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COMPLICATIONS OF TREATMENT

Dysphagia in head and neck cancer

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SUMMARY

Dysphagia is an important symptom of head and neck cancer (HNC), as well as representing a significant complication of its treatment. The treatment of HNC can result in neuromuscular and sensory damage affecting any stage of the swallow. The protective mechanisms during swallowing afforded by the structures in the pharynx are also affected in HNC. This article reviews the effect of the various treatment modalities in HNC on the swallowing mechanism. Various interventions which may play in role in relieving this dysphagia are also discussed. Due stress has been laid on the need for a multi-disciplinary approach for an optimal outcome in rehabilitating a patient's swallow after treatment for HNC.

Introduction

Dysphagia is a term derived from the Greek words dys (difficulty) and *phagein* (to eat). It is a symptom which indicates a delay in the passage of solids or liquids from the oral cavity to the stomach. Head and neck cancer patients may complain of dysphagia due to the disease itself or as a consequence of treatment. The use of organ-sparing treatment has been on the increase in recent years, but it is important to draw the clear distinction that these do not necessarily translate into functional preservation. Dysphagia and aspiration are recognised as potentially devastating complications of treatment of head and neck cancer. Anything which restricts the opening of the upper oesophageal sphincter, resulting in retention of residual material, may cause spillage into the airway. Aspiration can, thus, be a consequence of dysphagia.[1] Aspiration can be prevented by an intact cough reflex. The incidence of "silent aspiration" is not known. The causes of aspiration can be divided as those causing aspiration before the swallow, during the swallow and after the swallow. Causes of aspiration are as follows: before the swallow – reduced oromotor control, delayed or absent reflex; during the swallow – reduced laryngeal closure, decreased epiglottic inversion or decreased laryngeal elevation; and after the swallow – reduced pharyngeal peristalsis, cricopharyngeal sphincter dysfunction, reduced laryngeal elevation, and structural abnormalities.[2] Patients who undergo chemoradiation are considered to have a higher risk of aspiration and they may lack laryngeal sensation resulting in difficulty in detecting aspiration.[3]

In this review we look at the normal swallowing mechanism, the effects of various treatment modalities on the swallowing mechanism and swallowing rehabilitation methods in head and neck cancer patients.

Normal swallowing mechanism

The process of swallowing includes the conscious effort to ingest food and a subconscious or reflex effort of bolus preparation. The preparation of the bolus is referred to as the preparatory phase, the transport of the bolus from the oral cavity and pharynx to the oesophagus as the transport phase and through the oesophagus as the oesophageal transport phase. The rhythm and pattern of the swallowing mechanism is controlled by a central pattern generator located in the medulla.[4]

In the oral preparatory phase, food is chewed and prepared for swallowing. The tongue plays an important role in the preparatory phase by mixing the food and moving it towards the occlusal surface of the teeth. Sensory innervation across the oral mucosa and the tone of the facial muscles help in keeping the bolus within the oral cavity and in its manipulation. The soft palate approximates to the tongue to create a glossopalatal seal which prevents premature spillage in to the pharynx, while various movements of the mandible are imperative for the adequate grinding of the bolus. The bolus is mixed with saliva and when ready for the oral

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phase of swallowing, the tongue forms a trough containing the bolus with the lateral edges curved upwards. The tongue then contracts from anterior to posterior pushing the bolus back into the pharynx, the whole process taking about one second. This phase involves the Vth, VIIth and XIIth cranial nerves.[4–6]

The pharyngeal phase is involuntary, with sensations travelling through the IXth and Xth cranial nerves and usually lasting one second. In this phase, the soft palate closes the nasopharynx, the larynx is elevated and closed, the pharyngeal constrictors contract and the cricopharynx relaxes. The true cords, the false cords, the epiglottis and the aryepiglottic folds constrict to form a barrier of several layers preventing aspiration. Elevation of the larynx occurs by the contraction of the suprahyoid musculature.[6] The pharyngeal stage generally occurs during a brief phase of apnoea which occurs during the expiratory phase of respiration which continues post-swallow, thus providing a degree of inherent airway protection.[7]

When the larynx is elevated superiorly and anteriorly, the cricopharyngeus relaxes, due to inhibition of its normal resting tone. With this relaxation, negative pressure is created in the upper oesophagus which helps in the movement of the bolus. In addition to true and false vocal fold closure, the laryngeal inlet is closed through epiglottic deflection by the action of the aryepiglottic muscles, the elevation of the larynx, pressure exerted by the base of the tongue and the pressure exerted by the bolus itself.[6] This phase lasts for a second but may vary depending on size of the bolus.[8]

In the oesophageal phase there is a single primary peristaltic wave travelling at 3-4 cm/sec. Several secondary peristaltic waves occur spontaneously in an hour helping to clear residue and any gastric reflux. Oesophageal transit time varies with age.[5]

Head and neck cancer and swallowing

Head and neck cancer (HNC) is the sixth most common cancer worldwide, accounting for 2.8% of all malignancies. The main treatment modalities for HNC are surgery and radiotherapy, with an increasing role for chemotherapy. The choice of modality is dependent on patient variables, primary site, clinical stage, and resectability of the tumour. Patients presenting with early-stage disease can be managed by curative surgery or radiotherapy. Patients presenting with locoregionally advanced disease may be treated with complete surgical excision followed by post-operative (chemo) radiotherapy or with concomitant chemoradiotherapy. In spite of using an aggressive bimodality treatment approach, patients have a poor prognosis, with 5-year survival rates of 30% to 40%.[9] The presence of tumour itself, as well as the treatment, can result in neuromuscular damage affecting any stage of the swallow.[10]

