

# Chapter 6

## Multidisciplinary Decision Making and Head and Neck Tumor Boards

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### Squamous Cell Carcinoma of the Head and Neck: Introduction

#### *A Changing Population*

The incidence of head and neck cancer (HNC) is still increasing, now being the fifth most common tumor worldwide, with an estimated 688,000 new cases in 2012 [1]. The incidence of squamous cell carcinoma of the head and neck (SCCHN) peaks between the fifth and seventh decades of life and the proportion of elderly (65+) patients is expected to rise in the coming years [2]. Surveillance, epidemiology, and end results (SEER) data in the United States indicated that this category of patients comprised 54 % of all malignant HNC (larynx + oral cavity + pharynx) and that the incidence of HNC among these older patients is expected to increase with 37 % by 2020 and even with 63 % in 2030 [3]. The clinical profile of the elderly is somewhat different from that in the younger patients with respect to sex ratio, tobacco and alcohol (ab)use, primary disease site, disease stage, survival, and human papillomavirus (HPV) infection (see Chap. 16 on “Treatment in the Elderly”).

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## *A Changing Disease*

In the general SCCHN population, the prevalence of tobacco and alcohol consumption is over 70% of the patients, and tobacco still is the single most important risk factor for this disease worldwide. However, HPV has now been recognized as one of the primary causes of oropharyngeal squamous cell cancer (OPC), and the incidence of HPV-associated OPC is on the rise. Oncogenic HPV infection is a risk factor for OPC both in smokers and in nonsmokers and in fact is the strongest prognostic factor in this disease [4, 5]. The proportion of SCCHN caused by HPV varies widely but is particularly rising rapidly in the Western world. HPV-positive and HPV-negative tumors appear to be distinct entities based on different clinical and molecular presentations [6]. Clinically, HPV-positive OPC patients generally are younger, generally have a better performance status, more frequently consume less alcohol and tobacco, and more frequently have a history of multiple sex partners. However, it should be understood that HPV-associated OPC may occur also in individuals with few sexual partners and 8–40% of the interviewed patients with HPV-positive tumors indicated they never had oral sex [6, 7]. HPV-positive OPC frequently presents with a smaller primary tumor associated with multiple lymph nodes relative to HPV-negative OPC, is more responsive to chemotherapy and radiation than HPV-negative disease, and overall has a better outcome ([8]; see also Chap. 10 on viral-associated head and neck cancer).

## *Changing Treatments (Innovations)*

Innovations have occurred in all areas. The field of head and neck surgery has gone through numerous changes in the past two decades, whereby microvascular free flap reconstructions largely replaced other techniques. In addition, organ sparing surgical techniques, and in particular more recently transoral robotic surgery, are getting major attention. In the field of radiotherapy, dramatic advances have occurred in optimizing dose fractionation schedules, improving target delineation for staging and radiotherapy simulation/planning using anatomical and functional imaging, improving accuracy of radiotherapy delivery using daily image-guidance, as well as the emergence of new radiation techniques (rotational intensity-modulated radiotherapy, stereotactic radiotherapy, and particle therapy). Innovations in combining radiation and systemic agents have also taken place including with cytotoxic chemotherapy, hypoxic cell modifiers, and targeted agents [9].

## *Standard Treatment Options in SCCHN*

Taking the above into account, the present standard treatment options for early disease (stage I–II) include either a radiotherapeutic approach or a surgical approach, depending on patient and disease factors [10, 11]. With such approaches, the expected 5-year survival figures range from 60 to 90%. Patient factors, such as lifestyle habits, will have a major impact on the outcome.

Treatment approaches for locoregionally advanced disease include surgery (in patients with resectable disease) followed by radiation or chemoradiation, depending on the results reported in the pathology specimen (positive margins, extracapsular extension). In case surgery is not the selected primary option, there are different possibilities to choose from with different levels of evidence, i.e., concurrent chemoradiotherapy (CCRT), hypoxic modification of radiotherapy (standard in Denmark, not yet standard outside Denmark) and altered fractionation radiotherapy (all level IA evidence), and bioradiotherapy (BRT) with cetuximab or induction chemotherapy (ICT) followed by radiation alone, CCRT, or BRT. The latter two options do not reach level IA evidence and in fact ICT followed by CCRT or BRT is still considered investigational [12, 13]. Mainly because of disease factors there is a wide range in the expected outcome with 5-year overall survival ranging from 20 to 80 % (see also Chap. 11 on “Patient and Treatment Factors in Concurrent Chemoradiotherapy”).

