottic and supraglottic larynx. This resulted in significantly improved post-treatment swallow function [32,33].

6. CONCLUSION

Dysphagia is an important phenomenon in head and neck cancer presentation and outcome. There are several factors that make study of this phenomenon difficult. First, the swallow apparatus is a complex structure. There are several etiologies responsible for dysphagia which may occur at any point during the mechanism. Second, no standard measurement exists to quantify dysphagia across studies. Even within a given measure, there is a lack of consensus regarding the interpretation of data. Third, because head and neck cancers comprise such a wide variety of neoplasms, it is difficult to generalize findings between cancer groups. Finally, head and neck cancers, especially once classified by region and histology, are relatively rare. As the body of research continues to grow, investigators must work toward consensus on parameters such as tumor classification, functional measurement, and data interpretation. Such consensus will greatly improve the strength of studies limited in size by the rarity of such cancers.

REFERENCES

- [1] Surveillance, Epidemiology, and End Results (SEER) Program) SEER*Stat Database: Incidence—SEER 9 Regs Research Data, Nov 2011 Sub (1973-2010) <Katrina/Rita Population Adjustment> Linked to County Attributes—Total US, 1969-2010 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, Released April 2013, Based on the November 2012 Submission. www.seer.cancer.gov
- [2] Magendie, F. (1813) Vomissement. *Procès-verb Acad d Sc*, **5**, 152-159, 174-183.
- [3] Ertekin, C. and Aydogdu, I. (2003) Neurophysiology of swallowing. *Clinical Neurophysiology*, **114**, 2226-2244. [http://dx.doi.org/10.1016/S1388-2457\(03\)00237-2](http://dx.doi.org/10.1016/S1388-2457(03)00237-2)
- [4] Miller, A.J. (1982) Deglutition. *Physiol Rev*, **62**, 129-184.
- [5] Flint, P.W., Haughey, B.H., Lund, V.J., Niparko, J.K., Richardson, M.A., Robbins, T.K. and Thomas J.R. (2010) Cummings otolaryngology—Head & neck surgery. In *Chapter 90: Mechanisms of Normal and Abnormal Swallowing*, 5th Edition, Mosby Elsevier, Philadelphia.
- [6] Ekberg, O. and Olsson, R. (1997) Dynamic radiology of swallowing disorders. *Endoscopy*, **29**, 439-446. <http://dx.doi.org/10.1055/s-2007-1004248>
- [7] Kim, D., *et al.* (2012) Inter-rater reliability of videofluoroscopic dysphagia Scale. *Annals of Rehabilitation Medicine*, **36**, 791-796. <http://dx.doi.org/10.5535/arm.2012.36.6.791>
- [8] Bredenoord, A.J., Tutuian, R., Smout, A.J. and Castell, D.O. (2007) Technology review: Esophageal impedance monitoring. *American Journal of Gastroenterology*, **102**, 187-194. <http://dx.doi.org/10.1111/j.1572-0241.2006.00966.x>
- [9] Kessing, B.F., Smout, A.J.P.M. and Bredenoord, A.J. (2012) Clinical applications of esophageal impedance monitoring and high-resolution manometry. *Current Gastroenterology Reports*, **14**, 197-205. <http://dx.doi.org/10.1007/s11894-012-0253-9>
- [10] Ulualp, S., Brown, A., Sanghavi, R. and Rivera-Sanchez, Y. (2013) Assessment of laryngopharyngeal sensation in children with dysphagia. *Laryngoscope*, Epub.
- [11] Reilly, B.K., Holliday, M.A., Rock, A.N., Kang, X., Shekhar, R. and Preciado, D.A. (2013) Three-dimensional direct laryngoscopy and bronchoscopy: Enhanced visualization of the airway. *JAMA Otolaryngology Head and Neck Surgery*, **139**, 367-370. <http://dx.doi.org/10.1001/jamaoto.2013.156>
- [12] Villares, M., Risueno, T., Carbajo, S.R., Pello, F. and Calvo, D. (2003) Pretreatment dysphagia in patients with advanced head and neck cancer. *Nutricion Hospitalaria*, **18**, 238-242.
- [13] Stenson, K.M., MacCracken, E., List, M., *et al.* (2000) Swallowing function in patients with head and neck cancer prior to treatment. *Archives of Otolaryngology Head and Neck Surgery*, **126**, 371-377. <http://dx.doi.org/10.1001/archotol.126.3.371>
- [14] Pauloski, B.R., Rademaker, A.W., Logemann, J.A., *et al.* (2006) Pre-treatment swallowing function in patients with head and neck cancer. *Head Neck*, **22**, 474-482. [http://dx.doi.org/10.1002/1097-0347\(200008\)22:5<474::AID-HED6>3.0.CO;2-I](http://dx.doi.org/10.1002/1097-0347(200008)22:5<474::AID-HED6>3.0.CO;2-I)
- [15] Hoekzema, C.R., Massey, B.L., Blumin, J.H., Hunt, B.C. and Bock, J.M. (2012) Dysphagia due to adenoid cystic carcinoma of the base of the tongue. *Annals of Otolaryngology, Rhinology and Laryngology*, **121**, 402-406.
- [16] Lazarus, C.L., Husaini, H., Anand, S.M., Jacobson, A.S., Mojica, J.K., Buchbinder, D. and Urken, M.L. (2013) Tongue strength as a predictor of functional outcomes and quality of life after tongue cancer surgery. *Annals of Otolaryngology, Rhinology and Laryngology*, **122**, 386-397.
- [17] Parkin, D.M., Bray, F., Ferlay, J. and Pisani, P. (2005) Global cancer statistics, 2002. *CA—A Cancer Journal for Clinicians*, **55**, 74-108. <http://dx.doi.org/10.3322/canjclin.55.2.74>
- [18] Brown, L.M., Devesa, S.S. and Chow, W.H. (2008) Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. *Journal of the National Cancer Institute*, **100**, 1184-1187. <http://dx.doi.org/10.1093/jnci/djn211>
- [19] Siegel, R., Naishadham, D. and Jemal, A. (2013) Cancer statistics, 2013. *CA—A Cancer Journal for Clinicians*, **63**, 11-30. <http://dx.doi.org/10.3322/caac.21166>
- [20] Enzinger, P.C. and Mayer, R.J. (2003) Esophageal cancer. *The New England Journal of Medicine*, **349**, 2241-2252. <http://dx.doi.org/10.1056/NEJMra035010>
- [21] Thrift, A.P., Pandeya, N. and Whiteman, D.C. (2012) Current status and future perspectives on the etiology of esophageal adenocarcinoma. *Frontiers in Oncology*, **2**, 11. <http://dx.doi.org/10.3389/fonc.2012.00011>
- [22] Low, D.E. (2013) Evolution in surgical management of esophageal cancer. *Digestive Diseases*, **31**, 21-29.

