

Preservation of organ function in head and neck cancer

Abstract

Preservation of function is a crucial aspect for the evaluation of therapies applied in the field of head and neck cancer. However, preservation of anatomic structures cannot automatically be equated with preservation of function. Functional outcome becomes increasingly important particularly for the evaluation of alternative treatment options with equivalent oncological outcomes.

As a result, present studies take into account three topic areas with varying emphasis: (1) the effects of cancer therapy on essential physiological functions, (2) additional therapy-induced side-effects and complications, and (3) health-related quality of life.

The present article summarizes vital aspects of clinical research from recent years. Functional outcomes after surgical and non-surgical treatment approaches are presented according to tumor localization and staging criteria. Additional methodological aspects relating to data gathering and documentation as well as challenges in implementing the results in clinical practice are also discussed.

Keywords: head and neck cancer, oral cancer, oropharyngeal cancer, laryngeal cancer, organ preservation, toxicity, quality of life, functional outcome

Uta Tschiesner¹

1 Clinic for Otorhinolaryngology,
Ludwig Maximilians
University (LMU) Munich,
Munich, Germany

Introduction

From an oncological perspective, it is particularly important that recurrences and secondary malignancies have to be recognized and treated as early as possible in the course of cancer follow-up among patients with head and neck cancer (HNC). Further goals include the treatment of functional and psychosocial issues, and an efficiency assessment of the therapy that has taken place [1].

Patients with HNC suffer from a variety of problems, e.g. with breathing, eating, speaking, pain, and psychic difficulties, that follow a cancer diagnosis, and individual changes in their day-to-day lives. Examples of this are participating in meals within their usual social setting, conducting personal hygiene, oral communication, and pursuit of their professional and social activities. According to the World Health Organization (WHO), all these aspects are summarized under the term “functioning” [2]. The assessment of functioning after cancer treatment has become a key component of many clinical studies in recent years. The extent of functional problems is considered an independent predictor of patient survival [3], [4], [5], [6].

Beyond that, it would be desirable to make comparative statements on the (expected) functional results of oncologically equivalent therapies to be able to give patients more detailed advice on their therapy decisions.

Another term that is meaningful in this context is “health-related quality of life.” It represents a subjective psychological notion that assesses health status from the perspective of the patient affected. It is defined as a multidimensional notion that encompasses physical, mental,

social and behavioral components of well-being and functioning from the viewpoint of the patient [7].

Despite great interest and a correspondingly large number of publications on the topic, it is difficult overall to draw conclusions for clinical care. This is partly due to methodological limitations of the studies (imprecise details on tumor localization and the therapy conducted, small case numbers, few randomized controlled studies, limited longitudinal data, etc.), but also to two content-related challenges. First, the lack of a definition for the criteria of functioning across all health professional groups, and secondly a quite large and non-homogenous group of different instruments with which functioning is measured. Some of these instruments vary so much among each other, that it is hard to design suitable meta-analyses [8], [9], [10].

The goal of this review paper is to summarize the current status of knowledge on the topic of preservation of function in HNC. It will also discuss methodological aspects of data gathering and documentation as well as challenges of implementation in clinical practice.

Diagnostic methods

Many outcome instruments have been developed and validated for different study questions over the past few years. Comparisons of diverse target parameters for measuring functional outcome in clinical studies reveal a large spectrum of patient-, investigator- and/or technology-based outcome instruments [11], [12], [13]. There

is not a gold standard; different instruments are used depending on the issue being examined.

Documenting side-effects of therapy

The National Cancer Institute (NCI), the European Organisation for Research and Treatment of Cancer (EORTC), the Radiation Therapy Oncology Group (RTOG) and other groups have made various efforts to systematically document the effects of radiation therapy/chemotherapy on the organism, and to develop a uniform classification from various scores. The RTOG acute/late radiation morbidity scores [14] and NCI Common Terminology Criteria for adverse effects (CTC-AE_v4) [15] are regularly used for patients with head and neck malignancies. The LENT-SOMA score serves to document subjective and objective long-term consequences of therapy [16], [17], [18], [19], [20].

Generally the side-effects are divided into five degrees of severity (0: no side-effect, 1–5: increasing intensity of the side-effect). It is clearly defined which score should be selected for specific clinical parameters. Toxicities that score a 3 (“severe”), 4 (“life-threatening”), or 5 (“death”) are considered as “serious complications”. These scales are used in many clinical studies to evaluate and compare adverse effects of radio-/chemotherapy due to the clearly defined categorization of degrees of severity and simplified reporting.

However, the use of these instruments is very laborious. The CTC-AE_v4, for example, has 765 individual questions. Time will tell whether such instruments can hold their own in practice, outside clinical studies.

Clinical examinations and study end points

Various technology-assisted examinations are available particularly for a differentiated description of organotropic functional disorders, e.g., laryngo-(strobos)copy, videofluoroscopy and fiberoptic-endoscopic assessments of the swallowing process. The findings are systematically evaluated and graded along (partially) standardized assessment criteria by an experienced investigator [21], [22], [23], [24].

In addition, many clinical studies define a number of end points of their own to describe individual aspects of preserving function, such as laryngectomy-free survival, the number of tracheotomized patients, and the number of patients fed using a gastric-tube.

Questionnaires

Patient questionnaires are used alongside this. There is international consensus that quality of life can only be evaluated from the personal, subjective reality of the patient affected [25], [26]. The term “health-related quality of life” opens up the opportunity to reliably quantify the relative, personal character of the phenomenon of quality of life despite all the difficulties [27]. Various

patient questionnaires have been developed and validated to quantify this subjective assessment of a patient’s own quality of life specifically for various tumor entities. On the Internet-based platform “Pro Quolid,” a large number of different instruments are summarized, and their psychometric features are compared [28]. Well-known instruments for use with patients suffering from head and neck cancer are the European *EORTC Quality of Life questionnaires* (EORTC-QLQ modules c30 and hn35), the North American questionnaires *Functional Assessment of Cancer Therapy* (FACT, modules g and hn), and the *University of Washington Quality of Life questionnaire* (UW-QOL) [29], [30], [31].

Further questionnaires are available for the detailed assessment of speech, ability to swallow and sensation of pain, including the Voice Handicap Index (VHI) [32], the Voice-Related Quality of Life questionnaire (VR-QOL) [33], the MD Anderson Dysphagia Inventory (MDADI) [34], as well as the Brief Pain Inventory (BPI) [35], the McGill Pain questionnaire [36] and the Pain Thermometer, which is based on a visual analog scale.

An advantage of such questionnaires is that they are generally well received by patients [37]. The questionnaires mentioned here are available in different languages.

Beyond this, the Working Group for Psycho-Oncology in Germany in association with the German Cancer Society have investigated various brief screening procedures to assess the psycho-oncological stress of patients, and the practicability of these in day-to-day clinical practice. The criteria applied were brevity of the process and the availability of threshold and comparison values, their psychometric validity, acceptance among patients, and previous experience in clinical practice. The recommendation comprises five screening processes, including the Hospital Anxiety and Depression Scale (HADS), the Hornheider Screening Instrument (HSI), the Distress Thermometer (DT), the questionnaire on the disease-specific stress of cancer patients, and psycho-oncological base documentation [38].

Summary

Different questionnaires specific to HNC measure varying parameters. Therefore, their results are comparable only to a limited extent [12], [39].

In addition, an exclusionary evaluation of therapeutic success with patient-related quality of life questionnaires is problematic because objectifiable findings on ability to swallow, ability to speak, wound healing, etc., are assessed individually and differently by patients based on their personal psychological and social circumstances. Patient reported outcomes do not correlate sufficiently with objectifiable findings on intake of nutrition, etc. [40]. On the other side, technical procedures (e.g. video-esophagography) can localize the causes of a disturbance in swallowing more precisely, but do not allow conclusions on how this affects the life of the patient. Questions such

as those on “social eating” in EORTC-QLQ hn35 address this issues.

As a result, both types of patient- and investigator-based evaluation have to be jointly taken into account to fully evaluate preservation of function and quality of life of patients with HNC.

The following summarizes the functional results after treatment of head and neck cancer, depending on the tumor localization, tumor staging and treatment option.

Functional outcome after cancer treatment is tumor and therapy-related. Therefore, it is important to compare data before and after therapy. However, not many publications report corresponding information. In addition, a comparison of study results is complicated by the fact that the respective study end points and the applied outcome instruments are hard to compare with one another, so that appropriate meta-analyses are limited. Implications from this for the clinical research in years to come are discussed in the last section of this paper (“Outlook”).

Carcinomas of the oral cavity and oropharynx

Results with early oral cavity and oropharyngeal carcinomas

Surgical therapy

Patients with relatively small tumors of the oral cavity (stages I & II, UICC) that have only been treated surgically indicate the fewest problems in a comparative study over five years [5]. However, the exact tumor localization and surgical procedure applied are only reported incompletely, which limits the validity of the study.

Swallowing and speech problems

The intelligibility of speech among all patients with an oropharynx carcinoma appears to be reduced compared to a healthy comparison group [41]. Tumor localization has a particularly strong influence in this. Patients with tumors at the base of mouth have an especially reduced ability to swallow and poorer articulation compared to patients who have had surgery for tumors of the tongue [41], [42]. As expected, the findings worsen as T stage and tumor volume increase [41].

Brown et al. have described the effects of the resected volume on functional results. They come to the conclusion that larger (as against smaller) resections of the tongue affect speaking and swallowing more severely – incrementally – than resections of the soft palate [43].

Radiation therapy

Patients who have been treated with radiation therapy stated that they had more problems with xerostomy, mouth opening, swallowing and with sleep disturbances than the comparison group that had only been treated surgically [5].

Functional improvement after approximately one year is delayed among patients with adjuvant radiation therapy [44], [45]. Two thirds of the patients stated that they still had considerable problems with saliva consistency and swallowing five years after their therapy [5].

In addition, speech intelligibility is significantly reduced among patients who have received adjuvant radiation therapy as against those who have only been treated surgically [46]. However, quality of life is not influenced by adjuvant radiation therapy [46].

Digression: Intensity-modulated radiation therapy (IMRT)

An option for the prophylaxis of radiation-treatment-related side-effects is intensity-modulated radiation therapy (IMRT). This can particularly improve xerostomy if the parotid dose is reduced to <26 Gy [47], [48], [49]. In addition to this, there are also indications that swallowing function can be prevented by reducing the dose on sensitive structures in the larynx and the inferior pharyngeal constrictor muscle [50], [51].

Givens et al. have assessed the extent of therapy-related toxicity on a larger group of patients. Patients who were treated with IMRT had fewer therapy-related side-effects and evaluated their quality of life as better than patients after conventional radiation therapy [48].

Limited mouth opening is not a problem that only occurs in oropharyngeal carcinomas. However, the risk is considerably increased in this group of patients [52]. An overview paper on trismus in HNC has analyzed 22 publications. This shows that the weighted incidence for patients after conventional radiation therapy is 25%, and 5% for patients who were given IMRT. However, the analysis could only give few treatment recommendations for existing trismus [53].

Results with advanced oral cavity and oropharyngeal carcinomas

Radiochemotherapy

Meta-analyses have shown improved survival if radiation therapy and chemotherapy were combined compared to radiation therapy alone [54], [55].

Toxicity

On the other hand, combined radiation- and chemotherapy causes severe short- and long-term toxicity. Current studies indicate severe acute toxicity (grades 3–4) in up to 66% of the patients treated [56].

Acute toxicity frequently affects the oral mucosa (34–90%), causes hematological changes (39–60%), nausea and vomiting accompanied by undernutrition and dehydration (20–26%), neuro- and ototoxicity (7–26%), skin problems (16–34%), pneumonia (0–25%), functional disorders of the kidney (3–19%), severe fever (0–18%), and weight loss of over 10% (0–17%) [48], [57], [58], [59]. Various toxic side-effects of differing severity occur depending on the protocol.

Cetuximab, an antagonist to the epidermal growth factor receptor (EGFR), has proved effective combined with cisplatin in the therapy of metastasizing tumor stages [60]. Its role in combination treatments with radiochemotherapy is still being investigated in studies. Acne-like dermatitis occurs with the use of cetuximab [61], [62]. If cetuximab is combined with radiation therapy, complicated skin changes may occur [63], [64]. There are not (yet) any final recommendations on the treatment of side-effects after cetuximab [65].

Up to 50% of the patients described toxicity-related delays in therapy or a reduction in the planned chemotherapy cycles due to toxicity [48]. More current approaches have excluded toxicity-related delays in therapy [58]. To reduce these reductions or delays in therapy, intensive supportive therapies must be conducted by a multidisciplinary team [66].

Acute toxicity is characterized by the fact that it occurs in the course of therapy and after that subsides again within weeks. Late toxicity summarizes long-term restrictions that emerge after several months and persist for longer. Late toxicity includes xerostomy, persistent swallowing disorders, esophagus constrictions, lockjaw, osteoradionecrosis and hypothyroidism [59], [67].

A Cochrane analysis from 2011 fails to come up with clear indications of which chemotherapeutic substances and therapy schedules are most effective, or what additional toxicity is caused by the various substances in the combined therapeutic approaches [68].