Dysphagia following surgery for head and neck cancer

Surgical interventions for cancers of the head and neck result in specific anatomic or neurologic insults with site-specific patterns of dysphagia and aspiration.[5]

Oral and oropharyngeal surgery

Sessions et al.[11] showed that, for oral surgery, the size of the lesion excised was less predictive of subsequent dysphagia than the area excised. Logemann and Bytell[12] found that swallowing was worse in patients with tumours in the tongue base rather than the anterior floor of mouth. The swallowing deficits that occur after oral resections vary with the site of resection and type of reconstruction. The various reconstruction types for oral and pharyngeal defects are primary closure, skin graft, tissue flap, or microvascular free flap. McConnel et al.[13] found that skin grafts gave better results than when reconstruction is done with a distal flap. A multi-centre prospective study was undertaken to compare the swallowing function before and after oral and oropharyngeal surgery and to compare primary closure, distal myocutaneous flap and microvascular free flap reconstruction. Measurements made were the oral transit time, pharyngeal transit time, pharyngeal delay time, duration of laryngeal closure, duration of cricopharyngeal opening and oropharyngeal swallowing efficiency (OPSE), which is calculated by dividing the approximate percentage of bolus swallowed by the total transit time. Patients with distal flap reconstruction (50.9 ± 8.7) had significantly lower OPSE scores in comparison to patients with primary closure (79.9 ± 8.2) for liquid boluses ($p = 0.01$), the distal flap patients, however, had significantly faster oral transit times on paste boluses but had significantly more pharyngeal residue. Patients with free flaps had significantly lower OPSE scores and more pharyngeal residue when compared to primary closure. The distal flap group had significantly more pharyngeal residue in comparison to the free flap group. The study showed that resections of tongue (<30%) and tongue base (<60%) had better swallowing efficiency with primary closure on liquid boluses. The authors felt that a flap may be acting as an adynamic segment reducing the swallow efficiency by impairing the driving force of the tongue.[14]

In a pilot study for surgical variables affecting swallowing efficiency it was seen that as the percentage of the tongue and tongue base that was resected increased, the efficiency of the swallow decreased. Hence, it is better to replace oral and pharyngeal tissue with a flap so as to not affect the functional tongue. McConnel et al.[14] in a retrospective pilot study of 20 patients and Logemann and Bytell[12] showed better swallowing in patients without use of tongue for closure of oral cavity defects than in patients with tongue-flap closure. In a study of 278 consecutive patients with oral cancer assessed using the University of Washington Quality of Life (UW-QOL) questionnaire it was concluded that primary closure results in a better swallowing outcome than reconstruction with a distal or free flap.[15] The radial forearm free flap is a fasciocutaneous flap which has a wide use in head and neck cancer reconstruction. A bi-lobed sensate design of the flap was introduced by Urken and Biller to preserve tongue mobility.[16] The main disadvantage of this flap has been donor site morbidity. This has led authors to advocate the antero-lateral thigh flap. The antero-lateral thigh flap was first advocated by Song et al in 1984 and is a popular reconstructive method following head and neck surgery.[17] In a study of twenty patients who underwent hemiglossectomy, ten had primary reconstruction with a forearm free flap and ten with an antero-lateral thigh flap. Eight patients in each group received post-operative radiotherapy. The patients' functional outcome was assessed after six months and it was seen that there was no significant difference in the mean scores for deglutition ($p > 0.05$) between the two groups. The donor site was closed primarily in all cases for the antero-lateral thigh flaps and by skin graft and immobilisation for 1 week in all cases for the forearm free flaps. No complications were noted in the former but seen in 4 cases of the latter group. The authors concluded that the antero-lateral thigh flap is ideal for reconstruction of surgical defects following hemiglossectomy.[18]

A videofluoroscopic study of 15 patients who underwent total, subtotal (10% of base tongue is preserved) or partial glossectomies showed stasis in all areas of the oropharyngeal tract after subtotal and total glossectomies.[19] The oral transit times were greater for food of all consistencies and the laryngeal elevation and reduction in opening of the upper oesophageal sphincter. Moderate aspiration after deglutition was noted in 2 patients. Patients who underwent partial glossectomies showed increased oral transit times and required a greater number of swallows to clear the valleculae. Total glossectomy has been associated with the risk of aspiration, for which simultaneous total laryngectomy used to be carried out prophylactically. Laryngeal preservation with total glossectomy was proposed in 1973.[20] In a study of 30 patients who underwent total or subtotal glossectomy with reconstruction and with preservation of the larynx, the post-operative swallowing outcome was compared in patients as per the post-operative MRI appearance of the tongue.[21] Deglutition was significantly poorer in patients with flat or depressed tongues in comparison to patients with protuberant or semi-protuberant tongues ($p < 0.003$). The authors suggested that wider and thicker flaps such as rectus abdominis musculocutaneous flaps be used for reconstruction of the tongue and that the flaps be designed to be 30% wider than the defect. They also advocated laryngeal suspension to prevent prolapse of the flap.