For patients with recurrent and/or metastatic SCCHN, the most unfavorable group of patients, there are several treatment options depending on the presentation. In case of locoregionally recurrent disease, without distant metastases, surgery is the first choice and should always be considered, and patients are then treated with a curative intent. According to a meta-analysis of 32 studies with a total of 1,080 patients reported by Goodwin, a survival rate of 39 % can be expected at 5 years after salvage surgery [14]. Unfortunately, that will be possible only in a minority of patients (see also Chap. 12 on “Salvage Surgery of Head and Neck Cancer”). Postoperative radiotherapy might be indicated in some instances [15]. Reirradiation should also be considered in patients with unresectable recurrences and primary tumors arising in a previously irradiated area. However, retreatment is associated with an increased risk of serious toxicity and impaired quality of life (QoL). Therefore, a proper selection of patients based on disease-related factors, current comorbidities, and preexisting organ dysfunction for such treatment is essential. If so done, a meaningful survival in the range of 10–30 % at 2 years can be expected [15]. Patients with locoregional recurrence only who are not candidates for salvage surgery or reirradiation might be candidates for systemic therapy. The latter is also the case for patients with distant metastases with/without a local and/or regional recurrence. When in a good condition (Eastern Cooperative Oncology Group [ECOG] performance status [PS] 0/1), patients are candidate for platinum/5-FU plus cetuximab (the EXTREME regimen), the new standard chemotherapy regimen since 2008; patients with PS 2 are candidates for treatment with less aggressive regimens, which is commonly a single-agent therapy; for patients with PS 3 best supportive care only is advisable. At all times, patients should be offered the option of participating in a clinical trial, as results with so-called standard therapy in the recurrent/metastatic disease setting are still disappointing [12].

## Multidisciplinary Team Meetings

Cancer care is undergoing an important paradigm shift from a disease-focused management to a patient-centered approach, in which increasingly more attention is paid to psychological aspects, quality of life, patients’ rights and empowerment, and survivorship [16]. In this context, multidisciplinary teams have emerged as a practical necessity for optimal coordination among health professionals and clear

communication with patients. A new definition addressing the role of multidisciplinary teams was put forward in 2013 by the healthcare working group of the European Partnership for Action Against Cancer (EPAAC): “*Multidisciplinary teams (MDTs) are an alliance of all medical and health care professionals related to a specific tumour disease whose approach to cancer care is guided by their willingness to agree on evidence-based clinical decisions and to co-ordinate the delivery of care at all stages of the process, encouraging patients in turn to take an active role in their care*” [16]. The importance of MDTs in cancer care is becoming widely recognized as shown by international adoption of mandatory guidelines or legislation. This is illustrated by the fact that in Belgium, France, and the Netherlands, the use of MDTs is mandatory with make-up of multidisciplinary teams clearly defined. The United Kingdom, Canada, and Australia all have national or state-defined guidelines for the use of MDTs in cancer care [17]. In Italy and Germany, it is mandatory for cancer patients to be treated in expert centers.

### ***Goals and Benefits of MDTs***

The primary goal of an MDT is to improve the care management for individual patients. The early implementation of the discussion process in the pathway of an individual patient can prevent unnecessary diagnostic investigations and save valuable time. Ruhstaller et al. suggested that one multidisciplinary discussion with all the involved specialties is more effective and the joint decision more accurate than the sum of all individual opinions [18]. They also stressed that in such meetings, patients will be treated according to the same guidelines and to the same standard regardless to whom the patient was initially referred to. In principle, when treated in Europe the decision-making process should preferably be consistent with evidence-based European clinical practice guidelines, if available. Moreover, during MDT meeting discussions, guidelines should be tailored to the type of tumor and the specific condition of the patient, including comorbidities and frailty. Treatment decision, which impact patients’ QoL to varying degrees, should not be made without information on patients’ preferences for treatment and/or care [16]. Next to these positive elements in decision-making, there are some additional benefits of MDTs; for instance multidisciplinary discussed patients are more likely to be included in clinical trials; MDTs lead to a better understanding of the roles, possibilities, and limitations of each discipline and lead to a better communication between different specialties. MDTs are also an ideal learning opportunity for junior doctors or other health care professionals [18].