Findings related to swallowing

A meta-analysis on swallowing function after different radiochemotherapy protocols concludes that the swallowing function is moderately to severely restricted. Aspiration rates are cited at 23–78% [40].

Quality of life

The quality of life assessed by patients after radiochemotherapy was only surveyed in individual studies alongside the toxicity criteria. Quality of life was lowest three months after the beginning of therapy and improved gradually to a level the patients had reported followed at the time of cancer diagnosis and before the therapy began [69].

Quality of life after radiochemotherapy versus surgery and adjuvant radio(chemo)therapy was assessed in some studies and will be discussed at the end of the following section on the surgical approach.

Surgical therapy

Extensive tumors of the oral cavity and the oropharynx sometimes require large-scale resection to ensure an R0-situation. In any case the defects that occur have to be closed. In some cases it is not possible to close directly, and the pharynx has to be reconstructed with pedicled and or microvascular free flaps. Free flaps are used somewhat more frequently, and are evaluated according to oncological and functional perspectives [70]. For the reconstruction of defects in the oral cavity and oropharyngeal area, various donor regions are used, for example the radial forearm and the anterolateral thigh free flaps.

Surgical complications

Perioperative complications have to be documented as well as treatment-related toxicity after radio(chemo)therapy. In contrast to the standardized toxicity scores, perioperative complications are more often documented in non-standardized format. Complications that have been reported are for example blood loss, wound complications, fistulas, fissures, perioperative infections and necroses. The lack of standardization in the reporting of perioperative complications makes the specification of reliable data difficult.

Findings related to chewing, swallowing, and speaking

A review on the ability to swallow and speak after surgical therapy of advanced oral cavity and oropharyngeal carcinomas, Kreeft et al. conclude that the general intelligibility of speech is almost normal, at 92–98%. Problems occur especially in swallowing, where aspiration rates of 12–50% are mentioned [44]. Especially after oropharyngeal resection, pharyngeal transit time is delayed [44]. In addition, significant restrictions in opening the mouth (<36 mm), dentition and the chewing function appear [45], [52], [71].

Restrictions in movement of the tongue, swallowing function and articulation improve after one year to values that are similar to those before cancer therapy [72], [73], [74]. Over 80% of patients evaluate their ability to speak and swallow after (sub-)total glossectomy and reconstruction with free flaps as sufficient or good after three years [75]. In 90% of cases, objectifiable measurements with videofluoroscopy and speech analysis show sufficient mobility of the new tongue, sufficient oral bolus control at 74%, and a comprehensible voice in 75% of the patients [76]. In contrast to this, however, problems with opening the mouth, saliva secretion or coughing deteriorate, and remain impaired for years [52], [72].

After reconstruction of an oropharyngeal carcinoma, patients appear to be more severely functionally restricted than patients who have undergone reconstruction for a carcinoma of the oral cavity [72]. The operation in the case of an oropharyngeal carcinoma harbors the risk of velopharyngeal insufficiency. After reconstruction with radial forearm flaps, individual examinations reveal nor-

mal oral intake of nutrition and comprehensible speech, as well as (videofluoroscopically) complete velopharyngeal closure [77].

Publications on chewing and swallowing function after free mandibula-fibula grafts show that the chewing function after reconstruction is still significantly reduced. However, patients regain their former chewing function with post-operative prosthetic care [78].

Some groups describe the use of free flaps in the therapy of osteoradionecrosis of the lower jaw. Baumann et al. document full oral nutrition in around half the patients, and a combination of oral and tube feeding for a further 25% [79].

A comparison of functional results between various flaps from different institutions is not possible at present due to a variety of factors, including variance in study end points and the application of non-standardized outcome instruments. Still, one study compares their own experience with radial forearm versus anterolateral thigh flaps and concludes that both procedures are functionally equivalent [80].

Quality of life

Despite large-scale surgical interventions and adjuvant radiation, patients' quality of life six months after therapy is better than before therapy [81]. The social, emotional and cognitive areas of the patients' life also do not seem to have been negatively influenced. Pain and a general feeling of being sick even seem to improve [72].

Direct comparison of functional outcome depending on therapeutic approach

A study documents functional results of various therapeutic approaches for early T stage but advanced N stage oropharyngeal carcinomas. There was no difference in oncologic outcome nor in terms of hr-QOL between a surgical approach with adjuvant radiation therapy versus primary radiochemotherapy. Still, the surgical group demonstrated better functional results, particularly in the cognitive and social areas, and less need for supplements [82]. The unfavorable effects of radiochemotherapy on cognitive performance have also been described by other authors as well [83]. The reasons for this are not clear, and probably multifactorial. A possible connection between the radiation dose on the temporal lobe and memory constraints was described in the case of nasopharyngeal carcinoma [84].

Two studies compare the functional results among patients with oropharyngeal carcinomas who are either treated with primary radiochemotherapy or a surgical approach with adjuvant radiation therapy [85], [86]. Evaluations of the hr-QOL after two and three years, respectively, reveal either no significant difference according to therapeutic approach [85], or a slight advantage for the patients treated with surgery in the areas of general quality of life, cognition, social life, nausea and vomiting, xerostomy, as well as less need for analgesics

and fewer financial problems. Survival rates were comparable [86].

Larynx carcinomas

Results with early larynx carcinomas

Larynx carcinomas Stage I and II (according to UICC) are treated with transoral laser surgery or radiation therapy with equally good oncologic results. Local control after radiation therapy is somewhat poorer than with a laser surgery, and is accompanied by a higher rate of secondary removal of the larynx [87]. Reasons given for this are a) early recognition of local recurrences after radiation therapy is more difficult, and b) radiation therapy cannot be repeated [87].

Voice quality after both procedures was compared in several studies. Some authors describe greater hoarseness after laser surgery compared to radiation therapy. However, this impairment is rated as mild overall [88], [89]. Other studies demonstrate equally good voice quality for both therapies with patient-reported outcome instruments, investigator-based instruments and voice analyses [90], [91].

Open surgery shows similarly good oncologic results as laser surgery or radiation. The rates for larynx preservation are superior to those of radiation therapy [87].

Functionally, however, aspiration rates of 20% are cited after vertical and supraglottic hemilaryngectomies, which can generally be treated conservatively according to the authors [92]. After supracricoidal resection, silent signs of aspiration can be seen videofluoroscopically [93], [94]. Voice outcomes after supracricoid partial resection improve with logopedics in the course of the first year after the operation, but are still categorized as strained and hoarse [93]. Stroboscopically, varying regions of postoperative kinetics can be seen at the neoglottis. Still, acoustic parameters and patient-reported outcomes certify good verbal communication [94]. After cricohyoidepiglottopexy, reduced larynx elevation was also documented [95].

With preservation of the arytenoid cartilage, effects are especially described in the early post-operative period relating to decannulation, removal of the nasal catheter and duration of the inpatient stay. However, for the later voice and swallowing functions (which were assessed with voice analyses, dysphagia scores and the VHI) no differences are apparent between patients with one and two arytenoid cartilages [96].

Oncological and functional results have been compared using a large patient cohort with T2 larynx carcinoma patients following laser surgery and frontolateral larynx partial resection [97]. The incidence of tracheotomies and complications was lower in the patient cohort treated with laser surgery, while the oncological success rates were equivalent. The authors therefore conclude that open surgical procedures should be reserved for cases where the tumor cannot be sufficiently displayed microlaryngoscopically.

With larynx carcinomas there is a correlation between the localization of the primary tumor and subsequent functional problems. With glottic carcinomas, alongside good ability to swallow, voice problems are particularly to be expected, while supraglottic carcinomas tend to cause problems with swallowing, while voice results are rather good [98], [99]. There is a direct relation between the extent of the resection of the epiglottis and the severity of swallowing disturbances [99].

Results with advanced larynx carcinomas

The introduction of transoral laser surgery and new methods and protocols of radiation therapy with and without chemotherapy have led to new forms of treatment. The discussion on the importance of some of these combined protocols is not yet over. Alongside oncological results, some of the newer therapeutic approaches also document details on functioning that will be described in the following.

Surgical approaches for larynx preservation

Advanced larynx carcinomas of Stages III, IV a-b have been treated to preserve the larynx using laser surgery and adjuvant radio(chemo)therapy [100]. The five-year survival rate was 47%, and the rate for preservation of the larynx was 90%. More extensive analyses of functioning were conducted among some of the survivors. The patients' subjective assessment of their ability to swallow was satisfactory. In contrast to this, though, around half of the patients who underwent endoscopic evaluation were found to have aspiration; around a third of these patients were using a PEG tube. Voice quality was comprehensible; however, both patient evaluation using the Voice Handicap Index as well as the voice analysis revealed clear impairments in voice quality. Grade 3 toxicity was evident in 44% of the patients for mucositis, advanced dysphagia and severe changes in blood count [100].

Laryngectomy

Laryngectomy is a surgical approach that has been used for many years to treat advanced larynx carcinomas. However, it is associated with dramatic changes in the life of the patient. While ability to swallow is generally assessed as good [101], laryngeal voice production is no longer possible. Patients have to live with a permanent tracheostomy.

Rehabilitation of speech should therefore be initiated immediately, and generally takes place via one of three possibilities: esophageal speech, tracheo-esophageal voice prosthesis, or an electrolarynx. (1) Esophageal speech manages without any further prosthesis, and has the fewest complications. However, it is the most difficult to learn, and has a correspondingly lower success rate. (2) The tracheoesophageal shunt prosthesis is the

method most frequently used, and is applied surgically [102]. However, the prosthesis has to be exchanged regularly, and has corresponding complications. An enlarged stoma and/or leakage occurs in 1–29% of cases, and is linked to a tripled risk of pneumonia [103], [104]. Still, patients report the greatest satisfaction with this method. (3) The electrolarynx is the easiest technique to use, and requires little training. However, patient satisfaction with the electrolarynx is lowest of the three options described due to its mechanical-sounding voice [102].

Surgical complications

The most frequent surgical complication of laryngectomy are pharyngocutaneous fistulas, with an incidence of 0.5–32% [105]. These fistulas delay wound healing and the onset of oral feeding. Larger fistulas can even delay the start of post-operative radiation therapy, which can in turn negatively influence local tumor control [105].

Ability to speak and swallow

Dworkin et al. compare voice and swallowing functions after a laryngectomy versus supracricoidal hemilaryngectomy. The results of both groups are equivalent related to speech intelligibility and voice quality. However, on the path to complete oral feeding, hemilaryngectomized patients require considerably more training in swallowing [106]. The speech findings, however, are not supported by other authors who certify speech advantage for hemilaryngectomy.

Robertson et al. evaluate voice and swallowing functions using the patient questionnaires Voice Symptom Scale, the MD Anderson Dysphagia Inventory, and the UW-QOL. Patients who had "only" had a laryngectomy had better voice and swallowing results than patients who had adjuvant radiation therapy [107]. There is controversy over the areas in which adjuvant therapeutic procedures further increase functional problems after a laryngectomy [108], [109].

Quality of life

The Short Form 12 (SF-12) is a recognized instrument for recording quality of life in the general population, but is not specific for HNC. Interestingly, a comparison of quality of life of laryngectomized patients and the general population with SF-36 does not reveal any differences [108]. The health-related Quality of life of laryngectomized patients was examined in various studies using tumor-specific instruments. Three main areas are problematic: speech, external appearance, and altered activities in day-to-day life [110]. Despite moderate speech intelligibility when evaluated objectively, many patients state that they are not satisfied with their new voice, and withdraw from conversation [111].

Younger patients suffer more frequently from anxiety and problems due to their altered external appearance. Women complain about frequent difficulties swallowing. And

adjuvant radiochemotherapy are risk factors for increased anxiety and mood disturbances [108]. Knowing about such risk groups makes it possible for the physician to initiate suitable supportive measures early if necessary. Both speech and swallowing are evaluated better by patients as their survival time increases [112]. Comparisons of quality of life after a laryngectomy versus primary radiochemotherapy are described in the later section on radiochemotherapy.

Laryngopharyngectomy with microvascular defect reconstruction

Extensive tumors of the larynx and hypopharynx sometimes require extensive resections of the pharynx that have to be closed. A variety of surgical reconstruction options are available for this.

Surgical complications

Strictures occur in 13–15% of cases [113], [114], and the incidence of pharyngocutaneous fistulas are cited at 5–38% [115], [116]. A randomized prospective study compares perioperative complications of radial forearm and anterolateral thigh grafts, revealing a preference for radial flaps [117].

Again, we find that the documentation of treatment-related adverse effects with standardized protocols (namely CTCAE) is less often used in studies with surgical protocols compared to studies with radiochemotherapy protocols.

Ability to speak and swallow

Functional outcome after free flap reconstruction shows, that in the long run 88–93% of the patients resume oral nutrition of some kind, while 16% continue to require (additional) special nutrition. 84–92% of patients receive a tracheoesophageal puncture. Increased complication rates due to the puncture are reported by some authors [118], but not by others [114].

Comparisons of the functional outcome after reconstruction with different free flaps are not possible at present due to methodological differences in the studies [119], [120], [121].

Radiochemotherapy

Patients with larynx carcinomas of Stages III, IVa and IVb are also treated with different protocols of (concomitant) radiochemotherapy. The larynx was preserved in 74–84% of cases [122], [123].

