## **HEAD AND NECK CANCER Review Article**

# A relationship between quality-of-life and head and neck cancer: A systemic review

Sujal Mitul Parkar, Mihir N. Shah<sup>1</sup>

#### **Abstract**

Aim: The aim was to identify the literature and to assess the association between quality-of-life (QoL) and head and neck cancer (HNC) related outcomes systemically. Materials and Methods: The full articles published in English language bio-medical journals between 1992 and December 2014 were searched using Medline database. The keywords used for searching the articles include the combination of "health-related of QoL," "QoL," "HNC." The search limited only to the observational studies using questionnaires European Organization for Research and Treatment of Cancer (EORTC) QLQ C 30 and EORTC QLQ H and N 35. Purely psychological studies were excluded. Results: A total of 5055 articles were retrieved, and 16 articles were selected for this review. Of 16 observational studies, 13 (81.25%) were prospective cohort studies while remaining 3 (18.75%) were cross-sectional studies. The main findings of the studies revealed that the treatment of HNC had a statistically significant influence on QoL. Others associated factors like age, female sex, duration of treatment, advance tumor, and site of the tumor has also the impact on QoL on patients suffering from HNC. Conclusion: This review provides evidence for a positive relationship between cancer-related outcomes and QoL. Assessment of QoL in relation to HNC with proper methodology and validated instruments is lacking hence there is a need for further evidence to support the relation between cancer and QoL.

Key words: Head and neck cancer, neoplasm, observational studies, quality-of-life, review

#### Introduction

Head and neck cancer (HNC) is the one of the major threats to public health in the developed world and increasingly in the developing world. The global incidence of the oral cavity and pharynx cancer is approximately 400,000 cases/year, with 160,000 cancers of the laryngeal cancer, resulting in approximately 300,000 deaths.<sup>[1]</sup> The increase incidence of HNC cases is a cause of major concern as it is associated with high morbidity and mortality.

Quality-of-life (QoL) generally refers to the perception of the effects of disease and the impact on the patient's daily functioning. QoL is determined not only by the disease and its treatment, but also by other medical and sociodemographic characteristics. [2,3] It is important to develop an understanding of variables that may influence QoL for patients with advanced cancer, so that these can be accounted for in clinical trials; it is also important to identify vulnerable groups, so that their HR QoL can be specifically addressed and optimized. Both HNC and its treatment have significant and often devastating effects on the function, appearance, psychological status, socialization, and individual QoL of patients. Hence, to assess the QoL outcome in patients with HNC has been become popular in the recent past in the field of clinical oncology and psycho-social research.

The number of scientific papers published under the key words "QoL" and "HNC" had increased dramatically. A recent Medline search found that the number of scientific papers published between years 1995 and 2000 were 287 which had increased to 699 from 2001 to 2005 which further increase to 2237 by the end of 2014. Hence, the aim of this paper was to identify the literature on QoL and HNC, review systematically and assess the association between cancer-related outcomes.



Department of Public Health Dentistry,
Siddhpur Dental College and Hospital, Patan,
'Department of Periodontology, Ahmedabad Dental
College and Hospital, Ahmedabad, Gujarat, India
Correspondence to: Dr. Sujal Mitul Parkar,
E-mail: drsujal\_pcd@live.com

#### **Materials and Methods**

## Search engines and time period

A literature search was carried out using Medline database to assess the QoL in head and neck patients. The keywords and medical subject headings included the combination of "health-related of QoL," "QoL," "HNC." These words can appear in all fields of publication (e.g., Title, abstract and text of the articles). The present review was restricted to full articles published in English language bio-medical journals between 1992 and December 2014. The year 1992 was chosen because the first study to assess the QoL of patients treated surgically for HNC was published in that year. [4] Table 1 shows the search strings for Medline.

#### Inclusion and exclusion criteria

The purpose of this review was to identify the relationship between QoL and HNC hence, the original observational studies were included. Observational studies include cross-sectional studies, case-control studies, and cohort studies. Studies reporting on Head and Neck squamous cell carcinoma (HNSCC) patients were included. Studies reporting malignancies other than squamous cell carcinoma, recurrent cancer, and metastasis of HNC were excluded. Only those studies analyzed QoL using questionnaires European Organization for Research and Treatment of Cancer (EORTC) QLQ C 30 and EORTC QLQ H and N 35 were included. Studies related to validation of the questionnaire were also excluded. Purely psychological studies were excluded.

## **Data collection and extraction**

At first, the two reviewers (PS and SM) independently search for the title with "QoL in HNC patients" through the electronic search. Second, they checked the contents of these articles based on the criteria described above. The eligibility of selected articles was compared and discussed between two reviewers, and the final decision was made. The internal validity between two reviewers was determined by k value.

The data were extracted only from the original articles using a preformatted sheet with a set of predefined parameters: First author, year of publication, country of study, study design, number of study subjects, treatment modalities, and the main findings or conclusions.