Some tumours may infiltrate the mandible requiring resection. Mandibular defects that are not reconstructed and are not pure lateral defects give a poor functional and aesthetic outcome.[22] In a study of 10 patients with reconstruction of mandibular defects and 10 patients who did not undergo mandibular reconstruction it was seen that there was a clear advantage in function for the reconstructed patients.[23] The 3-dimensional anatomical relationship should be maintained during oro-mandibular reconstruction after composite resection of oral neoplasms in order to preserve physiological function.[24] Complications of bone graft resorption and wound healing were often faced when non-vascularised bone grafts were used. The combination of tissue match and favourable attributes of pedicle length, no repositioning and remote distance from the defect have led to the popularity of the free-fibular flap for reconstruction of composite head and neck defects.[25] In a retrospective study of 163 patients undergoing mandibular reconstruction which compared osseo-cutaneous radial forearm free flap with free-fibular and scapular flaps it was seen that the swallowing outcome was similar between the flap types.[24] In the study the maximum length of bone harvested from radial forearm was 12 cm. The authors felt for larger defects, the fibula graft can offer up to 25 cm of bone. Seikaly et al.[26] in a prospective study of free-fibular reconstruction of mandibular defects compared the swallowing outcome across treatment times pre-operatively, pre-radiation and post-radiation therapy and found no significant difference in swallowing. They concluded that free-fibular grafts are an excellent option for reconstruction of mandibular defects.

Tumours involving the palate and maxillary sinus that are treated by surgical extirpation often require the creation of large oronasal, oromaxillary fistulae and loss of tooth bearing segments which impair oral alimentation.[27] These defects can be managed by skin for lining the defect and a prosthesis for swallowing. The prosthesis requires regular cleaning.[28] The oral and nasal cavities can be sealed by local flaps or by microvascular free tissue transfer. In a retrospective study of 56 patients who underwent partial or total maxillectomy with free flap reconstruction, it was seen that 37 returned to a normal diet and 19 were able to eat a soft diet.[29]

Tracheostomy

Tracheostomy may be used as a short- or long-term solution when the tumour occludes the airway, for post-operative oedema or where supraglottic and glottic oedema may occur during chemoradiation. It may also be indicated due to significant laryngeal incompetence and aspiration risk.

It is reported that the presence of an inflated cuff may have an impact on the range of laryngeal motion and, thus, airway protection and cricopharyngeal opening.[30]

Material collecting above the cuff has passed the true cords and is considered aspirated and micro-aspiration can occur with an inflated cuff. Manometers are essential for cuff pressure management and deflation trials are needed to prevent blunting of the cough reflex. In a retrospective study of videofluoroscopy results of 623 tracheostomised patients with inflated and deflated cuffs, it was concluded that there was a higher incidence of silent aspiration and reduction in laryngeal elevation in the cuff-inflated condition. They also concluded that patients should undergo instrumental evaluation in both a cuff-inflated and -deflated condition, thus returning those with adequate swallow function to oral intake at the earliest opportunity.[30]

The causes of aspiration after tracheostomy were divided into mechanical and neurophysiological factors.[31] The mechanical factors were decreased laryngeal elevation due to suturing of the trachea to the skin and stasis of secretions in the upper airway and cervical oesophagus due to local compressive forces exerted by the inflated cuff. The neurophysiologic factors were desensitization of the protective cough reflex and a loss of co-ordination of laryngeal closure. An inflated cuff is not protective against aspiration in tracheostomised patients. High volume, low pressure cuffs significantly decrease this risk of aspiration.[32] It is key that prior to decannulation of the post-surgical patient, the supraglottic airway should be evaluated to ensure successful removal of the tube.

Endoscopic laser surgery on the larynx

In a study of 117 patients who underwent transoral laser microsurgery for stage III or stage IV glottic or supraglottic carcinoma of the larynx, swallowing was assessed by the functional outcome of swallowing scale (FOSS).[33] Out of the 68 patients alive on latest follow-up, 7% were feeding tube-dependent, 44% of the patients could be assessed by the FOSS system and it was seen that the overall median post-treatment FOSS stage was stage 1 which is normal function with episodic or daily symptoms of dysphagia. The authors used a definition of FOSS stage 2 or better as the functional endpoint and found that 22 of the 28 patients for whom follow-up data were available met the criteria.

Partial laryngectomy

Partial laryngectomy procedures were introduced to decrease the functional impact of total laryngectomy on swallowing and speech. A study comparing the dysphagia outcome in 25 total laryngectomy and 11 frontolateral laryngectomy patients found a statistically significant difference between the two, with 36% patients having difficulties of whom 12 had undergone total laryngectomy and 1 frontolateral laryngectomy ($p < 0.027$).[34] The patients were interviewed by a speech language pathologist using a semi-structured questionnaire. In a study of functional outcome of 29 male patients undergoing cricohyoidopexy, frontolateral laryngectomy or laryngofissure cordectomy it was found that time to return to oral feeding was significantly longer in patients undergoing cricohyoidopexy (day 20) and frontolateral laryngectomy (day 6) in comparison to cordectomy (day 0).[35] There was no statistically significant difference on the swallowing outcome when these procedures were combined with arytenoidectomy. In a study comparing 17 patients treated by cricohyoidoepiglottopexy (CHEP) with 21 patients of near total laryngectomy with epiglottic reconstruction (NTLER), nasogastric tubes were removed at a mean of 23.0 (SD 13.6) days in the CHEP group and 17.0 (SD 11.4) days in the NTLER group. The difference was not significant ($p > 0.05$) and the swallow function was good on long term follow-up in both groups. All the patients selected for the study had T1b glottic cancer.[36]