Toxicity

However, preservation of the larynx after primary radiochemotherapy and the associated natural speech is in some cases accompanied by huge therapy-related toxicity. In up to 82% of the patients treated, toxic side-effects of grade 3 (“severe”) to 4 (“life-threatening”) were

documented [123]. Other studies on simultaneous radiation therapy and chemotherapy reported toxicity of grades 3–4 for mucositis (53%), dysphagia (54%), and dermatitis (19%). 80% of the patients were affected by severe changes to their blood count [122].

While early toxicity after radiochemotherapy is reduced over the course of several weeks, it is particularly late toxicity that has a long-term influence on the life of those affected. An accepted method for this is the above-described LENT-SOMA system, which links objective and subjective evaluations [124].

Findings related to speech and swallowing

Investigations on speech intelligibility among patients with advanced carcinomas after radiochemotherapy reveal normal values neither before nor after the therapy [8]. Meta-analysis of the findings are again difficult due to methodological deficits in the study design (lack of initial values and unclear allocation of the findings to the regions exposed to radiation therapy and tumor localization) [8].

Patients treated with primary radiochemotherapy for advanced larynx carcinoma suffer from considerable swallowing problems that are linked to strictures. They may lead to aspiration pneumonia and require an increased use of a PEG tubes [125]. In general, women tend to have more difficulties with regaining speech, while older patients have a greater risk of swallowing problems [126].

Quality of life

Studies that compare the quality of life of patients after primary radiochemotherapy (pRCT) with total laryngectomy come to different results: Some state that the quality of life after pRCT is better than after laryngectomy [127], [128] while others conclude that the quality of life is equal after both therapeutic procedures [129], [130].

Recurrences after radiochemotherapy

Specificities of speech after laryngectomy as salvage surgery

A phoniatic group investigated speech function after various therapies for advanced larynx carcinoma. Patients after primary radiochemotherapy or primary laryngectomy had a speech handicap that was assessed as “slight.” In contrast to this, speech after salvage laryngectomy after primary radiochemotherapy had failed was much worse [131]. Other recent findings also show significantly reduced voice functions after pRCT and salvage laryngectomy compared to primary laryngectomy [107]. The functionally poorer results of salvage surgery possibly occur after just one cycle of induction chemotherapy [112]. This hypothesis, however, must be tested in further studies.

Specificities of wound healing in recurrences after radio(chemo)therapy

A familiar problem with salvage surgery after radiochemotherapy is impaired wound healing in tissue that has already been exposed to radiation therapy. The risk of developing pharyngocutaneous fistulas is increased if radiation therapy has taken place previously [132], [133]. Data of the Radiation Therapy Oncology Group 91-11 and investigations from Japan reveal wound complication rates of 46–59%, with rates for pharyngocutaneous fistulas of 15–38% [134], [135]. Fung et al. showed that reconstruction with microvascular free flaps in salvage surgery does avoid more extensive wound healing disorders [136].

Cross-localization analyses

Functional results of selective neck dissection

Selective neck dissection (SND) seems superior in functional outcome compared to radical or modified radical neck dissection.

Still, after SND constricted shoulder mobility and pain appear compared to the neck side that has not been treated. They have a negative effect on patients' professional life, their leisure time and sleep. Additional influence of adjuvant radio(chemo)therapy is not described [137].

The role of SND in a cN0-stage neck is under investigation. Addressing this question oncologically is not the topic of this review paper. From a functional perspective, post-operative examinations of 100 patients show satisfying results from functional and esthetic perspectives [138].

Pain therapy

Another important topic among patients with head and neck cancer is pain. A meta-analysis of 39 publications on orofacial cancer pain reveals that a majority of the pain continues despite pain therapy [139]. The causes of pain in these cases are manifold. Alongside mucositis induced by radiation therapy, there are other causes such as inflammation, wound healing disorders, the injury of sensory nerves, or necroses of the lower jaw and/or larynx cartilage. In these cases greater pain levels are linked to fears and episodes of depression, reduced quality of life and reduced food intake.

Pain in the shoulder region arises both after neck dissection – the most frequent cause – and also after radiation therapy. It has to be recognized and appropriately treated [140].

There is common consensus on how pain should be recorded: systematically using validated questionnaires and scales, and from a patient perspective. Here, visual

analog scales are a valuable option. Patient questionnaires also cover the pain issue, for example the EORTC-QLQ questionnaires, the University of Washington Quality of Life questionnaire, or the Hospital Anxiety and Depression Scale.

Clinical management of limited effectiveness and tolerance of oral opioids among some cancer patients still remains a challenge [141]. Aggressive RCT-protocols open up new challenges in the treatment of pain. Pain is rare overall in chemotherapy, but the pain that does arise is sometimes so severe that it cannot be effectively treated with opioids in up to 20% of cases [142]. When the diagnosis is made, many patients are suffering pain, and this affects around 50–75% of patients with HNC in the course of their treatment. After therapy has been concluded, the prevalence of orofacial pain declines, but in some cases never reaches the level that it was before therapy. Especially after combined RCT, patients complain of long-term pain that is more severe than before treatment began (despite analgesics) [139].

Mucositis

Mucositis is a side-effect that frequently occurs with radiation therapy, with a prevalence of 10–100% depending on the therapy regime [143]. The extent of the damage is linked to the volume of mucosa exposed to radiation, the intensity of the therapy, and the individual predisposition of the patient [144]. The clinical consequence of advanced mucositis is severe dysphagia that leads to inadequate nutrition, dehydration, and severe weight loss and, eventually, requires inpatient treatment. In many cases feeding tubes are required [144].

Currently various substances are being tested to prevent radiation-induced mucositis. Recommendations on therapy for mucositis are partially contradictory, so uniform therapy recommendations are not (yet) available [145].

Nutrition & feeding tubes

Various measures have been tested in randomized controlled studies to ensure sufficient nutrition when a carcinoma is being treated. Synthesizing the data, three pillars of supportive therapy can be identified: 1) advice on nutritional therapy by an experienced specialist from the outset, and the preparation of a tailored therapy plan, 2) the use of megesterol acetate, and 3) the insertion of a feeding tube [146].

The insertion of feeding tubes is primarily reserved for tumors in advanced stages [147]. There are various ways in which they can be inserted, including nasogastric tubes or percutaneous endoscopic gastrostomy (PEG). A PEG tube is generally associated with few complications, but remains in place much longer than a nasogastric tube. The secondary effects of a PEG tube on swallowing function are not (yet) fully understood [147].

There is controversy on the ideal point in time for a PEG tube. Some authors recommend intensified swallowing training to practice the act of swallowing and prevent

fibroses in the sense of a “use it or lose it” strategy [148]. Against this, however, one has to weigh up the greater risk of aspiration [149].

The use of feeding tubes is linked to a significant decline in quality of life, and is a considerable burden on the patients in their private and social environment. However, the impact of a feeding tube on quality of life is reversible after its removal [150].

When evaluating swallowing disorders and PEG-dependency as a consequence of inadequate oral intake of nutrition, it is also important to differentiate between anatomical narrowing and a swallowing disorder that cannot be explained anatomically, e.g., due to sensory deficit [119].

Tracheostomy

A tracheostomy impairs swallowing function [151]. A prospective randomized study investigates the influence of the technology of the tracheostoma closure mechanism on the subsequent ability to swallow and length of stay in the clinic/hospital. The study showed that suturing the edges of the tracheotomy wound early after decannulation results in a much better swallowing function, and that (from an economic perspective) this reduces the patient's hospital stay [152].

Dysgeusia

Dysgeusia has a series of causes, such as radiation therapy, infections or ulcerations of the oral cavity, gastrointestinal reflux diseases, and systemic zinc deficiency. It is also a well-known side-effect of medications such as cyclophosphamide, doxorubicin, fluoruracil, methotrexate, cisplatin, vincristine, and others. Dysgeusia occurs within several days after the beginning of radiation therapy. 90% of patients who receive radiation therapy at 60 Gy complain of significant dysgeusia [153]. Normal dysgeusia generally reverts after 6–24 months; remaining dysgeusia was not described [139].

Dysgeusia is documented using the CTC-AE_v4 or with the aid of (electro-)gustometry as well as with evoked potential in MRT or PET. However, the two latter methods are not common for monitoring dysgeusia in HNC patients. No method has been found to prevent this dysgeusia. Zinc substitution failed to prevent taste alterations in a randomized study [154]. Clonazepam, which is generally used for the treatment of dysgeusia, is not very suitable in HNC due to its well-known side-effect of xerostomy. Studies on intensity-modulated radiation therapy (IMRT) do not yet allow definite conclusions.

Quality of life and psychosocial aspects

Evaluations on the quality of life of patients after HNC have already been described from an organ-related perspective at several points in this review article, and therefore do not need to be repeated.

In summary, it can be stated that patients with HNC are under greater psychic pressure than patients with other cancer localizations. This difference becomes particularly evident around six months after therapy, and is related to lack of support from the patient's social environment [155]. Social support and self-efficacy are key factors for the appraisal of life [108], [156].

In all HNC patients we find, that the prevalence of anxiety disorders declines after therapy, while the prevalence of depressive moods increases during the same period [157]. The incidence of anxiety disorders and/or depression is cited around 25% [158]. Alongside tumor-specific details, the extent of these psychic problems particularly correlates with individual coping strategies [158]. In particular self-efficacy and accepting intrapersonal mechanisms have a protective effect [159]. On the physical side, speech and feeding difficulties in particular (especially a feeding tube) cause higher stress levels [150], [160].

Various studies have investigated feelings of being stigmatized. Especially after laryngectomy, 87% of those asked stated that they felt stigmatized, and 40% withdrew from conversation [111].

Professional activity & financial problems

Of patients who had worked before their diagnosis, a large share return to their former or a different professional activity within six months [161]. Still, financial problems are an unsolved problem for many patients [162], [163].

Time periods

Most physical impairments occur most intensively during and immediately after therapy. They improve over the following three to six months if rehabilitation measures are undertaken [162]. Sleep disorders and emotional problems improve within the next one to five years [5]. However, problems particularly with xerostomy, saliva consistency, difficulties opening the mouth, and dental status persist for longer [164]. Poor dental status is correlated with greater pain and more problems in day-to-day life [165].

Outlook

Meta-analyses in HNC oncology are based on uniform concepts, such as five-year survival rates and the TNM-classification. However, uniform concepts are not established in the evaluation of functioning. Systematic evaluations of the findings on functional outcome from various studies is still quite difficult because the outcome instruments and study end points in the studies vary greatly and hamper appropriate meta-analyses [9], [12], [166]. As already mentioned at the introduction, the assessment of functional data is not an end in itself, but pursues the aim of efficiency evaluation of therapies, identifying risk

groups among patients and obtaining data on the expected functional outcome after alternative therapy options. So far it has not been possible to define the term *functional outcome* among patients with HNC across health professional groups – despite of broad global interest in the topic and many publications on various aspects of the theme.

A prerequisite for successfully communication is first of all uniform language and terminology. In the communication of medical diagnoses, the “International Classification of Diseases” (ICD-10) by the World Health Organization (WHO) is well established. In 2001, WHO approved a further classification, the “International Classification of Functioning, Disability and Health” (ICF) to describe the various aspects of functioning and disability in an internationally accepted language [2].

The International Classification of Functioning, Disability and Health (ICF)

WHO makes the ICF available alongside the ICD-10. While the ICD classifies disease, the ICF classifies the impact on functioning and disability. The ICD is stretched to its limits when the topic is no longer disease as such, but associated functional issues [167]. The application of an internationally accepted and comprehensive description of functioning can be applied to aspects such as planning, evaluation and optimization of therapeutic care, the definition of care requirements, and in clinical research [167].

The increasing importance of the ICF results from the growing significance of functional problems and their management in the social security system [168].

The ICF is based on a comprehensive bio-psycho-social model for describing health. It has a dual structure, and consists of two sections 1) *Functioning and disability*, and 2) *Contextual factors*. The key characteristic of the ICF is its comprehensiveness. Alongside changes and limitations in anatomy and (patho-)physiology, the ICF also records aspects that take into account differing individual factors from the patient’s personal, social and professional environment. These aspects are primarily independent from the medical diagnosis, but still have impact on the success of therapy concepts. Various studies emphasize the relevance of the ICF in evaluating problems after head and neck cancer [166], [169]. The proximity between the two classifications of WHO – the ICD-10 and the ICF – also offers further opportunities to make comparisons that extend beyond diagnoses and specialisms.

The ICF contains over 1,400 different categories on various levels of detail. This scope is an advantage because it promises to reflect individual problems as precisely as possible. On the other hand, this is also a huge challenge because the length represents an implementation hurdle in clinical practice. Therefore, disease-specific “ICF Core Sets” are being developed. ICF Core Sets are a tool to adapt the ICF specifically to the diagnosis-specific requirements of patients. ICF Core Sets have been developed in

a standardized process for a series of diseases, including coronary heart disease, obstructive pulmonary diseases, diabetes mellitus and breast cancer [170], [171], [172], [173], [174].