- <http://dx.doi.org/10.1159/000343650>
- [23] Dolan, J.P., Kaur, T. and Diggs, B.S., Luna R.A., Schipper P.H., Tieu B.H., Sheppard B.C. and Hunter J.G. (2013) Impact of comorbidity on outcomes and overall survival after open and minimally invasive esophagectomy for locally advanced esophageal cancer. *Surgical Endoscopy*, **27**, 4094-4103.
- [24] Sihag, S., Wright, C.D., Wain, J.C., Gaissert, H.A., Lanuti, M., Allan, J.S., Mathisen, D.J. and Morse, C.R. (2012) Comparison of perioperative outcomes following open versus minimally invasive Ivor Lewis oesophagectomy at a single, high-volume centre. *European Journal of Cardio-Thoracic Surgery* **42**, 430-437. <http://dx.doi.org/10.1093/ejcts/ezs031>
- [25] Li, X., Gao, L., Li, H., Gao, J., Yang, Y., Zhou, F., Gao, C., Li, M. and Jin, Q. (2013) Human papillomavirus infection and laryngeal cancer risk: a systematic review and meta-analysis. *Journal of Infectious Diseases*, **207**, 479-488.
- [26] Starmer, H., Gourin, C., Lua, L. and Burkhead, L. (2011) Pretreatment swallowing assessment in head and neck cancer patients. *Laryngoscope*, **121**, 1208-1211. <http://dx.doi.org/10.1002/lary.21800>
- [27] Fritsch, V.A. and Lentsch, E.J. (2013) Basaloid squamous cell carcinoma of the larynx: Analysis of 145 cases with comparison to conventional squamous cell carcinoma. Epub.
- [28] Hod, R., Bachar, G., Sternov, Y. and Shvero, J. (2013) Insular thyroid carcinoma: A retrospective clinicopathologic study. *American Journal of Otolaryngology*, **34**, 292-295. <http://dx.doi.org/10.1016/j.amjoto.2012.12.009>
- [29] Banks, C., Ayers C., Hornig J., Lentsch E., Day T., Nguyen S. and Gillespie M. (2012) Thyroid disease and compressive symptoms. *Laryngoscope*, **122**, 13-16. <http://dx.doi.org/10.1002/lary.22366>
- [30] Logemann, J.A., Rademaker, A.W., Pauloski, B.R., *et al.* (2005) Site of disease and treatment protocol as correlates of swallowing function in patients with head and neck cancer treated with chemoradiation. *Head & Neck*, **28**, 64-73. <http://dx.doi.org/10.1002/hed.20299>
- [31] Patterson, J., McColl, E., Carding, P., Hildreth, A., Kelly, C. and Wilson, J. (2013) Swallowing in the first year after chemoradiotherapy for head and neck cancer: Clinician- and patient-reported outcomes. *Head & Neck*, Epub.
- [32] Paleri, V., Roe, J.W., Strojan, P., Corry, J., Grégoire, V., Hamoir, M., Eisbruch, A., Mendenhall, W.M., Silver, C.E., Rinaldo, A., Takes, R.P. and Ferlito, A. (2013) Strategies to reduce long-term postchemoradiation dysphagia in patients with head and neck cancer: An evidence-based review. *Head & Neck*. <http://dx.doi.org/10.1002/hed.23251>
- [33] Eisbruch, A., Schwartz, M., Rasch, C., *et al.* (2004) Dysphagia and aspiration after chemoradiotherapy for head-and-neck cancer: Which anatomic structures are affected and can they be spared by IMRT? *International Journal of Radiation Oncology & Biology & Physics*, **60**, 1425-1439. <http://dx.doi.org/10.1016/j.ijrobp.2004.05.050>