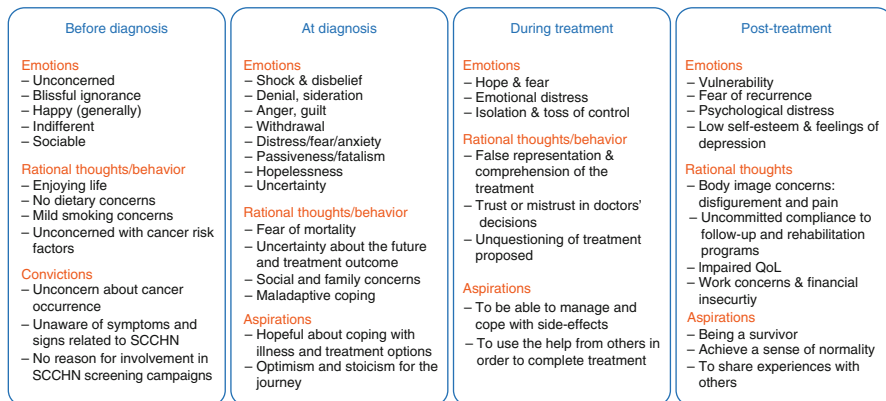
### ***MDT Management in Head and Neck Cancer Patients***

Because HNCs are a complex, heterogeneous group of malignancies, which require multifaceted treatment strategies and the input of a number of specialties, they are an ideal example to benefit from MDTs. Moreover, as mentioned earlier, the HNC

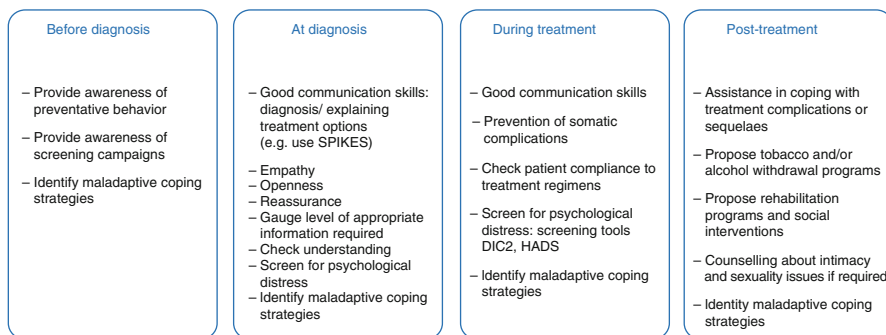
population is changing, there are new entities in HNC coming up with different biology, presentation, and outcome, and there is a tremendous evolution in treatment possibilities, both in surgical and nonsurgical approaches. Molecular biology has proven to be vital in our understanding of the disease; at the same time we start to understand now that the molecular characteristics of no two tumors are identical. Nevertheless, a more personalized approach is coming closer and closer. Smarter drugs are needed to make optimal use of the specific genetic make-up of a patient's tumor [19]. In addition to this development, a spectacular revival in immunology and evolution of immunological therapies in oncology in general but in particular also in HNC is ongoing [20]. During the MDTs, all these aspects have to be taken into account in order to make an optimal choice of treatment for an individual patient. Basically, it means that we should take into account: (1) disease factors, i.e., site, stage, biology (HPV, epidermal growth factor receptor [EGFR]), specific risk factors for locoregional or distant relapse; (2) patients factors, such as age sex, performance status, nutritional status, comorbid chronic disease, oral health, lifestyle habits, socioeconomic status, etc.; (3) treatment factors (surgery, radiotherapy, chemotherapy, targeted therapy, immunotherapy with all the possible side effects they may induce); and (4) adequate communication with and information to the patient, giving sufficient support, taking into account the wish of the patient. It has become increasingly apparent that patients need emotional support to navigate their cancer journey and successfully integrate back into society and daily life. Emotional support is vital as many people who have been through SCCHN, in particular younger patients, may have impaired physical and psychological well-being.

MDT for head and neck cancer patients should include a surgical oncologist (head and neck surgeon), a radiation oncologist and a medical oncologist, a pathologist, a radiologist, a plastic (reconstruction) surgeon, an otolaryngologist, an oncologic dentist or oral oncologist, a speech therapist, an audiologist, a dedicated oncology nurse, and preferably a datamanager involved in all ongoing trials in HNC and a case manager. In addition, MDTs may be enriched by a variety of other care professionals, such a physical therapist, a social worker, a dietician, and a psychologist and/or psychiatrist and for elderly patients a geriatrician.