ICF Core Sets for head and neck cancer

The development process of the ICF Core Sets for head and neck cancer (ICF-HNC) is based on a standardized process consisting of (1) four pre-studies to identify the relevant criteria using patient interviews, multidisciplinary expert opinion, an international multicentre study on feasibility of the ICF in clinical practice, and a systematic literature review [163], [175], [176], [177]. (2) Building on this, a first version of the ICF-HNC was voted in a formal decision-making process during an international, multidisciplinary consensus conference [174]. (3) The ICF-HNC was validated at 14 international study centers as well as through health-professional-specific Delphi exercises [178], [179], [180], [181], [182].

The ICF-HNC were approved on two different levels of detail: (1) as a “short ICF Core Sets” with 19 categories for day-to-day clinical practice, and (2) as a “comprehensive ICF Core Set” with 112 categories for interdisciplinary approaches, and comprehensive assessment.

The increasing complexity of the oncological therapy of HNC and an overproportionally large variety of vital functions that are potentially affected require an interdisciplinary team. Therefore, HNC is considered one of the cancer entities with an especially high need for interdisciplinary cooperation [183], [184]. Treatment includes close cooperation between physicians (otorhinolaryngologists, oral and maxillofacial surgeons, radiation therapists, oncologists), psycho-oncologists, physiotherapists, logopedists, inpatient and outpatient nursing care assistants, social workers and other health professions. Therefore, a key aspect in the development of ICF-HNC was to integrate multidisciplinary expertise throughout the entire development and validation processes [174], [175], [178], [179]. Creating the ICF-HNC was the first step to define the term “preservation of function” comprehensively.

It should be emphasized that the ICF and ICF-HNC are not outcome instruments in a classical sense. They are primarily meta-tools and offer the opportunity to translate existing outcome instruments and their results into a unique “language” of functioning [185], [186]. The methodology of translating different outcome instruments and their results into ICF-terminology has already been demonstrated for various diseases, including head and neck cancer [39], [187], [188].

Evidence-based medicine and methodological challenges

In terms of methodological quality of the studies conducted in the field of functional and supportive aspects, one must admit that many studies were carried out retrospectively and/or were cross-sectional studies. Many studies

were performed at individual centers, and case numbers were low in some of them. Multicenter studies can lead to higher case numbers, increasing their statistical informational value. Also the call for longitudinal data, that compares pre- and post-therapeutic values, intensifies [9], [189].

In addition, various cancer localizations and therapeutic approaches are often aggregated in the publications, and it is not possible for the reader to trace back functional or toxic findings to individual groups of patients. All of this limits the informational value of research in the field of functional outcome.

Prospectively randomized studies are a gold standard in terms of statistical significance. However, they are rare in the field of HNC therapy, especially when substantially different approaches to fight cancer are concerned, e.g. radiotherapy versus surgery [87], [190]. As expected, many patients and physicians find it difficult to subject themselves to randomization when life-critical decisions on therapy are concerned.

In times of evidence-based medicine, however, the selection of methodology in the study design critically influences the later value of the findings.

Clinical implementation

Patients are very willing to accept questionnaires in cancer follow-up sessions [37]. In contrast, surveys with physicians and dentists reveal that questionnaires are only used to a limited extent in day-to-day clinical practice [191]. They are considered too time-consuming and do not easily facilitate clinical decision making [191], [192]. Another factor even complicates this: When comparing objectifiable investigator-based outcome instruments and patient reported outcomes, the data do not sufficiently correlate in several cases [10], [100], [193].

Therefore, work over the last few years has increasingly been concerned with the question how results from patient reported outcomes and from clinical investigations (such as fiber-optic endoscopic examination or speech intelligibility analyses) can be linked. This is how threshold values from patient questionnaires such as the UW-QOL were defined. Such threshold values open up the opportunity to use patient reported outcomes as screening instruments for substantial swallowing or speech problems [194], [195]. Work of this kind considerably increases the clinical feasibility of patient questionnaires.

Beyond this, careful examination of the experience from studies in which the outcome instruments were used is required to reveal significant differences in the scaling and clinically relevant threshold values within the instruments. Knowledge of this data could allow the development of a first model on how the functional aspects of cancer follow-up can be systematically and practicably implemented into clinical routine.

Notes

Competing interests

The author declares that she has no competing interests.

References

1. Haas I, Hauser U, Ganzer U. The dilemma of follow-up in head and neck cancer patients. *Eur Arch Otorhinolaryngol.* 2001 May;258(4):177-83. DOI: 10.1007/s004050100333
2. World Health Organization. ICF – International Classification of Functioning, Disability and Health. Geneva; 2001.
3. Oskam IM, Verdonck-de Leeuw IM, Aaronson NK, Kuik DJ, de Bree R, Doornaert P, Langendijk JA, Leemans RC. Quality of life as predictor of survival: a prospective study on patients treated with combined surgery and radiotherapy for advanced oral and oropharyngeal cancer. *Radiother Oncol.* 2010 Nov;97(2):258-62. DOI: 10.1016/j.radonc.2010.02.005
4. MacKenzie R, Franssen E, Balogh J, Birt D, Gilbert R. The prognostic significance of tracheostomy in carcinoma of the larynx treated with radiotherapy and surgery for salvage. *Int J Radiat Oncol Biol Phys.* 1998 Apr 1;41(1):43-51. DOI: 10.1016/S0360-3016(98)00030-3
5. Nordgren M, Hammerlid E, Bjordal K, Ahlner-Elmqvist M, Boysen M, Jannert M. Quality of life in oral carcinoma: a 5-year prospective study. *Head Neck.* 2008 Apr;30(4):461-70. DOI: 10.1002/hed.20735
6. Korfage A, Schoen PJ, Raghoebar GM, Bouma J, Burlage FR, Roodenburg JL, Vissink A, Reintsema H. Five-year follow-up of oral functioning and quality of life in patients with oral cancer with implant-retained mandibular overdentures. *Head Neck.* 2011 Jun;33(6):831-9. DOI: 10.1002/hed.21544
7. Gabler Verlag, ed. Stichwort: Gesundheitsbezogene Lebensqualität. In: Gabler Wirtschaftslexikon. Springer Gabler; 2011. Available from: <http://wirtschaftslexikon.gabler.de/Archiv/18103/gesundheitsbezogene-lebensqualitaet-v9.html>
8. Jacobi I, van der Molen L, Huiskens H, van Rossum MA, Hilgers FJ. Voice and speech outcomes of chemoradiation for advanced head and neck cancer: a systematic review. *Eur Arch Otorhinolaryngol.* 2010 Oct;267(10):1495-505. DOI: 10.1007/s00405-010-1316-x
9. Kreeft AM, van der Molen L, Hilgers FJ, Balm AJ. Speech and swallowing after surgical treatment of advanced oral and oropharyngeal carcinoma: a systematic review of the literature. *Eur Arch Otorhinolaryngol.* 2009 Nov;266(11):1687-98. DOI: 10.1007/s00405-009-1089-2
10. van der Molen L, van Rossum MA, Ackerstaff AH, Smelee LE, Rasch CR, Hilgers FJ. Pretreatment organ function in patients with advanced head and neck cancer: clinical outcome measures and patients' views. *BMC Ear Nose Throat Disord.* 2009 Nov 15;9:10. DOI: 10.1186/1472-6815-9-10
11. Kanatas AN, Rogers SN. A systematic review of patient self-completed questionnaires suitable for oral and maxillofacial surgery. *Br J Oral Maxillofac Surg.* 2010 Dec;48(8):579-90. DOI: 10.1016/j.bjoms.2009.12.004
12. Rogers SN, Ahad SA, Murphy AP. A structured review and theme analysis of papers published on 'quality of life' in head and neck cancer: 2000-2005. *Oral Oncol.* 2007 Oct;43(9):843-68. DOI: 10.1016/j.oraloncology.2007.02.006

13. van der Molen L, van Rossum MA, Burkhead LM, Smeele LE, Hilgers FJ. Functional outcomes and rehabilitation strategies in patients treated with chemoradiotherapy for advanced head and neck cancer: a systematic review. *Eur Arch Otorhinolaryngol*. 2009 Jun;266(6):901-2. DOI: 10.1007/s00405-008-0845-z
14. Radiation Therapy Oncology Group. Acute Radiation Morbidity Scoring Criteria. RTOG; 2012. Available from: <http://www.rtog.org/ResearchAssociates/AdverseEventReporting/AcuteRadiationMorbidityScoringCriteria.aspx>
15. Trotti A, Colevas AD, Setser A, Rusch V, Jaques D, Budach V, Langer C, Murphy B, Cumberlin R, Coleman CN, Rubin P. CTCAE v3.0: development of a comprehensive grading system for the adverse effects of cancer treatment. *Semin Radiat Oncol*. 2003 Jul;13(3):176-81. DOI: 10.1016/S1053-4296(03)00031-6
16. Maguire PD, Papagikos M, Hamann S, Neal C, Meyerson M, Hayes N, Ungaro P, Kotz K, Couch M, Pollock H, Tepper J. Phase II trial of hyperfractionated intensity-modulated radiation therapy and concurrent weekly cisplatin for Stage III and IVa head-and-neck cancer. *Int J Radiat Oncol Biol Phys*. 2011 Mar 15;79(4):1081-8. DOI: 10.1016/j.ijrobp.2009.12.046
17. Givens DJ, Karnell LH, Gupta AK, Clamon GH, Pagedar NA, Chang KE, Van Daele DJ, Funk GF. Adverse events associated with concurrent chemoradiation therapy in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg*. 2009 Dec;135(12):1209-17. DOI: 10.1001/archoto.2009.174
18. Dietz A, Rudat V, Dreyhaupt J, Pritsch M, Hoppe F, Hagen R, Pfreundner L, Schröder U, Eckel H, Hess M, Schröder M, Schneider P, Jens B, Zenner HP, Werner JA, Engenhardt-Cabillic R, Vanselow B, Plinkert P, Niewald M, Kuhnt T, Budach W, Flentje M. Induction chemotherapy with paclitaxel and cisplatin followed by radiotherapy for larynx organ preservation in advanced laryngeal and hypopharyngeal cancer offers moderate late toxicity outcome (DeLOS-I-trial). *Eur Arch Otorhinolaryngol*. 2009 Aug;266(8):1291-300. DOI: 10.1007/s00405-008-0846-y
19. LENT SOMA scales for all anatomic sites. *Int J Radiat Oncol Biol Phys*. 1995 Mar 30;31(5):1049-91. DOI: 10.1016/0360-3016(95)90159-0
20. Ho KF, Farnell DJ, Routledge JA, Burns MP, Sykes AJ, Slevin NJ, Davidson SE. Comparison of patient-reported late treatment toxicity (LENT-SOMA) with quality of life (EORTC QLQ-C30 and QLQ-H&N35) assessment after head and neck radiotherapy. *Radiother Oncol*. 2010 Nov;97(2):270-5. DOI: 10.1016/j.radonc.2010.01.017
21. Seidl R, Nusser-Müller-Busch R, Ernst A. Evaluation eines Untersuchungsbogens zur endoskopischen Schluckuntersuchung. *Sprache Stimme Gehör*. 2002;26:28-36. DOI: 10.1055/s-2002-23116
22. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. *Dysphagia*. 1996 Spring;11(2):93-8. DOI: 10.1007/BF00417897
23. Logemann J. Manual for the videofluorographic study of swallowing. 2nd ed. Pro-Ed. Austin, TX: 1993. p. 170.
24. Schneider B, Wendler J, Seidner W. The relevance of stroboscopy in functional dysphonias(1). *Folia Phoniatri Logop*. 2002 Jan-Feb;54(1):44-54. DOI: 10.1159/000048595
25. Laugsand EA, Sprangers MA, Bjordal K, Skorpen F, Kaasa S, Klepstad P. Health care providers underestimate symptom intensities of cancer patients: a multicenter European study. *Health Qual Life Outcomes*. 2010 Sep 21;8:104. DOI: 10.1186/1477-7525-8-104
26. Weymuller EA Jr, Yueh B, Deleyiannis FW, Kuntz AL, Alsarraf R, Coltrera MD. Quality of life in head and neck cancer. *Laryngoscope*. 2000 Mar;110(3 Pt 3):4-7. DOI: 10.1097/00005537-200003002-00002
27. Dietz A, Meyer A, Singer S. Lebensqualitätsmessungen bei Patienten mit Kopf-Hals-Malignomen: Aktueller Stand und zukünftige Anforderungen [Measuring quality of life in head and neck cancer. Current status and future needs]. *HNO*. 2009 Sep;57(9):857-65. DOI: 10.1007/s00106-009-1969-1
28. Mapi Research Institute. ProQuolid: patient reported outcome and quality of life instruments database. 2010.
29. Bjordal K, Hammerlid E, Ahlner-Elmqvist M, de Graeff A, Boysen M, Evensen JF, Biörklund A, de Leeuw JR, Fayers PM, Jannert M, Westin T, Kaasa S. Quality of life in head and neck cancer patients: validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-H&N35. *J Clin Oncol*. 1999 Mar;17(3):1008-19.
30. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, Silberman M, Yellen SB, Winicour P, Brannon J, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol*. 1993 Mar;11(3):570-9.
31. Rogers SN, Gwanne S, Lowe D, Humphris G, Yueh B, Weymuller EA Jr. The addition of mood and anxiety domains to the University of Washington quality of life scale. *Head Neck*. 2002 Jun;24(6):521-9. DOI: 10.1002/hed.10106
32. Nawka T, Wiesmann U, Gonnermann U. Validierung des Voice Handicap Index (VHI) in der deutschen Fassung [Validation of the German version of the Voice Handicap Index]. *HNO*. 2003 Nov;51(11):921-30. DOI: 10.1007/s00106-003-0909-8
33. Hogikyan ND, Sethuraman G. Validation of an instrument to measure voice-related quality of life (V-RQOL). *J Voice*. 1999 Dec;13(4):557-69. DOI: 10.1016/S0892-1997(99)80010-1
34. Bauer F, Seiss M, Grässel E, Stelzle F, Klotz M, Rosanowski F. Schluckbezogene Lebensqualität bei Mundhöhlenkarzinomen. Anderson-Dysphagia-Inventary, deutsche Version [Swallowing-related quality of life in oral cavity cancer. The German version of the Anderson Dysphagia Inventory]. *HNO*. 2010 Jul;58(7):692-7. DOI: 10.1007/s00106-010-2117-7
35. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore*. 1994 Mar;23(2):129-38.
36. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. *Pain*. 1975 Sep;1(3):277-99. DOI: 10.1016/0304-3959(75)90044-5
37. Sadura A, Pater J, Osoba D, Levine M, Palmer M, Bennett K. Quality-of-life assessment: patient compliance with questionnaire completion. *J Natl Cancer Inst*. 1992 Jul 1;84(13):1023-6. DOI: 10.1093/jnci/84.13.1023
38. Arbeitsgemeinschaft Psychoonkologie, Herschbach P, Weis J. Screeningverfahren in der Psychoonkologie. Testinstrumente zur Identifikation betreuungsbedürftiger Krebspatienten. Eine Empfehlung der PSO. Deutsche Krebsgesellschaft; 2008.
39. Tschiesner U, Rogers SN, Harréus U, Berghaus A, Cieza A. Content comparison of quality of life questionnaires used in head and neck cancer based on the international classification of functioning, disability and health: a systematic review. *Eur Arch Otorhinolaryngol*. 2008 Jun;265(6):627-37. DOI: 10.1007/s00405-008-0641-9
40. van der Molen L, van Rossum MA, Burkhead LM, Smeele LE, Hilgers FJ. Functional outcomes and rehabilitation strategies in patients treated with chemoradiotherapy for advanced head and neck cancer: a systematic review. *Eur Arch Otorhinolaryngol*. 2009 Jun;266(6):889-900. DOI: 10.1007/s00405-008-0817-3
41. Stelzle F, Maier A, Nöth E, Bocklet T, Knipfer C, Schuster M, Neukam FW, Nkenke E. Automatic quantification of speech intelligibility in patients after treatment for oral squamous cell carcinoma. *J Oral Maxillofac Surg*. 2011 May;69(5):1493-500. DOI: 10.1016/j.joms.2010.05.077