Supraglottic laryngectomy

Supraglottic laryngectomy involves the removal of the epiglottis, aryepiglottic folds, false cords and one or both superior laryngeal nerves. Aspiration can occur following supraglottic laryngectomy due to incomplete airway closure, secondary to pharyngeal residue spilling in to the airway, inadequate laryngeal elevation or weak propulsive forces.[37] When the supraglottic laryngectomy is extended to involve the tongue base or arytenoids, aspiration is more likely. In a study of 55 patients undergoing partial laryngectomy it was seen that patients who underwent extended supraglottic laryngectomy took significantly longer to achieve swallowing rehabilitation.[38]

Supracricoid laryngectomy

Supracricoid laryngectomy includes the removal of the true and false cords of both sides, paraglottic space, the thyroid cartilage and occasionally the epiglottis and one arytenoid. A study of 27 patients who underwent supracricoid partial laryngectomy evaluated by modified barium swallow showed that all patients aspirated initially and had impaired base of tongue and laryngeal movements. The median tube removal was 9.4 weeks and 81% of patients returned to normal diet. The most common complications reported by the authors were pneumonia and subcutaneous emphysema.[39]

Total laryngectomy

Dysphagia, as a predominant negative sequela following total laryngectomy, and has been reported to range from 10% to 60%.[40] It may be as a result of tumour recurrence, a benign stricture, a second primary, post-radiation,[41] pseudo-epiglottis[12] formation or loss of co-ordination of the pharyngeal constrictors. A spatial distortion may occur in the hypopharynx and cervical oesophagus due to the tethering of the tracheostomy.[41] Following total laryngectomy, patients take longer to clear the bolus from their pharynx.[42] In an evaluation of lifestyle changes post-total laryngectomy, Ackerstaff et al.[43] reported that 25% patients had a change in diet, consistency and style of eating. Authors have variously described successful swallowing as maintenance of nutrition without tube feeding and ability to swallow modified consistencies as the optimal outcome. Hillman et al.[44] reported 76% of laryngectomy patients resuming normal diet by 2 years post-surgery. In a study of 55 patients[45] who underwent total laryngectomy and 37 who underwent laryngopharyngectomy with jejunal reconstruction, it was seen that 27% of the laryngectomy group and 65% of the laryngopharyngectomy group developed swallowing-related complications in the one month post-surgery. This was statistically significant ($p < 0.001$). All patients were on post-operative nasogastric (NG) tube feeding, with the mean duration to oral feeding in the total laryngectomy group at 10.7 ± 2.0 days. Late complications requiring non-oral nutrition on follow-up were seen in 27% of the laryngectomy group. Percutaneous endoscopic gastrostomy (PEG) feeding for a mean duration of 23.3 ± 17.9 days was required in 5% of the laryngectomy patients. On discharge, one laryngectomy patient was on normal diet and 98% were unable to consume diet of normal consistency. On long term follow-up, 58% of patients continued to have dysphagia. The authors of the study classified dysphagia as an inability to achieve normal dietary status, stating that this may be the reason for the higher incidence of dysphagia reported. Following laryngectomy, the drop in hypopharyngeal pressure that occurs on laryngeal elevation during the pharyngeal phase of the swallow is lost.[41] The pseudo-epiglottis is a mucosal fold at the junction between the tongue base and the reconstructed pharynx.[12] Lateral radiographic visualisation gives the appearance of the contour of an epiglottis, hence the term "pseudo-epiglottis". On clinical examination, due to the resting state, the pseudo-epiglottis tends to collapse against the tongue base giving the false impression of adequate space. However, as a result of pharyngeal contraction, this pseudo-epiglottis forms a pocket during a swallow accumulating food and causing dysphagia[41] (Fig 1).

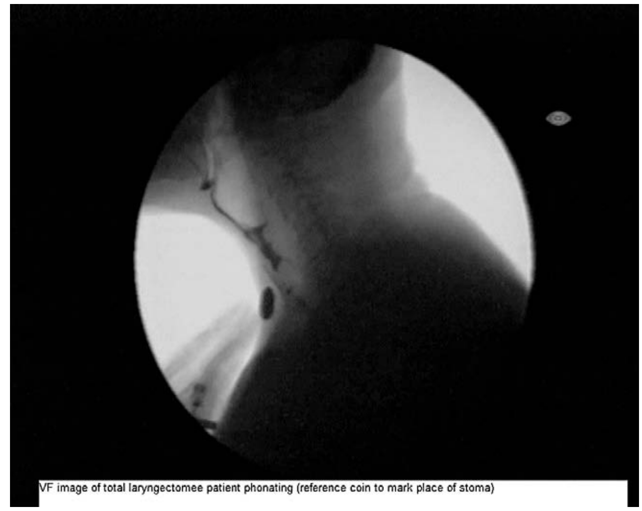

Fig. 1. VF image of total laryngectomee patient phonating (reference coin to mark place of stoma).