The attendance in such meetings of primary care physicians (general practitioners) should be promoted, as they know their patients best and are able to provide advice on comorbidities and a holistic health assessment of their patients' care needs [16]. The case manager, which could be an expert nurse or a qualified staff member, should provide case management throughout the care process, acting as a point of contact for both patient/families and the team. Some of the most important tasks assigned to this case manager is giving expert clinical advice to patients, exchanging key patient information and care recommendations with the physicians, attending MDT meetings, and ensuring that diagnostic and treatment times are consistent with the targets set in this regard [16]. Case managers can also play an important role in the emotional support that the patients need throughout their journey, i.e., from diagnosis, during treatment, and posttreatment. Reich et al. defined emotional support in this context as a sensitive, empathic, and understanding approach to patients to help them to cope with their disease and to allow patients to express and communicate their concerns and feelings [21]. Figures 6.1 and 6.2, derived from that article, are summarizing the expected emotions and reactions from the SCCHN



**Fig. 6.1** Expected emotions and reactions for the SCCHN patient



**Fig. 6.2** Recommended actions for the healthcare professional. *DIC2* Distress Inventory for Cancer version 2, *HADS* Hospital Anxiety and Depression Scale, *SCCHN* squamous cell carcinoma of the head and neck, *QoL* quality of life (From Reich et al. [21], reproduced with permission)

patients and the recommended actions that need to be taken by the health care professional.

### ***Do MDT Meetings Impact on Diagnosis, Treatment Decision, and Outcome?***

It seems self-evident that the variety of specialist team members with their combined knowledge and expertise will improve decision-making and therefore ultimately patient management and outcome. Although that is very likely so, evidence for that has not been easy to demonstrate because, as outlined above, over time cancer care is changing, there is improvement in staging and diagnosis, and more

effective treatments become available. These aspects are, of course, confounding factors in retrospective studies where one looked at whether the introduction of MDT meetings had any impact on outcome (so-called “before and after” studies). Prades et al. undertook a literature search in the Medline database for peer-reviewed articles (partly retrospective, partly prospective) published between November 2005 and June 2012 that examined multidisciplinary clinical practice and organization in cancer care [22]. MDTs resulted in better clinical and process outcomes for cancer patients with evidence of improved survival among colorectal, head and neck, breast, esophageal, and lung cancer patients in this study period. However, unfortunately the two studies in that survey that concerned HNC were both retrospective [23, 24].

Friedland et al. [23] analyzed the outcomes of 726 cases of primary HNC patients managed between 1996 and 2008, including 395 patients managed in a multidisciplinary clinic or team setting and 331 managed outside of an MDT by individual disciplines. Data were collected from the Hospital Based Cancer Registry (HBCR) and a database within the Head and Neck Cancer Clinic of the Sir Charles Gairdner Hospital, Perth, Australia. The MDT patients were younger by about 2 years of age on average ( $p=0.046$ ), which is a potential source of bias. On the other hand, patients seen in the multidisciplinary clinic were more likely to have advanced disease ( $p<0.001$ ). The authors reported a better outcome for the patients in the MDT group (for all patients with stage I–IV a hazard ratio [HR] of 0.79,  $p=0.024$ ), but this was mainly due to a different outcome in the stage IV patients (HR=0.69,  $p=0.004$ ). There was no difference observed in stage I–III, although the numbers in each of these stages were too small to provide statistical power. Over time there was an increasing incidence in the use of CCRT (2.1 % in 1996 and 42.5 % in 2008; test for trend  $p<0.001$ ) and at the same time a decline in the use of radiotherapy alone (27.1 % in 1996 and 15 % in 2008; test for trend  $p<0.001$ ). Patients in the multidisciplinary clinic were significantly less likely to receive radiotherapy alone for positive nodes or surgery alone for their cancer and positive nodes. The MDT group used significantly more CCRT ( $p=0.004$ ) and the non-MDT group significantly more radiotherapy alone ( $p=0.002$ ).

Wang et al. [24] reported on a study performed in Taiwan, where the incidence of oral cavity cancer is very high (about 60 % of all HNC). They used for their study the National Health Database (2004–2008) and applied matching based on propensity of receiving MDT care. After the propensity score matching, 3099 MDT care participants and 6198 non-MDT care participants were included in the study. The relative risk of death was lower with MDT care than for those without MDT care (HR=0.84; 95 % CI 0.78–0.90,  $p<0.001$ ). The effect of MDT care was stronger for older patients.