42. Suarez-Cunqueiro MM, Schramm A, Schoen R, Seoane-Lestón J, Otero-Cepeda XL, Bormann KH, Kokemueller H, Metzger M, Diz-Dios P, Geilrich NC. Speech and swallowing impairment after treatment for oral and oropharyngeal cancer. *Arch Otolaryngol Head Neck Surg.* 2008 Dec;134(12):1299-304. DOI: 10.1001/archotol.134.12.1299
43. Brown JS, Rogers SN, Lowe D. A comparison of tongue and soft palate squamous cell carcinoma treated by primary surgery in terms of survival and quality of life outcomes. *Int J Oral Maxillofac Surg.* 2006 Mar;35(3):208-14. DOI: 10.1016/j.ijom.2005.09.005
44. Kreeft AM, van der Molen L, Hilgers FJ, Balm AJ. Speech and swallowing after surgical treatment of advanced oral and oropharyngeal carcinoma: a systematic review of the literature. *Eur Arch Otorhinolaryngol.* 2009 Nov;266(11):1687-1698. DOI: 10.1007/s00405-009-1089-2
45. Speksnijder CM, van der Bilt A, Abbink JH, Merks MA, Koole R. Mastication in patients treated for malignancies in tongue and/or floor of mouth: A 1-year prospective study. *Head Neck.* 2011 Jul;33(7):1013-20. DOI: 10.1002/hed.21573
46. Hahn TR, Kruskemper G. Auswirkung der Strahlentherapie auf die Lebensqualität: Eine Untersuchung von 1411 Patienten mit Mundhöhlenkarzinom [The impact of radiotherapy on quality of life – a survey of 1411 patients with oral cancer]. *Mund Kiefer Gesichtschir.* 2007 Apr;11(2):99-106. DOI: 10.1007/s10006-007-0049-5
47. van Rij CM, Oughlane-Heemsbergen WD, Ackerstaff AH, Lamers EA, Balm AJ, Rasch CR. Parotid gland sparing IMRT for head and neck cancer improves xerostomia related quality of life. *Radiat Oncol.* 2008 Dec 9;3:41. DOI: 10.1186/1748-717X-3-41
48. Givens DJ, Karnell LH, Gupta AK, Clamon GH, Pagedar NA, Chang KE, Van Daele DJ, Funk GF. Adverse events associated with concurrent chemoradiation therapy in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg.* 2009 Dec;135(12):1209-17. DOI: 10.1001/archoto.2009.174
49. Wan Leung S, Lee TF, Chien CY, Chao PJ, Tsai WL, Fang FM. Health-related quality of life in 640 head and neck cancer survivors after radiotherapy using EORTC QLQ-C30 and QLQ-H&N35 questionnaires. *BMC Cancer.* 2011 Apr 12;11:128. DOI: 10.1186/1471-2407-11-128
50. Caglar HB, Tishler RB, Othus M, Burke E, Li Y, Goguen L, Wirth LJ, Haddad RI, Norris CM, Court LE, Aninno DJ, Posner MR, Allen AM. Dose to larynx predicts for swallowing complications after intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys.* 2008 Nov 15;72(4):1110-8. DOI: 10.1016/j.ijrobp.2008.02.048
51. Peponi E, Glanzmann C, Willi B, Huber G, Studer G. Dysphagia in head and neck cancer patients following intensity modulated radiotherapy (IMRT). *Radiat Oncol.* 2011 Jan 5;6:1. DOI: 10.1186/1748-717X-6-1
52. Weber C, Dommerich S, Pau HW, Kramp B. Limited mouth opening after primary therapy of head and neck cancer. *Oral Maxillofac Surg.* 2010 Sep;14(3):169-73. DOI: 10.1007/s10006-010-0220-2
53. Bensadoun RJ, Riesenbeck D, Lockhart PB, Elting LS, Spijkervet FK, Brennan MT; Trismus Section; Oral Care Study Group; Multinational Association for Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO). A systematic review of trismus induced by cancer therapies in head and neck cancer patients. *Support Care Cancer.* 2010 Aug;18(8):1033-8. DOI: 10.1007/s00520-010-0847-4
54. Browman GP, Hodson DI, Mackenzie RJ, Bestic N, Zuraw L; Cancer Care Ontario Practice Guideline Initiative Head and Neck Cancer Disease Site Group. Choosing a concomitant chemotherapy and radiotherapy regimen for squamous cell head and neck cancer: A systematic review of the published literature with subgroup analysis. *Head Neck.* 2001 Jul;23(7):579-89. DOI: 10.1002/hed.1081
55. Pignon JP, Bourhis J, Domenge C, Designé L. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. *Lancet.* 2000 Mar 18;355(9208):949-55. DOI: 10.1016/S0140-6736(00)90011-0
56. Boscolo-Rizzo P, Muzzi E, Trabalzini F, Gava A, Stellin M, Da Mosto MC. Functional organ preservation after chemoradiotherapy in elderly patients with loco-regionally advanced head and neck squamous cell carcinoma. *Eur Arch Otorhinolaryngol.* 2011 Sep;268(9):1349-55. DOI: 10.1007/s00405-011-1489-y
57. Boscolo-Rizzo P, Gava A, Marchiori C, Baggio V, Da Mosto MC. Functional organ preservation in patients with locoregionally advanced head and neck squamous cell carcinoma treated by platinum-based multidrug induction chemotherapy and concurrent chemoradiotherapy. *Ann Oncol.* 2011 Aug;22(8):1894-901. DOI: 10.1093/annonc/mdq681
58. Semrau S, Waldfahrer F, Lell M, Linke R, Klautke G, Kuwert T, Uder M, Iro H, Fietkau R. Feasibility, toxicity, and efficacy of short induction chemotherapy of docetaxel plus cisplatin or carboplatin (TP) followed by concurrent chemoradio-therapy for organ preservation in advanced cancer of the hypopharynx, larynx, and base of tongue. Early results. *Strahlenther Onkol.* 2011 Jan;187(1):15-22. DOI: 10.1007/s00066-010-2178-2
59. Al-Saleh K, Safwat R, Hooda HS, Bedair A, Al-Basmy A, Al-Wikeel H, Naseer M, Thotathil Z. Hyperfractionated Radiation Therapy and Concurrent Chemotherapy for advanced Head and Neck Cancer. *Gulf J Oncolog.* 2011 Jan;(9):12-9.
60. Bonner JA, Harari PM, Giralt J, Azarnia N, Shin DM, Cohen RB, Jones CU, Sur R, Raben D, Jassem J, Ove R, Kies MS, Baselga J, Youssoufian H, Amellal N, Rowinsky EK, Ang KK. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med.* 2006 Feb 9;354(6):567-78. DOI: 10.1056/NEJMoa053422
61. Walsh L, Gillham C, Dunne M, Fraser I, Hollywood D, Armstrong J, Thirion P. Toxicity of cetuximab versus cisplatin concurrent with radiotherapy in locally advanced head and neck squamous cell cancer (LAHNSCC). *Radiat Oncol.* 2011 Jan;98(1):38-41. DOI: 10.1016/j.radonc.2010.11.009
62. Kies MS, Holsinger FC, Lee JJ, William WN Jr, Glisson BS, Lin HY, Lewin JS, Ginsberg LE, Gillaspay KA, Massarelli E, Byers L, Lippman SM, Hong WK, El-Naggar AK, Garden AS, Papadimitrakopoulou V. Induction chemotherapy and cetuximab for locally advanced squamous cell carcinoma of the head and neck: results from a phase II prospective trial. *J Clin Oncol.* 2010 Jan 1;28(1):8-14. DOI: 10.1200/JCO.2009.23.0425
63. Scarpace SL, Brodzik FA, Mehdi S, Belgam R. Treatment of head and neck cancers: issues for clinical pharmacists. *Pharmacotherapy.* 2009 May;29(5):578-92. DOI: 10.1592/phco.29.5.578
64. Budach W, Bölke E, Homey B. Severe cutaneous reaction during radiation therapy with concurrent cetuximab. *N Engl J Med.* 2007 Aug 2;357(5):514-5. DOI: 10.1056/NEJMc071075
65. Pinto C, Barone CA, Girolomoni G, Russi EG, Merlano MC, Ferrari D, Maiello E; American Society of Clinical Oncology; European Society of Medical Oncology. Management of skin toxicity associated with cetuximab treatment in combination with chemotherapy or radiotherapy. *Oncologist.* 2011;16(2):228-38. DOI: 10.1634/theoncologist.2010-0298
66. Lambertz CK, Gruell J, Robenstein V, Mueller-Funaiole V, Cummings K, Knapp V. NO StOPS: Reducing treatment breaks during chemoradiation for head and neck cancer. *Clin J Oncol Nurs.* 2010 Oct;14(5):585-93. DOI: 10.1188/10.CJON.585-593