Hypopharyngeal surgery

Minimal morbidity and mortality with single stage reconstruction, short hospital stay and early restoration of swallowing has been the goal of hypopharyngeal surgery. Ogura and Biller[46] advocated partial pharyngolaryngectomy in patients whose tumour did not involve the true cords and arytenoids, the apex of the pyriform sinus and did not invade the thyroid cartilage. When the resection does not involve the lateral wall of the pyrifrom sinus the defect can be closed by a hinge flap or local mucosal flap.[46] In a study of 20 patients who underwent partial pharyngolaryngectomy with reconstruction using a radial forearm free flap, 50% of patients returned to a normal diet and 35% to a soft diet at 6 months post-surgery.[47] Aspiration was seen in 45% of patients, but data were absent in 20% of patients. In a study of 55 patients who underwent transoral laser surgery for pharyngeal and pharyngolaryngeal tumours of T1, T2 and T3 stage, 67% patients required a feeding tube, which was removed at a median period of 7 days. Of the 32 patients followed up, 16 patients had returned to a normal diet.[48] Myocutaneous flaps, visceral transpositions and free flaps have been used for circumferential reconstruction of the hypopharynx. Myocutaneous flaps have the problem of developing local complications such as fistulae and dysphagia which are difficult to treat due to the thickness of the flaps. Proximal lesions of the pharynx and hypopharynx are reconstructed by free jejunal transfer, whereas gastric transposition is used for reconstruction when the resection extends beyond the thoracic inlet. In an analysis of 209 patients who underwent total laryngopharyngectomy between 1982 and 1999,[49] 61% of patients underwent total oesophagectomy with pharyngogastric anastomosis, 37% cervical oesophagectomy with free jejunal transfer and 2% pharyngocolic anastomosis. The average time of resumption of feeding was 19.7 days and 98.4% of patients achieved swallowing. Survival rate without dysphagia was higher for gastric anastomosis (89%) than for jejunal grafts (76%). Swallowing is better with gastric transposition because of the low rate of fistula and stricture formation. In a study of 29 patients who underwent hypopharyngeal resection with jejunal free transfer, the nasogastric tube was removed at a mean of 15 days (9–150 days) and in 25 it was removed before the 15th day. Patients who received adjuvant radiotherapy (15 patients) did not show any swallowing impairment.[50]

Skull base surgery

Surgery involving the skull base poses a problem due to the presence of vital structures in its vicinity. In a retrospective study of 19 patients with nerve sheath tumours of the skull base,[51] 57.8% patients presented with a soft tissue lump, dysphagia was a presenting symptom in 3 patients with a neck lump. Patients with extensive tumours usually do not present with significant dysphagia as the swallowing mechanism adapts to the slow onset of the cranial nerve paresis, however post-operative dysphagia can be acute due to injuries to the adjoining cranial nerves.[52] The various approaches used for accessing the skull base may affect the swallowing mechanism in various ways. The anterior approach involving maxillectomies may cause palatal defects and nasal reflux. The lateral approach through the zygoma and mandible may injure cranial nerves V, VII, IX, X, XI and XII. Temporal bone resections and temporal bone approaches may injure the VIIth cranial nerve with subsequent difficulties.[53] In fact, not just the nerves, but the pharynx itself may be injured in a skull base surgery.[52]

Radiotherapy

The conventional radiotherapy dosage for cure in HNC is daily fractions of 1.8–2.0 Gray (Gy), up to total doses of 66–70 Gy over 6 or 7 weeks. There is now evidence that suggests that alterations in the fractionation schedule, as well as concomitant chemotherapy, may significantly improve tumour responses. However, these aggressive treatment regimens have also contributed to significant dysphagia.[1] Radiotherapy to the head and neck results in appreciable dose delivery to critical structures necessary for normal deglutition, such as the tongue, larynx and pharyngeal muscles. Acute side-effects of radiotherapy are mucositis, dysphagia, hoarseness, erythema and desquamation of the skin. The potential late sequelae of this high radiation dose include osteonecrosis, dental decay, trismus, hypogeusia, subcutaneous fibrosis, thyroid dysfunction, oesophageal stenosis, hoarseness, and damage to the middle or inner ear.[54] The various structures within the head and neck region have their own inherent responses to radiation. Mucocutaneous tissues subjected to irradiation develop increased vascular permeability leading to fibrin deposition, collagen formation and eventually fibrosis.[55] The type and severity of the effects are related directly to radiation dosimetry, including total dose, fraction size, and duration of treatment.[56] A study was conducted in 100 patients with head and neck cancer treated by radiotherapy to evaluate the oral sequelae. The mean post-radiotherapy time when the patients were evaluated was 28 months. It was seen that 30% of the patients had dysgeusia, 38% had dysphagia and 68% had xerostomia. The authors concluded that the post-radiotherapy sequelae are dependent on radiation field, radiation dose, use of anti-xerostomic medication and post-radiotherapy time.[57] EORTC protocol 22791 compared daily fractionation to pure hyperfractionation of 80.5 Gy in 70 fractions in 7 weeks using 3 fractions of 1.15 Gy per day in advanced oropharyngeal carcinoma.[58] There was an improved locoregional control noted in the hyperfractionation schedule and there was no difference in the late normal tissue damage between the modalities. In an analysis of 39 patients for late complications of rapid hyperfractionated radiotherapy, it was seen that complications of cervical fibrosis, mucosal necrosis, bone necrosis, trismus and laryngeal oedema were common.[59] Late complications were seen in 70% of the patients and in 54% of the patients it was considered severe. There was no relationship seen between the field sizes, dosimetric data and frequency of late effects. The authors concluded that the interval between the daily sessions is of critical importance in hyperfractionation schedules. An analysis of 784 patients with squamous cell carcinoma of the pharynx or larynx treated by external beam radiotherapy compared site and size of the tumour, total dose, fraction size and treatment time.[60] There was a weak relationship between the late effects to patient and fractionation schedules. The size of the primary had a significant influence on the complication rate independent of the fractionation schedule. In recent years, there have been favourable results reported with the introduction of conformal 3-dimensional radiotherapy techniques and, in particular, intensity modulated radiation therapy (IMRT) which allows for radiation to be delivered to the tumour while sparing surrounding healthy tissues.[61] Studies relating to swallowing in IMRT suggest that there is the potential for improved functional outcomes with targeted therapy avoiding key structures.[62] In particular, the superior and middle constrictor muscles have been implicated as key swallowing structures to avoid.[63] A study was conducted among 31 dysphagic nasopharyngeal carcinoma patients, treated by radiotherapy alone with a mean follow-up of 8.5 years, to see the functional and anatomic changes.[64] It was seen that 93.5% of patients had pharyngeal retention and an incidence of 77.4% of post-swallow aspiration. Other disorders which were observed were atrophy of the tongue (54.8%), vocal cord palsy (29%), velopharyngeal insufficiency (58%), premature leakage (41.9%), delay or absence of the swallow reflex (87.1%), poor pharyngeal constriction (80.6%) and silent aspiration (41.9%). It was seen that there was a significant role of poor pharyngeal constriction and abnormal upper oesophageal sphincter function in post-swallow aspiration. In a study of 40 patients receiving radiotherapy for advanced laryngeal carcinoma,[65] aspiration was identified in 84% of patients and 44% aspirated silently. Impaired hyolaryngeal motion, incomplete epiglottic inversion and reduced base of tongue retraction to the posterior pharyngeal wall were the most prevalent abnormalities identified. Only 15% of the total number of patients required a feeding tube prior to radiotherapy. During the course of treatment 78% of the patients had a feeding tube at some point of time and 52% of these were removed eventually. Of the disease-free patients 72% returned to oral nutrition. Patients who were feeding tube-dependent in the pre-treatment stage remained so on assessment post-radiotherapy. Fibrosis and functional deterioration of the swallow is said to be avoided by encouraging patients to swallow during therapy.[1] However, the ability to maintain normal diet or swallow does not indicate a normal swallow mechanism and safe limits of aspiration have not been quantified. In a retrospective study of 158 patients[66] who underwent treatment for head and neck cancer, it was seen that 16 out of 50 patients undergoing radiotherapy needed tube placement, whereas 75 patients of 108 undergoing chemoradiotherapy underwent tube placement ($p < 0.001$). They also concluded that a PEG was required for longer periods of time and was associated with more dysphagia and required pharyngo-oesophageal dilatation in comparison to NG tubes. In a multi-centre cross-sectional study for the clinical factors influencing the placement of an enteral feeding tube in head and neck cancer patients, it was found that 28% of patients receiving chemoradiation required tube feeding.[67] As per the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on enteral nutrition for non-surgical oncology,[68] patients with obstructive head and neck cancer lesions interfering with swallowing should be started on enteral feeding delivered by a tube. Tube feeding is also indicated for severe oral and oesophageal mucositis with dysphagia and a PEG is preferred to an NG tube. In a recent randomised study of 33 patients undergoing chemoradiation for head and neck cancer, no evidence was found to support the use of PEG over NG tubes for enteral nutrition.[69]