In two prospective studies, treatment plan changed in about one third of cases after MDT. The first study was performed at the Department of Otolaryngology-Head and Neck Surgery of the University of North Carolina Hospital in North Carolina, in the USA, and concerned 120 new patients (84 with malignant, 36 with benign tumors) whose clinical findings were presented for review at the MDT meeting between December 2009 and February 2010 [25]. Approximately 27 %

(32/120) had some change in either tumor diagnosis or treatment plan due to the input from the multidisciplinary tumor board. Three (9%) of these 32 patients had changes in both diagnosis and treatment, 19/32 (59%) had a change in their treatment plan without a change in diagnosis, and 10/32 (31%) had a change in diagnosis without a change in treatment. Approximately 7% of patients required further diagnostic workup before definitive treatment planning. The second study was executed at the Sydney Head and Neck Cancer Institute at the Royal Prince Alfred Hospital, a tertiary care hospital in Central Sydney, Australia [26]. One hundred seventy-two patients with head and neck tumors (160 malignant, 12 benign) were discussed in 39 meetings over the period from December 2011 until October 2012. The proposed management plans were documented before the MDT meeting, and the MDT meeting recommendations and potential changes to the initial plan were recorded after the meeting. The changes were categorized as major or minor: changes were considered major when they concerned a change in treatment modality, while changes were considered minor when they comprised alterations in the extent of a chosen modality, the addition of diagnostic tools or research decisions. Compliance with MDT recommendation was evaluated after completion of treatment. Of the 172 patients, 52 (30%) had management changes, 35 (67%) of which were considered major and 12 (33%) considered minor. Interestingly, a significant association was found between the frequency of changes in treatment plan and the referring consultant's specialty (more likely in case referrals by medical oncologists or radiation oncologists than by surgical oncologists), the initial treatment plan (when the treatment plan did not include surgery) and the histological tumor source (least likely in case of mucosal tumors). The recommendations of the MDT meeting were followed in 132 (84%) of the 158 patients on which data were available. Of the 26 cases where the treatment plan was not followed, a more aggressive plan was chosen by the treating physician in 50%, in 40% it was less aggressive, and in 10% the modality changed (surgery replacing RT or vice versa). Reasons for this non-compliance were variable: unexpected findings in the surgical specimen, patient preference, and/or change in functional status between the MDT meeting and the actual start of the treatment. Given the complex and mutilating nature of SCCHN treatments and the advanced age and frequent comorbidities in HNC patients, the authors considered the compliance to the recommendations in this study high (84% overall, 70% for patients with changes). On the other hand, still worrisome is the fact that in 15% of cases the treatment agreed upon was not carried out.

A disadvantage of MDT meetings that sometimes has been mentioned by some authors is that this might potentially lead to delay in starting treatment [26]. However, this will be particularly the case when the interval between MDT meetings are long. In most institutions, MDT meetings take place at weekly intervals. However, the point is well taken. It is very well known that treatment delay is associated with a less favorable outcome [27, 28]. A recently performed systematic review with meta-analysis of ten studies showed that the estimated relative risk (RR) of mortality related to any diagnostic delay (either patient or professional delay) was 1.34 (95% CI, 1.12–1.61) [29]. Therefore, studies that investigate how to reduce time intervals are of interest. One such initiative was taken by the Danish



group and showed that a fast-track program through logistic changes, employment of a full-time case manager, strengthening the multidisciplinary tumor board, and giving higher priority to HNC patients (by introducing a hotline for referrals, having prebooked slots in the outpatient clinic, having faster pathology reports and imaging procedures), the overall time from first suspicion of cancer until treatment start could be reduced from 57 calendar days to 29 calendar days [30].

## Conclusions

Head and neck cancer management is a typical example of a complex treatment involving multiple disciplines. There is not much doubt that multidisciplinary care is needed for an adequate coordination of the multidisciplinary care pathway with respect to logistics, reducing any treatment delays, and communication with the patient. MDT meetings have a positive effect on decision making and management, as in about one third of cases the initial proposed management will be changed in these meetings. A case manager seems to play a crucial role in this whole process, and although prospective trials on the impact of MDTs on outcome are lacking, because having a valid control group is almost impossible, the expectation is that it does have an impact on outcome. Therefore, not only centralization of care for HNC patients is a major issue, but within this MDT meetings nowadays are considered standard of care.

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