67. Montejo ME, Shrieve DC, Bentz BG, Hunt JP, Buchman LO, Agarwal N, Hitchcock YJ. IMRT with simultaneous integrated boost and concurrent chemotherapy for locoregionally advanced squamous cell carcinoma of the head and neck. *Int J Radiat Oncol Biol Phys.* 2011 Dec 1;81(5):e845-52. DOI: 10.1016/j.ijrobp.2010.10.021
68. Furness S, Glennly AM, Worthington HV, Pavitt S, Oliver R, Clarkson JE, Macluskey M, Chan KK, Conway DI. Interventions for the treatment of oral cavity and oropharyngeal cancer: chemotherapy. *Cochrane Database Syst Rev.* 2011 Apr 13;(4):CD006386.
69. Argiris A, Heron DE, Smith RP, Kim S, Gibson MK, Lai SY, Branstetter BF, Posluszny DM, Wang L, Seethala RR, Dacic S, Gooding W, Grandis JR, Johnson JT, Ferris RL. Induction docetaxel, cisplatin, and cetuximab followed by concurrent radiotherapy, cisplatin, and cetuximab and maintenance cetuximab in patients with locally advanced head and neck cancer. *J Clin Oncol.* 2010 Dec 20;28(36):5294-300. DOI: 10.1200/JCO.2010.30.6423
70. Villaret AB, Cappiello J, Piazza C, Pedruzzi B, Nicolai P. Quality of life in patients treated for cancer of the oral cavity requiring reconstruction: a prospective study. *Acta Otorhinolaryngol Ital.* 2008 Jun;28(3):120-5.
71. Biazevic MG, Antunes JL, Togni J, de Andrade FP, de Carvalho MB, Wünsch-Filho V. Survival and quality of life of patients with oral and oropharyngeal cancer at 1-year follow-up of tumor resection. *J Appl Oral Sci.* 2010 May-Jun;18(3):279-84. DOI: 10.1590/S1678-77572010000300015
72. Borggreven PA, Aaronson NK, Verdonck-de Leeuw IM, Muller MJ, Heiligers ML, Bree R, Langendijk JA, Leemans CR. Quality of life after surgical treatment for oral and oropharyngeal cancer: a prospective longitudinal assessment of patients reconstructed by a microvascular flap. *Oral Oncol.* 2007 Nov;43(10):1034-42. DOI: 10.1016/j.oraloncology.2006.11.017
73. Brown L, Rieger JM, Harris J, Seikaly H. A longitudinal study of functional outcomes after surgical resection and microvascular reconstruction for oral cancer: tongue mobility and swallowing function. *J Oral Maxillofac Surg.* 2010 Nov;68(11):2690-700. DOI: 10.1016/j.joms.2010.05.004
74. Bozec A, Poissonnet G, Chamorey E, Casanova C, Vallicioni J, Demard F, Mahdyoun P, Peyrade F, Follana P, Bensadoun RJ, Benezery K, Thariat J, Marcy PY, Sudaka A, Dassonville O. Free-flap head and neck reconstruction and quality of life: a 2-year prospective study. *Laryngoscope.* 2008 May;118(5):874-80. DOI: 10.1097/MLG.0b013e3181644abd
75. Yanai C, Kikutani T, Adachi M, Thoren H, Suzuki M, Iizuka T. Functional outcome after total and subtotal glossectomy with free flap reconstruction. *Head Neck.* 2008 Jul;30(7):909-18. DOI: 10.1002/hed.20804
76. Archontaki M, Athanasiou A, Stavrianos SD, Korkolis DP, Faratzis G, Papadopoulou F, Kokkalis G, Rapis AD. Functional results of speech and swallowing after oral microvascular free flap reconstruction. *Eur Arch Otorhinolaryngol.* 2010 Nov;267(11):1771-7. DOI: 10.1007/s00405-010-1275-2
77. Moerman M, Vermeersch H, Van Lierde K, Fahimi H, Van Cauwenberge P. Refinement of the free radial forearm flap reconstructive technique after resection of large oropharyngeal malignancies with excellent functional results. *Head Neck.* 2003 Sep;25(9):772-7. <http://dx.doi.org/10.1002/hed.10295>
78. Roumanas ED, Garrett N, Blackwell KE, Freymiller E, Abemayor E, Wong WK, Beumer J 3rd, Fueki K, Fueki W, Kapur KK. Masticatory and swallowing threshold performances with conventional and implant-supported prostheses after mandibular fibula free-flap reconstruction. *J Prosthet Dent.* 2006 Oct;96(4):289-97. DOI: 10.1016/j.prosdent.2006.08.015
79. Baumann DP, Yu P, Hanasono MM, Skoracki RJ. Free flap reconstruction of osteoradionecrosis of the mandible: a 10-year review and defect classification. *Head Neck.* 2011 Jun;33(6):800-7. DOI: 10.1002/hed.21537
80. Hsiao HT, Leu YS, Liu CJ, Tung KY, Lin CC. Radial forearm versus anterolateral thigh flap reconstruction after hemiglossectomy: functional assessment of swallowing and speech. *J Reconstr Microsurg.* 2008 Feb;24(2):85-8. DOI: 10.1055/s-2008-1076097
81. Rizvi TA, Rashid M, Ahmed B, Haq EU, Sarwar SU, Zia-ul-Islam M, Tamimy MS. Quality of life assessment in patients with locally advanced head and neck malignancy after ablative surgery and reconstruction with microvascular free flaps. *J Coll Physicians Surg Pak.* 2009 Feb;19(2):108-12.
82. Chung MK, Son YI, Cho JK, So YK, Woo SH, Jeong HS, Baek CH. Therapeutic options in patients with early T stage and advanced N stage of tonsillar squamous cell carcinomas. *Otolaryngol Head Neck Surg.* 2010 Dec;143(6):808-14. DOI: 10.1016/j.otohns.2010.06.914
83. Gan HK, Bernstein LJ, Brown J, Ringash J, Vakilha M, Wang L, Goldstein D, Kim J, Hope A, O'Sullivan B, Waldron J, Abdul Razak AR, Chen EX, Siu LL. Cognitive functioning after radiotherapy or chemoradiotherapy for head-and-neck cancer. *Int J Radiat Oncol Biol Phys.* 2011 Sep 1;81(1):126-34. DOI: 10.1016/j.ijrobp.2010.05.004
84. Hsiao KY, Yeh SA, Chang CC, Tsai PC, Wu JM, Gau JS. Cognitive function before and after intensity-modulated radiation therapy in patients with nasopharyngeal carcinoma: a prospective study. *Int J Radiat Oncol Biol Phys.* 2010 Jul 1;77(3):722-6. DOI: 10.1016/j.ijrobp.2009.06.080
85. Mowry SE, Ho A, Lotempio MM, Sadeghi A, Blackwell KE, Wang MB. Quality of life in advanced oropharyngeal carcinoma after chemoradiation versus surgery and radiation. *Laryngoscope.* 2006 Sep;116(9):1589-93. DOI: 10.1097/01.mlg.0000233244.18901.44
86. Kim TW, Youm HY, Byun H, Son YI, Baek CH. Treatment Outcomes and Quality of Life in Oropharyngeal Cancer after Surgery-based versus Radiation-based Treatment. *Clin Exp Otorhinolaryngol.* 2010 Sep;3(3):153-60. DOI: 10.3342/ceo.2010.3.3.153
87. Ambrosch P, Fazel A. Funktionserhaltende Therapie des Kehlkopf- und des Hypopharynxkarzinoms [Functional organ preservation in laryngeal and hypopharyngeal cancer]. *Laryngorhinologie.* 2011 Mar;90 Suppl 1:S83-109. DOI: 10.1055/s-0030-1270449
88. Kujath M, Kerr P, Myers C, Bammeke F, Lambert P, Cooke A, Sutherland D. Functional outcomes and laryngectomy-free survival after transoral CO2 laser microsurgery for stage 1 and 2 glottic carcinoma. *J Otolaryngol Head Neck Surg.* 2011 Feb;40(Suppl 1):S49-58.
89. Núñez Batalla F, Caminero Cueva MJ, Señaris González B, Llorente Pendás JL, Gorri Gil C, López Llamas A, Alonso Pantiga R, Suárez Nieto C. Voice quality after endoscopic laser surgery and radiotherapy for early glottic cancer: objective measurements emphasizing the Voice Handicap Index. *Eur Arch Otorhinolaryngol.* 2008 May;265(5):543-8. DOI: 10.1007/s00405-007-0512-9
90. Loughran S, Calder N, MacGregor FB, Carding P, MacKenzie K. Quality of life and voice following endoscopic resection or radiotherapy for early glottic cancer. *Clin Otolaryngol.* 2005 Feb;30(1):42-7. DOI: 10.1111/j.1365-2273.2004.00919.x
91. Spielmann PM, Majumdar S, Morton RP. Quality of life and functional outcomes in the management of early glottic carcinoma: a systematic review of studies comparing radiotherapy and transoral laser microsurgery. *Clin Otolaryngol.* 2010 Oct;35(5):373-82. DOI: 10.1111/j.1749-4486.2010.02191.x

92. Mostafa BE, Youssef AM. Conservation surgery for early laryngeal carcinoma. *ORL J Otorhinolaryngol Relat Spec.* 2010;72(4):220-4. DOI: 10.1159/000316649
93. Webster KT, Samlan RA, Jones B, Bunton K, Tufano RP. Supracricoid partial laryngectomy: swallowing, voice, and speech outcomes. *Ann Otol Rhinol Laryngol.* 2010 Jan;119(1):10-6.
94. Saito K, Araki K, Ogawa K, Shiotani A. Laryngeal function after supracricoid laryngectomy. *Otolaryngol Head Neck Surg.* 2009 Apr;140(4):487-92. DOI: 10.1016/j.otohns.2008.12.036
95. Portas JG, Queija Ddos S, Arine LP, Ferreira AS, Dedivitis RA, Lehn CN, Barros AP. Voice and swallowing disorders: functional results and quality of life following supracricoid laryngectomy with cricothyroidopiglottopexy. *Ear Nose Throat J.* 2009 Oct;88(10):E23-30.
96. Yüce I, Cagli S, Bayram A, Karasu F, Sati I, Güney E. The effect of arytenoid resection on functional results of cricothyroidopexy. *Otolaryngol Head Neck Surg.* 2009 Aug;141(2):272-5. DOI: 10.1016/j.otohns.2009.04.012
97. Mantsopoulos K, Psychogios G, Koch M, Zenk J, Waldfahrer F, Iro H. Comparison of different surgical approaches in T2 glottic cancer. *Head Neck.* 2012 Jan;34(1):73-7. DOI: 10.1002/hed.21687
98. Jepsen MC, Gurushanthaiah D, Roy N, Smith ME, Gray SD, Davis RK. Voice, speech, and swallowing outcomes in laser-treated laryngeal cancer. *Laryngoscope.* 2003 Jun;113(6):923-8. DOI: 10.1097/00005537-200306000-00001
99. Nemr NK, de Carvalho MB, Köhle J, Leite GC, Rapoport A, Szeliga RM. Functional study of the voice and swallowing following supracricoid laryngectomy. *Braz J Otorhinolaryngol.* 2007 Mar-Apr;73(2):151-5.
100. Olthoff A, Ewen A, Wolff HA, Hermann RM, Vorwerk H, Hille A, Rödel R, Hess CF, Steiner W, Pradier O, Christiansen H. Organ function and quality of life after transoral laser microsurgery and adjuvant radiotherapy for locally advanced laryngeal cancer. *Strahlenther Onkol.* 2009 May;185(5):303-9. DOI: 10.1007/s00066-009-1967-y
101. Kazi R, Prasad V, Venkitaraman R, Nutting CM, Clarke P, Rhys-Evans P, Harrington KJ. Questionnaire analysis of the swallowing-related outcomes following total laryngectomy. *Clin Otolaryngol.* 2006 Dec;31(6):525-30. DOI: 10.1111/j.1365-2273.2006.01335.x
102. Xi S. Effectiveness of voice rehabilitation on vocalisation in postlaryngectomy patients: a systematic review. *Int J Evid Based Healthc.* 2010 Dec;8(4):256-8. DOI: 10.1111/j.1744-1609.2010.00177.x
103. Hutcheson KA, Lewin JS, Sturgis EM, Kapadia A, Risser J. Enlarged tracheoesophageal puncture after total laryngectomy: a systematic review and meta-analysis. *Head Neck.* 2011 Jan;33(1):20-30. DOI: 10.1002/hed.21399
104. Hutcheson KA, Lewin JS, Sturgis EM, Risser J. Outcomes and adverse events of enlarged tracheoesophageal puncture after total laryngectomy. *Laryngoscope.* 2011 Jul;121(7):1455-61. DOI: 10.1002/lary.21807
105. van la Parra RF, Kon M, Schellekens PP, Braunius WW, Pameijer FA. The prognostic value of abnormal findings on radiographic swallowing studies after total laryngectomy. *Cancer Imaging.* 2007 Jun 11;7:119-25. DOI: 10.1102/1470-7330.2007.0015
106. Dworkin JP, Meleca RJ, Zacharek MA, Stachler RJ, Pasha R, Abkarian GG, Culatta RA, Jacobs JR. Voice and deglutition functions after the supracricoid and total laryngectomy procedures for advanced stage laryngeal carcinoma. *Otolaryngol Head Neck Surg.* 2003 Oct;129(4):311-20. DOI: 10.1016/S0194-5998(03)01314-7
107. Robertson SM, Yeo JC, Dunnet C, Young D, Mackenzie K. Voice, swallowing, and quality of life after total laryngectomy: results of the west of Scotland laryngectomy audit. *Head Neck.* 2012 Jan;34(1):59-65. DOI: 10.1002/hed.21692
108. Vilaseca I, Chen AY, Backscheider AG. Long-term quality of life after total laryngectomy. *Head Neck.* 2006 Apr;28(4):313-20. DOI: 10.1002/hed.20268
109. de Casso C, Slevin NJ, Homer JJ. The impact of radiotherapy on swallowing and speech in patients who undergo total laryngectomy. *Otolaryngol Head Neck Surg.* 2008 Dec;139(6):792-7. DOI: 10.1016/j.otohns.2008.08.023
110. Vilaseca I, Chen AY, Backscheider AG. Long-term quality of life after total laryngectomy. *Head Neck.* 2006 Apr;28(4):313-20. DOI: 10.1002/hed.20268
111. Danker H, Wollbrück D, Singer S, Fuchs M, Brähler E, Meyer A. Social withdrawal after laryngectomy. *Eur Arch Otorhinolaryngol.* 2010 Apr;267(4):593-600. DOI: 10.1007/s00405-009-1087-4
112. Fung K, Lyden TH, Lee J, Urba SG, Worden F, Eisbruch A, Tsien C, Bradford CR, Chepeha DB, Hogikyan ND, Prince ME, Teknos TN, Wolf GT. Voice and swallowing outcomes of an organ-preservation trial for advanced laryngeal cancer. *Int J Radiat Oncol Biol Phys.* 2005 Dec 1;63(5):1395-9. DOI: 10.1016/j.ijrobp.2005.05.004
113. Clark JR, Gilbert R, Irish J, Brown D, Neligan P, Gullane PJ. Morbidity after flap reconstruction of hypopharyngeal defects. *Laryngoscope.* 2006 Feb;116(2):173-81. DOI: 10.1097/01.mlg.0000191459.40059.fd
114. Lewin JS, Barringer DA, May AH, Gillenwater AM, Arnold KA, Roberts DB, Yu P. Functional outcomes after laryngopharyngectomy with anterolateral thigh flap reconstruction. *Head Neck.* 2006 Feb;28(2):142-9. DOI: 10.1002/hed.20308
115. Moradi P, Glass GE, Atherton DD, Eccles S, Coffey M, Majithia A, Speirs AJ, Clarke PM, Wood SH. Reconstruction of pharyngolaryngectomy defects using the jejunal free flap: a 10-year experience from a single reconstructive center. *Plast Reconstr Surg.* 2010 Dec;126(6):1960-6. DOI: 10.1097/PRS.0b013e3181f446a6
116. Wu PY, Kuo YR, Jeng SF, Hsu CM, Su CY. Functional outcomes of patients with advanced pyriform sinus cancer treated with extended near-total laryngopharyngectomy and free fasciocutaneous flap reconstruction. *Eur Arch Otorhinolaryngol.* 2010 Dec;267(12):1951-6. DOI: 10.1007/s00405-010-1311-2
117. Morrissey AT, O'Connell DA, Garg S, Seikaly H, Harris JR. Radial forearm versus anterolateral thigh free flaps for laryngopharyngectomy defects: prospective, randomized trial. *J Otolaryngol Head Neck Surg.* 2010 Aug;39(4):448-53.
118. Nyquist GG, Hier MP, Dionisopoulos T, Black MJ. Stricture associated with primary tracheoesophageal puncture after pharyngolaryngectomy and free jejunal interposition. *Head Neck.* 2006 Mar;28(3):205-9. DOI: 10.1002/hed.20330
119. Oniscu GC, Walker WS, Sanderson R. Functional results following pharyngolaryngoesophagectomy with free jejunal graft reconstruction. *Eur J Cardiothorac Surg.* 2001 Apr;19(4):406-10. DOI: 10.1016/S1010-7940(01)00618-2
120. Scharpf J, Esclamado RM. Reconstruction with radial forearm flaps after ablative surgery for hypopharyngeal cancer. *Head Neck.* 2003 Apr;25(4):261-6. DOI: 10.1002/hed.10197
121. Hanasono MM, Lin D, Wax MK, Rosenthal EL. Closure of laryngectomy defects in the age of chemoradiation therapy. *Head Neck.* 2012 Apr;34(4):580-8. doi: 10.1002/hed.21712. DOI: 10.1002/hed.21712