Xerostomia is a common side effect of radiotherapy. Due to the challenges of bolus formation in the absence of saliva, patients may have to make permanent changes to their diet.[9] Research has shown that while patients with xerostomia perceive that their swallowing is impaired from a sensory and comfort perspective, swallowing physiology and bolus transport was unaffected.[70] Transforming growth factor β1 (TGFβ1) expression can be activated after high dose radiation and this is known to be involved in collagen deposition and degradation. As a result, swallowing can be affected several years after treatment with a fixation of the hyolaryngeal complex, reduced range of tongue motion, reduced glottic closure and cricopharyngeal relaxation, resulting in the potential for aspiration.[56] Irradiated patients have longer oral transit times, increased pharyngeal residue, and reduced cricopharyngeal opening times.[9]

Chemotherapy

Chemotherapeutic agents can impact the ability to swallow and affect nutrition in HNC. Various side-effects like nausea, vomiting, neutropenia, generalised weakness and fatigue can occur. Nutritional supplementation by routes other than oral may be required when the pain from mucositis prevents adequate nutrition. Approximately 40% of patients undergoing chemotherapy are reported to have mucositis; however, almost 100% of patients receiving chemoradiation report mucositis.[71] Symptoms of mucositis include odynophagia, dysphagia, dehydration, heartburn, vomiting, nausea, and sensitivity to salty, spicy, and hot/cold foods. Stomatitis may result in eating difficulty. The anti-metabolites such as methotrexate and 5-fluorouracil are the cytotoxic agents most commonly associated with oral, pharyngeal, and oesophageal symptoms of dysphagia.[72,73]