122. Cmelak AJ, Li S, Goldwasser MA, Murphy B, Cannon M, Pinto H, Rosenthal DI, Gillison M, Forastiere AA. Phase II trial of chemoradiation for organ preservation in resectable stage III or IV squamous cell carcinomas of the larynx or oropharynx: results of Eastern Cooperative Oncology Group Study E2399. *J Clin Oncol*. 2007 Sep 1;25(25):3971-7. DOI: 10.1200/JCO.2007.10.8951
123. Forastiere AA, Goepfert H, Maor M, Pajak TF, Weber R, Morrison W, Glisson B, Trotti A, Ridge JA, Chao C, Peters G, Lee DJ, Leaf A, Ensley J, Cooper J. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med*. 2003 Nov 27;349(22):2091-8. DOI: 10.1056/NEJMoa031317
124. LENT SOMA scales for all anatomic sites. *Int J Radiat Oncol Biol Phys*. 1995 Mar 30;31(5):1049-91. DOI: 10.1016/0360-3016(95)90159-0
125. Dworkin JP, Hill SL, Stachler RJ, Meleca RJ, Kewson D. Swallowing function outcomes following nonsurgical therapy for advanced-stage laryngeal carcinoma. *Dysphagia*. 2006 Jan;21(1):66-74. DOI: 10.1007/s00455-005-9001-8
126. Mouw KW, Haraf DJ, Stenson KM, Cohen EE, Xi X, Witt ME, List M, Blair EA, Vokes EE, Salama JK. Factors associated with long-term speech and swallowing outcomes after chemoradiotherapy for locoregionally advanced head and neck cancer. *Arch Otolaryngol Head Neck Surg*. 2010 Dec;136(12):1226-34. DOI: 10.1001/archoto.2010.218
127. Boscolo-Rizzo P, Maronato F, Marchiori C, Gava A, Da Mosto MC. Long-term quality of life after total laryngectomy and postoperative radiotherapy versus concurrent chemoradiotherapy for laryngeal preservation. *Laryngoscope*. 2008 Feb;118(2):300-6. DOI: 10.1097/MLG.0b013e31815a9ed3
128. Guibert M, Lepage B, Woisard V, Rives M, Serrano E, Vergez S. Quality of life in patients treated for advanced hypopharyngeal or laryngeal cancer. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2011 Nov;128(5):218-23. DOI: 10.1016/j.anorl.2011.02.010
129. Hanna E, Sherman A, Cash D, Adams D, Vural E, Fan CY, Suen JY. Quality of life for patients following total laryngectomy vs chemoradiation for laryngeal preservation. *Arch Otolaryngol Head Neck Surg*. 2004 Jul;130(7):875-9. DOI: 10.1001/archotol.130.7.875
130. Trivedi NP, Swaminathan DK, Thankappan K, Chatni S, Kuriakose MA, Iyer S. Comparison of quality of life in advanced laryngeal cancer patients after concurrent chemoradiotherapy vs total laryngectomy. *Otolaryngol Head Neck Surg*. 2008 Nov;139(5):702-7. DOI: 10.1016/j.otohns.2008.06.002
131. Azevedo EH, Montoni N, Gonçalves Filho J, Kowalski LP, Carrara-de Angelis E. Vocal handicap and quality of life after treatment of advanced squamous carcinoma of the larynx and/or hypopharynx. *J Voice*. 2012 Mar;26(2):e63-71. DOI: 10.1016/j.jvoice.2011.02.007
132. Klozar J, Cada Z, Koslabova E. Complications of total laryngectomy in the era of chemoradiation. *Eur Arch Otorhinolaryngol*. 2012 Jan;269(1):289-93. DOI: 10.1007/s00405-011-1598-7
133. Cavalot AL, Gervasio CF, Nazionale G, Albera R, Bussi M, Staffieri A, Ferrero V, Cortesina G. Pharyngocutaneous fistula as a complication of total laryngectomy: review of the literature and analysis of case records. *Otolaryngol Head Neck Surg*. 2000 Nov;123(5):587-92. DOI: 10.1067/mhn.2000.110617
134. Weber RS, Berkey BA, Forastiere A, Cooper J, Maor M, Goepfert H, Morrison W, Glisson B, Trotti A, Ridge JA, Chao KS, Peters G, Lee DJ, Leaf A, Ensley J. Outcome of salvage total laryngectomy following organ preservation therapy: the Radiation Therapy Oncology Group trial 91-11. *Arch Otolaryngol Head Neck Surg*. 2003 Jan;129(1):44-9. DOI: 10.1001/archotol.129.1.44
135. Sakai A, Okami K, Sugimoto R, Ebisumoto K, Yamamoto H, Furuya H, Iida M. Multivariate analysis of wound complications after surgery for laryngeal and hypopharyngeal cancers. *ORL J Otorhinolaryngol Relat Spec*. 2011;73(2):100-4. DOI: 10.1159/000323832
136. Fung K, Teknos TN, Vandenberg CD, Lyden TH, Bradford CR, Hogikyan ND, Kim J, Prince ME, Wolf GT, Chepeha DB. Prevention of wound complications following salvage laryngectomy using free vascularized tissue. *Head Neck*. 2007 May;29(5):425-30. DOI: 10.1002/hed.20492
137. Watkins JP, Williams GB, Mascioli AA, Wan JY, Samant S. Shoulder function in patients undergoing selective neck dissection with or without radiation and chemotherapy. *Head Neck*. 2011 May;33(5):615-9. DOI: 10.1002/hed.21503
138. Teymoortash A, Hoch S, Eivazi B, Werner J. Postoperative morbidity after different types of selective neck dissection. *Laryngoscope*. 2010 May;120(5):924-9.
139. Epstein JB, Hong C, Logan RM, Barasch A, Gordon SM, Oberle-Edwards L, McGuire D, Napenas JJ, Elting LS, Spijkervet FK, Brennan MT. A systematic review of orofacial pain in patients receiving cancer therapy. *Support Care Cancer*. 2010 Aug;18(8):1023-31. DOI: 10.1007/s00520-010-0897-7
140. van Wouwe M, de Bree R, Kuik DJ, de Goede CJ, Verdonck-de Leeuw IM, Doornaert P, Leemans CR. Shoulder morbidity after non-surgical treatment of the neck. *Radiother Oncol*. 2009 Feb;90(2):196-201. DOI: 10.1016/j.radonc.2008.11.003
141. Pigni A, Brunelli C, Caraceni A. The role of hydromorphone in cancer pain treatment: a systematic review. *Palliat Med*. 2011 Jul;25(5):471-7. DOI: 10.1177/0269216310387962
142. Navez ML. Douleur des cancers ORL au stade des sequelles [Otolaryngological cancer pain at the after-effects stage]. *Ann Otolaryngol Chir Cervicofac*. 2007 Oct;124 Suppl 1:S39-44. DOI: 10.1016/S0003-438X(07)80009-0
143. Raber-Durlacher JE, Elad S, Barasch A. Oral mucositis. *Oral Oncol*. 2010 Jun;46(6):452-6. DOI: 10.1016/j.oraloncology.2010.03.012
144. Rosenthal DI, Trotti A. Strategies for managing radiation-induced mucositis in head and neck cancer. *Semin Radiat Oncol*. 2009 Jan;19(1):29-34. DOI: 10.1016/j.semradonc.2008.09.006
145. Feller L, Essop R, Wood NH, Khammissa RA, Chikte UM, Meyerov R, Lemmer J. Chemotherapy- and radiotherapy-induced oral mucositis: pathobiology, epidemiology and management. *SADJ*. 2010 Sep;65(8):372-4.
146. Garg S, Yoo J, Winquist E. Nutritional support for head and neck cancer patients receiving radiotherapy: a systematic review. *Support Care Cancer*. 2010 Jun;18(6):667-77. DOI: 10.1007/s00520-009-0686-3
147. Paleri V, Patterson J. Use of gastrostomy in head and neck cancer: a systematic review to identify areas for future research. *Clin Otolaryngol*. 2010 Jun;35(3):177-89. DOI: 10.1111/j.1749-4486.2010.02128.x
148. Rosenthal DI, Lewin JS, Eisbruch A. Prevention and treatment of dysphagia and aspiration after chemoradiation for head and neck cancer. *J Clin Oncol*. 2006 Jun 10;24(17):2636-43. DOI: 10.1200/JCO.2006.06.0079
149. Nguyen NP, Frank C, Moltz CC, Vos P, Smith HJ, Nguyen PD, Martinez T, Karlsson U, Dutta S, Lemanski C, Nguyen LM, Sallah S. Analysis of factors influencing aspiration risk following chemoradiation for oropharyngeal cancer. *Br J Radiol*. 2009 Aug;82(980):675-80. DOI: 10.1259/bjr/72852974
150. Rogers SN, Thomson R, O'Toole P, Lowe D. Patients experience with long-term percutaneous endoscopic gastrostomy feeding following primary surgery for oral and oropharyngeal cancer. *Oral Oncol*. 2007 May;43(5):499-507. DOI: 10.1016/j.oraloncology.2006.05.002

151. Kazi R, Prasad V, Venkitaraman R, Nutting CM, Clarke P, Rhys-Evans P, Harrington KJ. Questionnaire analysis of swallowing-related outcomes following glossectomy. *ORL J Otorhinolaryngol Relat Spec.* 2008;70(3):151-5. DOI: 10.1159/000124287
152. Brookes JT, Seikaly H, Diamond C, Mechor B, Harris JR. Prospective randomized trial comparing the effect of early suturing of tracheostomy sites on postoperative patient swallowing and rehabilitation. *J Otolaryngol.* 2006 Apr;35(2):77-82. DOI: 10.2310/7070.2005.4035
153. Ruo Redda MG, Allis S. Radiotherapy-induced taste impairment. *Cancer Treat Rev.* 2006 Nov;32(7):541-7. DOI: 10.1016/j.ctrv.2006.06.003
154. Halyard MY, Jatoi A, Sloan JA, Bearden JD 3rd, Vora SA, Atherton PJ, Perez EA, Soori G, Zalduendo AC, Zhu A, Stella PJ, Loprinzi CL. Does zinc sulfate prevent therapy-induced taste alterations in head and neck cancer patients? Results of phase III double-blind, placebo-controlled trial from the North Central Cancer Treatment Group (N01C4). *Int J Radiat Oncol Biol Phys.* 2007 Apr 1;67(5):1318-22. DOI: 10.1016/j.ijrobp.2006.10.046
155. Singer S, Krauss O, Keszte J, Siegl G, Papsdorf K, Severi E, Hauss J, Briest S, Dietz A, Brähler E, Kortmann RD. Predictors of emotional distress in patients with head and neck cancer. *Head Neck.* 2012 Feb;34(2):180-7. DOI: 10.1002/hed.21702
156. Deno M, Tashiro M, Miyashita M, Asakage T, Takahashi K, Saito K, Busujima Y, Mori Y, Saito H, Ichikawa Y. The mediating effects of social support and self-efficacy on the relationship between social distress and emotional distress in head and neck cancer outpatients with facial disfigurement. *Psychooncology.* 2012 Feb;21(2):144-52. DOI: 10.1002/pon.1877
157. Neilson KA, Pollard AC, Boonzaier AM, Corry J, Castle DJ, Mead KR, Gray MC, Smith DI, Trauer T, Couper JW. Psychological distress (depression and anxiety) in people with head and neck cancers. *Med J Aust.* 2010 Sep 6;193(5 Suppl):S48-51.
158. Hassanein KA, Musgrove BT, Bradbury E. Psychological outcome of patients following treatment of oral cancer and its relation with functional status and coping mechanisms. *J Craniomaxillofac Surg.* 2005 Dec;33(6):404-9. DOI: 10.1016/j.jcms.2005.05.005
159. Horney DJ, Smith HE, McGurk M, Weinman J, Herold J, Altman K, Llewellyn CD. Associations between quality of life, coping styles, optimism, and anxiety and depression in pretreatment patients with head and neck cancer. *Head Neck.* 2011 Jan;33(1):65-71. DOI: 10.1002/hed.21407
160. Verdonck-de Leeuw IM, Eerenstein SE, Van der Linden MH, Kuik DJ, de Bree R, Leemans CR. Distress in spouses and patients after treatment for head and neck cancer. *Laryngoscope.* 2007 Feb;117(2):238-41. DOI: 10.1097/01.mlg.0000250169.10241.58
161. Verdonck-de Leeuw IM, van Bleek WJ, Leemans CR, de Bree R. Employment and return to work in head and neck cancer survivors. *Oral Oncol.* 2010 Jan;46(1):56-60. DOI: 10.1016/j.oraloncology.2009.11.001
162. Hamid OA, El Fiky LM, Medani MM, Abdelhady A, Ali HH. Laryngeal cancer in Egypt: quality of life measurement with different treatment modalities. *Head Neck.* 2011 Aug;33(8):1162-9. DOI: 10.1002/hed.21591
163. Tschiesner U, Linseisen E, Baumann S, Siedek V, Stelter K, Berghaus A, Cieza A. Assessment of functioning in patients with head and neck cancer according to the International Classification of Functioning, Disability, and Health (ICF): a multicenter study. *Laryngoscope.* 2009 May;119(5):915-23. DOI: 10.1002/lary.20211
164. Abendstein H, Nordgren M, Boysen M, Jannert M, Silander E, Ahlner-Elmqvist M, Hammerlid E, Bjordal K. Quality of life and head and neck cancer: a 5 year prospective study. *Laryngoscope.* 2005 Dec;115(12):2183-92. DOI: 10.1097/01.MLG.0000181507.69620.14
165. Duke RL, Campbell BH, Indresano AT, Eaton DJ, Marbella AM, Myers KB, Layde PM. Dental status and quality of life in long-term head and neck cancer survivors. *Laryngoscope.* 2005 Apr;115(4):678-83. DOI: 10.1097/01.mlg.0000161354.28073.bc
166. Frowen JJ, Perry AR. Swallowing outcomes after radiotherapy for head and neck cancer: a systematic review. *Head Neck.* 2006 Oct;28(10):932-44. DOI: 10.1002/hed.20438
167. Stucki G, Ewert T, Cieza A. Value and application of the ICF in rehabilitation medicine. *Disabil Rehabil.* 2002 Nov 20;24(17):932-8. DOI: 10.1080/09638280210148594
168. Schuntermann M. Einführung in die ICF. 2. Auflage. *eco med Medizin;* 2007.
169. Roe JW, Carding PN, Dwivedi RC, Kazi RA, Rhys-Evans PH, Harrington KJ, Nutting CM. Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head & neck cancer - a systematic review. *Oral Oncol.* 2010 Oct;46(10):727-33. DOI: 10.1016/j.oraloncology.2010.07.012
170. Brach M, Cieza A, Stucki G, Füssl M, Cole A, Ellerin B, Fialka-Moser V, Kostanjsek N, Melvin J. ICF Core Sets for breast cancer. *J Rehabil Med.* 2004 Jul;(44 Suppl):121-7. DOI: 10.1080/16501960410016811
171. Cieza A, Stucki A, Geyh S, Berteau M, Quittan M, Simon A, Kostanjsek N, Stucki G, Walsh N. ICF Core Sets for chronic ischaemic heart disease. *J Rehabil Med.* 2004 Jul;(44 Suppl):94-9. DOI: 10.1080/16501960410016785
172. Ruof J, Cieza A, Wolff B, Angst F, Ergeletzis D, Omar Z, Kostanjsek N, Stucki G. ICF Core Sets for diabetes mellitus. *J Rehabil Med.* 2004 Jul;(44 Suppl):100-6.
173. Stucki A, Stoll T, Cieza A, Weigl M, Giardini A, Wever D, Kostanjsek N, Stucki G. ICF Core Sets for obstructive pulmonary diseases. *J Rehabil Med.* 2004 Jul;(44 Suppl):114-20. DOI: 10.1080/16501960410016794
174. Tschiesner U, Rogers S, Dietz A, Yueh B, Cieza A. Development of ICF core sets for head and neck cancer. *Head Neck.* 2010 Feb;32(2):210-20.
175. Tschiesner U, Becker S, Cieza A. Health professional perspective on disability in head and neck cancer. *Arch Otolaryngol Head Neck Surg.* 2010 Jun;136(6):576-83. DOI: 10.1001/archoto.2010.78
176. Tschiesner U, Linseisen E, Coenen M, Rogers S, Harreus U, Berghaus A, Cieza A. Evaluating sequelae after head and neck cancer from the patient perspective with the help of the International Classification of Functioning, Disability and Health. *Eur Arch Otorhinolaryngol.* 2009 Mar;266(3):425-36. DOI: 10.1007/s00405-008-0764-z
177. Tschiesner UM, Rogers SN, Harreus U, Berghaus A, Cieza A. Comparison of outcome measures in head and neck cancer—literature review 2000-2006. *Head Neck.* 2009 Feb;31(2):251-9. DOI: 10.1002/hed.20960
178. Becker S, Kirchberger I, Cieza A, Berghaus A, Harreus U, Reichel O, Tschiesner U. Content validation of the Comprehensive ICF Core Set for Head and Neck Cancer (HNC): the perspective of psychologists. *Psychooncology.* 2010 Jun;19(6):594-605. DOI: 10.1002/pon.1608
179. Leib A, Cieza A, Tschiesner U. Perspective of physicians within a multidisciplinary team: Content validation of the comprehensive ICF core set for head and neck cancer. *Head Neck.* 2012 Jul;34(7):956-66. DOI: 10.1002/hed.21844
180. Tschiesner U, Linseisen E, Becker S, Mast G, Rogers SN, Walvekar RR, Berghaus A, Cieza A. Content validation of the international classification of functioning, disability and health core sets for head and neck cancer: a multicentre study. *J Otolaryngol Head Neck Surg.* 2010 Dec;39(6):674-87.

181. Tschiesner U, Oberhauser C, Cieza A. ICF Core Set for head and neck cancer: do the categories discriminate among clinically relevant subgroups of patients? *Int J Rehabil Res.* 2011 Jun;34(2):121-30. DOI: 10.1097/MRR.0b013e328343d4bc
182. Rogers SN, Forgie S, Lowe D, Precious L, Haran S, Tschiesner U. Development of the International Classification of Functioning, Disability and Health as a brief head and neck cancer patient questionnaire. *Int J Oral Maxillofac Surg.* 2010 Oct;39(10):975-82. DOI: 10.1016/j.ijom.2010.06.006
183. Licitra L, Bossi P, Locati LD. A multidisciplinary approach to squamous cell carcinomas of the head and neck: what is new? *Curr Opin Oncol.* 2006 May;18(3):253-7. DOI: 10.1097/O1.cco.0000219254.53091.35
184. Westin T, Stafors J. Tumour boards/multidisciplinary head and neck cancer meetings: are they of value to patients, treating staff or a political additional drain on healthcare resources? *Curr Opin Otolaryngol Head Neck Surg.* 2008 Apr;16(2):103-7. DOI: 10.1097/MOO.0b013e3282f6a4c4
185. Cieza A, Brockow T, Ewert T, Amman E, Kollerits B, Chatterji S, Ustün TB, Stucki G. Linking health-status measurements to the international classification of functioning, disability and health. *J Rehabil Med.* 2002 Sep;34(5):205-10. DOI: 10.1080/165019702760279189
186. Cieza A, Geyh S, Chatterji S, Kostanjsek N, Ustün B, Stucki G. ICF linking rules: an update based on lessons learned. *J Rehabil Med.* 2005 Jul;37(4):212-8. DOI: 10.1080/16501970510040263
187. Brockow T, Duddeck K, Geyh S, Schwarzkopf S, Weigl M, Franke T, Brach M. Identifying the concepts contained in outcome measures of clinical trials on breast cancer using the International Classification of Functioning, Disability and Health as a reference. *J Rehabil Med.* 2004 Jul;(44 Suppl):43-8. DOI: 10.1080/16501960410015434
188. Geyh S, Kurt T, Brockow T, Cieza A, Ewert T, Omar Z, Resch KL. Identifying the concepts contained in outcome measures of clinical trials on stroke using the International Classification of Functioning, Disability and Health as a reference. *J Rehabil Med.* 2004 Jul;(44 Suppl):56-62. DOI: 10.1080/16501960410015399
189. Dwivedi RC, Kazi RA, Agrawal N, Nutting CM, Clarke PM, Kerawala CJ, Rhys-Evans PH, Harrington KJ. Evaluation of speech outcomes following treatment of oral and oropharyngeal cancers. *Cancer Treat Rev.* 2009 Aug;35(5):417-24. DOI: 10.1016/j.ctrv.2009.04.013
190. Dey P, Arnold D, Wight R, MacKenzie K, Kelly C, Wilson J. Radiotherapy versus open surgery versus endolaryngeal surgery (with or without laser) for early laryngeal squamous cell cancer. *Cochrane Database Syst Rev.* 2002;(2):CD002027. DOI: 10.1002/14651858.CD002027
191. Kanatas AN, Mehanna HM, Lowe D, Rogers SN. A second national survey of health-related quality of life questionnaires in head and neck oncology. *Ann R Coll Surg Engl.* 2009 Jul;91(5):420-5. DOI: 10.1308/003588409X428306
192. Funk GF, Karnell LH, Smith RB, Christensen AJ. Clinical significance of health status assessment measures in head and neck cancer: what do quality-of-life scores mean? *Arch Otolaryngol Head Neck Surg.* 2004 Jul;130(7):825-9. DOI: 10.1001/archotol.130.7.825
193. Orlikoff R, Kraus D, Budnick A, Pfister D. Vocal function following successful chemoradiation treatment for advanced laryngeal cancer: preliminary results. *Phonoscope.* 1999;2:67-77.
194. Thomas L, Jones TM, Tandon S, Katre C, Lowe D, Rogers SN. An evaluation of the University of Washington Quality of Life swallowing domain following oropharyngeal cancer. *Eur Arch Otorhinolaryngol.* 2008 Jul;265(Suppl 1):S29-37. DOI: 10.1007/s00405-007-0470-2
195. Thomas L, Jones TM, Tandon S, Carding P, Lowe D, Rogers S. Speech and voice outcomes in oropharyngeal cancer and evaluation of the University of Washington Quality of Life speech domain. *Clin Otolaryngol.* 2009 Feb;34(1):34-42. DOI: 10.1111/j.1749-4486.2008.01830.x

Corresponding author:

Priv. Doz. Dr. med. Uta Tschiesner, M.D.
Clinic for Otorhinolaryngology, Ludwig Maximilians
University (LMU) Munich, Marchioninstr. 15, 81377
Munich, Germany, Phone: +49 89-7095-0
Uta.Tschiesner@med.uni-muenchen.de

Please cite as

Tschiesner U. Preservation of organ function in head and neck cancer. *GMS Curr Top Otorhinolaryngol Head Neck Surg.* 2012;11:Doc07.
DOI: 10.3205/cto000089, URN: urn:nbn:de:0183-cto0000898

This article is freely available from

<http://www.egms.de/en/journals/cto/2012-11/cto000089.shtml>

Published: 2012-12-20

Copyright

©2012 Tschiesner. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en>). You are free: to Share – to copy, distribute and transmit the work, provided the original author and source are credited.