Concurrent chemoradiation was introduced to improve prognosis by increasing tumour cell killing with chemotherapy which also acts as a radiosensitiser.[74] Inoperable tumours showed good control rates, but the toxicity of the two modalities was significant with severe mucositis.[75] Videofluoroscopic swallowing studies performed following chemoradiation showed that there was severe dysfunction of the base of the tongue, larynx and pharyngeal muscles, leading to stasis of the bolus, vallecular residue, epiglottic dysmotility and, in severe cases, aspiration.[56] The combination of aspiration with neutropenia arising from chemotherapy, may lead to aspiration pneumonia, sepsis and respiratory failure.[56] It is also believed that aspiration is under reported in chemoradiation patients, because it is often silent.[76] In a cross-sectional study comparing the swallowing outcome (by MD Anderson Dysphagia Inventory (MDADI)) after treatment with chemoradiation or surgery followed by radiation in stage III and stage IV patients with oropharynx, larynx and hypopharynx cancers, the swallowing outcome was better in patients with chemoradiation for oropharyngeal primaries.[77] Of the total of 40 subjects, 22 underwent surgery followed by radiation and 18 underwent chemoradiation. The MDADI scores for patients treated by chemoradiation for oropharyngeal tumours was significantly better than patients treated by surgery followed by radiation. There was no difference in the scores for the laryngeal and hypopharyngeal tumours and between the oropharynx and larynx/hypopharynx tumours. Another cross-sectional study conducted in patients with advanced oropharyngeal cancer compared the laryngeal penetration and aspiration between patients treated by chemoradiation (CRT) and surgery followed by radiation (SRT).[78] Of the total of 21 subjects in the study, 11 were in the SRT group and 10 in the CRT group and they were all seen 12 months after completion of their treatment. The patients were assessed using the validated penetration–aspiration scale and the MDADI. It was seen that significantly fewer patients in the SRT group (2/11) were able to consume a complex diet of all solids and liquids after treatment in comparison to patients of the CRT group (8/10). Patients of the CRT group demonstrated better airway protection during swallowing and swallow-related quality of life when their scores were compared. Hanna et al conducted a retrospective study in 127 patients with advanced HNC treated by intensive CRT to evaluate the efficacy and toxic effects of this therapy.[79] The toxic effect data collected included the rate and grade of treatment-related complications and the rate of unscheduled hospital admissions for the management of treatment-related toxic effects. Primary tumour sites were oropharynx in 46%, larynx in 28%, hypopharynx in 16%, oral cavity in 8% and oesophageal and sinonasal in 3% patients. Neutropenia was seen in 50% of the patients and of these 50% had grade 3–4 neutropenia. Mucositis was seen in 64% of the patients of which 33% were severe. Nausea was seen in 44% of patients and severe nausea in 15% and vomiting was seen in 11% of the patients. Gastrostomy tubes were placed in 73% of the patients. Dysphagia was the most common long-term complication and 40% of the patients required a change from their pre-treatment diet. The authors felt that early or pre-treatment placement of a gastrostomy tube resulted in "defunctioning" of the swallowing mechanism which may have had a detrimental effect on the long-term outcome of swallowing function. They also felt that active swallowing rehabilitation should be continued even when a gastrostomy tube is placed. The authors felt that the cause of dysphagia may be due to stricture formation as a consequence of ulcerative mucositis. Therefore, in cases of dysphagia it may be better to use a nasogastric tube than a gastrostomy tube for nutritional support, as it helps to maintain a patent lumen. The causes of dysphagia after CRT could be more likely due to generalised weakness and lack of co-ordination in deglutition. This could be due to fibrosis of the musculature or toxic effects on the neuromuscular junctions. Pharyngeal dysmotility and aspiration could result from muscular weakness and lack of sensation.[80]

Swallowing rehabilitation

Swallowing disorders arising as a result of head and neck cancer impairs the quality of life of the patient. Any available biochemical, technical and physical measures need to be used to improve the swallowing function of the patient. Teams should be alert to patients who have undergone treatment for HNC and are reporting swallowing difficulty. Patients should undergo a comprehensive clinical assessment and instrumental assessment will be selected based on the recommendation of the speech language pathologist. Recurrence is a possibility that has to be kept in mind when post-treatment patients present with recent-onset dysphagia or any worsening of existing dysphagia. Optimal rehabilitation planning should include detailed pre-treatment assessment and be informed by both clinical and instrumental assessment of deglutition by the speech language pathologist.

There are similarities between radiation mucositis and mucosal toxicity of chemotherapy but radiation mucositis is more difficult to prevent and treat. The Consensus Development Panel of the National Institutes of Health stated that no drug can prevent mucositis.[81] The oral care programs aim to remove mucosal irritating factors, cleanse the oral mucosa, maintain the moisture of the lips and the oral cavity, relieve mucosal inflammation and prevent and treat the inflammation.[82,83] Sharp teeth and fillings need to be smoothened or polished to reduce the chances of trauma. Irritating factors like spices, alcohol, tobacco and spicy foods need to be avoided.[82] Aqueous chlorhexidine rinses have been shown to benefit chemotherapy- but not radiotherapy-induced mucositis.[82] Sutherland and Browman rated several anaesthetics, analgesics and mucosal coating agents as cytoprotective but not therapeutic.[84] They also showed that narrow-spectrum antibiotic lozenges have benefit in the prophylaxis of radiation mucositis. The results with the administration of growth factors and free radical scavengers are promising but need further study.

Dysgeusia occurs as a result of radiation effects on the taste buds and salivary changes. This usually returns to normal within a year in most cases.[85,86] Taste loss can be prevented by the use of shields and by repositioning the fields. Zinc supplements are reported to be helpful in reducing dysgeusia after radiotherapy.[87]

Prevention is the best intervention for salivary gland hypofunction post-radiotherapy.[55] This is best achieved by radiation beam arrangement to avoid the salivary glands. IMRT is shown to reduce the radiation-induced salivary gland impairment and improve the xerostomia-related quality of life compared with conventional radiotherapy.[88] Post-radiotherapy salivary loss can be prevented by the use of sialogogues, amongst which pilocarpine has been extensively studied.[89] The effect of pilocarpine can be attributed to the stimulation of the minor salivary glands which are more resistant to the effects of radiation than the parotid glands. Amifostine, a free radical scavenger, when administered systemically has been shown to reduce xerostomia during and after radiation therapy.[90] The drug has also shown to have the undesirable effect of tumour protection.[91] If the amount of saliva produced after stimulation is insufficient then stored autologous saliva collected prior to radiotherapy or donor saliva is an option, however most patients find this gruesome.[92] A variety of rinsing solutions are available which moisten the mucosa. Other options are frequent moistening of the mouth with water, tea, saline, sodium bicarbonate solutions and diluted milk of magnesia.[93] Viscous glycerine-containing mouthwashes require less frequent applications. Complex saliva substitutes which moisten the mucosa, maintain viscosity and retard enamel solubility have also been developed. These are based on carboxymethylcellulose or mucin.[94] Other substitutes are xanthan gum-based and polyglycerylmethacrylate-based substitutes.[95] Each of these substitutes has its own advantages and disadvantages. Several authors believe the effectiveness of artificial saliva can be judged by indices like degree of night time discomfort and difficulty in talking. The effectiveness is also dependent on provision of adequate instructions.[93]

Rehabilitation can be broadly divided in to 3 main areas: (i) preventative; (ii) compensatory: and (iii) therapeutic exercises and manoeuvres.[80] From the preventative perspective, there is a growing body of evidence to suggest that patients should commence prophylactic swallowing exercises prior to commencing radiotherapy.[96,97] However, it is recognised that patients receiving chemoradiotherapy may find it difficult to continue the exercises during treatment due to the side-effects of the therapy.[98] Amifostine decreases the mucositis and xerostomia associated with chemotherapy.[90] However, there are no objective data on the effectiveness of this therapy in reducing swallowing disorders. There are a range of compensatory approaches which include postural changes such as a chin tuck posture to increase airway protection, or manoeuvres such as the supraglottic swallow which requires the patient to consciously protect the airway by breath holding during the swallow and coughing immediately post-swallow to expectorate penetrated or aspirated material from the airway. In addition, changes to consistency, temperature and taste may also be introduced. Postural changes and manoeuvres may be used in isolation or in combination, including adaptation of foods and fluids. Any strategies should only be implemented after evaluation of the nature and extent of any oropharyngeal dysphagia under videofluoroscopy or functional endoscopic evaluation of swallowing (FEES), especially when it is known silent aspiration is a risk factor in HNC patients, for example following chemoradiation.[76] Compensatory approaches can yield immediate benefit and may facilitate some oral intake. Instrumental evaluation allows for the speech language pathologist to evaluate the most appropriate rehabilitative strategies. These may be strengthening, as well as range of motion, exercises.[99] Some strategies have a dual compensation-exercise role such as the Mendelsohn manoeuvre which involves voluntary elevation of the larynx and prolonged opening of the cricopharyngeal sphincter. A range of exercises may be implemented following instrumental assessment, such as exercises to improve base of tongue strength.[100] In the post-operative period, after adequate healing, exercises can be introduced following assessment. A detailed specific review of preventative and rehabilitative strategies for HNC patients undergoing radiotherapy, chemotherapy and surgery has recently been published.[80]

Post-surgical cases may have decreased sensory feedback from the oral cavity and pharynx. Sensory feedback can be increased by changing the size of the bolus, temperature of the bolus and pressure on the tongue. Instruments such as a cold spoon, ice-cream sticks, chop-sticks can be used to apply pressure on the back of the tongue to increase the sensory feedback in the patient. Encouraging the patient to feed themselves also increases sensory feedback.[98] Post-operative patients can be taught range of motion exercises for strengthening musculature of the head and neck.[101] These exercises specifically address musculature of sites such as jaws, lips, tongue, and closure of the airway and for laryngeal elevation. FEES and videofluoroscopy can be used to study the success of therapy.[98]

Prosthetic devices can be used to improve the efficiency of the swallowing mechanism. Palatal defects can be closed by prosthetics for the oral phase of swallowing and, at the same time, they also prevent nasal leak of the food.[102] The prosthetic device should be designed so as to provide maximum functional rehabilitation. It is advantageous to have a prosthodontist working with the speech pathologist for the design of the prosthetic device.[98] In addition to functional rehabilitation, another matter of concern is the malnutrition that is associated with the treatment of the cancer. Factors influencing the development of malnutrition and its severity are the pre-treatment nutritional status of the patient, the site of the primary tumour and the type of treatment delivered.[103]

Dysphagia arising from the treatment of HNC also affects the psychosocial behaviour of the patient.[104] The patient may have special requirements when eating which may curtail his social activities. Patients may be more dependent on care-providers and family members for their feeding. The alteration of the feeding process and the various adaptive strategies may cause distress and anxiety to the patient. The cosmetic changes post-surgically may have an impact on the psychological status of the patient. Pre-treatment counselling and psychosocial support can help in the social and physical rehabilitation of the patient.[104]

Conclusion

Successful management of the HNC patient is underpinned by committed partnership working in the MDT. While disease control is paramount, this should be considered in tandem with the likely functional impact on swallowing function and subsequent quality of life. An accurate knowledge of the anatomy and physiology of the swallowing mechanism is essential for optimal management of dysphagia following treatment of HNC. The site of tumour, stage, extent of surgical excision and any reconstruction done affects the swallowing post-surgery. Radiotherapy and chemoradiotherapy affect the oral and pharyngeal phase of swallowing. Strategies such as exercises, IMRT and cytoprotectors may improve the swallowing function and overall quality of life of the patient. However, further studies are needed to develop better strategies and exercises.

Conflict of interest statement

There was no conflict of interest between the authors in the conception or in the content of this article.

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