### **Table 1: Search strings for Medline**

(("Quality-of-life" [MeSH Terms] OR ("quality" [All Fields] AND "life" [All Fields]) OR "quality-of-life" [All Fields]) AND ("head and neck neoplasms" [MeSH Terms] OR ("head" [All Fields] AND "neck" [All Fields] AND "neoplasms" [All Fields]) OR "head and neck neoplasms" [All Fields] OR ("head" [All Fields] AND "neck" [All Fields]) OR "head and neck cancer" [All Fields]) OR "head and neck cancer" [All Fields]) AND eortc [All Fields] AND ((Comparative Study [ptyp]) OR Multicenter Study [ptyp]) AND "loattr [ult text" [sb])

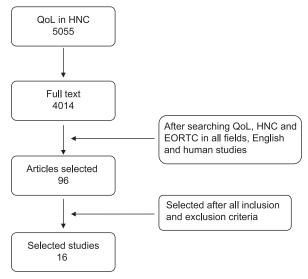


Figure 1: The systemic review process for selection of articles

#### **Results**

The flow chart of the review process is show in Figure 1. The initial search yield 5055 original articles of which access to full text was available for 4014 articles. Based on the title and description of studies, 96 articles were selected. After considering the predetermined criteria, 80 articles were excluded and remaining 16 articles were included at the end for this systemic review. The agreement between two reviewers has k value of 0.88 which indicates strong agreement. 16 studies included were published from 2001 to 2014 and are listed in chronological order in Table 2.

Of 16 observational studies, 13 (81.25%) were prospective cohort studies while remaining 3 (18.75%) were cross-sectional studies. These studies include the total of 2700 head and neck patients having a range from 42 to 357. Majority of studies, 12 (75%) were conducted in European countries while 2 (12.5%) studies were conducted in Middle East and one study in each in Asia and USA. The main findings of the reviewed studies revealed that the treatment of HNC had a statistically significant influence on QoL. Furthermore, the age, female sex, duration of treatment, advance tumor, and site of tumor (hypopharyngeal and larynx) were found to be associated with more symptomatic problems and worse QoL.

#### **Discussion**

In the recent years, the QoL in HNC patients had gain popularity in the field of oncological as well as in psychosocial research pertaining to important parameters like treatment outcomes, survival, mortality, and complication rates. [20,21] QoL can yield information that is relevant for clinical decision-making and help to inform patients about the long-term consequences of cancer. Keeping this in mind, this systematic review was conducted to review the studies showing the association between QoL and HNC-related outcomes.

An electronic literature search was conducted using Medline databases with the intention of retrieving all original studies. There might be the chances of selection bias while reviewing the articles due to: (1) Only the articles published in English language are included hence there is a risk that some relevant papers were missed which were published in other languages and (2) only a proportion of research projects are published in indexed journals and are readily available for systematic reviews. Furthermore, systematic review of published studies can lead to publication bias as studies with significant results are more likely to be published than studies with negative results. Although HNC and its associated factors may have some impact on QoL, it is not easy to evaluate the extent of this impact. It is also be necessary to determine whether this impact is meaningful in the clinical setting. More evidence of this kind is therefore needed for further exploration between the relationship of HNC and QoL.

A variety of instruments were developed and validated to assess the QoL in patients with HNC. They are mainly based on the general measures of health-related QoL, disease-specific instruments for patients with HNC, treatment specific instruments, and symptoms specific instruments to evaluate QoL in patients with HNC. In the current systemic review to increase the homogeneity, only studies using EORTC QLQ C30 and H and N module 35 were included. The reasons of selecting the combination of these instruments are: (1) Commonly used by many investigators throughout the world, (2) had been translated and validated into different languages showing a high rates of cultural acceptance and (3) provides a better measure of QoL as affected by HNC treatment side effects.

In the current review, the studies related to HNC are included without any subsite specification. When the general term "head and neck" is used, it may include cancers that we wanted to exclude in this review. Hence, this could have introduced selection bias to this review. HNC include many different types of cancer. The etiology and histopathology of cancers may vary from each other, making it difficult to go for a direct comparison hence to make more uniform only the patients diagnosed as squamous cell carcinoma histopathologically were reviewed. Very few studies were conducted selecting a specific group of HNC patients, paying attention to tumor stage and different treatment modalities and other factors that affect the generalizability of results. Furthermore, the studies included in this review were conducted in different countries. The prevalence of HNC can vary within cultures, and etiological and geographical changes can also play a role. Therefore, the results of this type of review may not be generalizable to other population.

This review excludes purely psychological studies. Psychological problems may, in addition to adversely affecting QoL, interfere with the treatment and rehabilitation of patients

Table 2: Studies on relationship between quality-of-life and HNC

Author	Year	Country	Study design	Study subjects	Treatment	Findings
Hammerlid et al.[5]	2001	Sweden	Prospective cohort study	357	S	Female sex, tumor site (hypopharynx) and advance tumor stage had the most powerful impact on QoL
Tschudi et al. [6]	2003	Switzerland	Prospective cohort study	217	S, RT	QoL after curative treatment was improved. QoL manifest in HN35 module not in QLQ C30
Derks et al.[7]	2003	Netherland	Prospective cohort study	129	S	No age wise significant differences in QoL after surgical treatment
Derks et al.[8]	2004	Netherland	Prospective cohort study	183	S	Treatment did not affect QoL differently with respect to age
Hanna et al.[9]	2004	USA	Cross-sectional	42	S, CT, RT	Treatment affects the QoL for advanced cancer however there no difference between the treatment groups
Abendstein et al.[10]	2005	Norway	Prospective cohort study	357	S, RT	Significant improvements in HRQL were not found as the duration progress
Cengiz et al.[11]	2005	Turkey	Prospective cohort study	187	RT, CT	QoL adversely affected by combined therapies. Tumor stage, female and long-term follow-up
Olthoff et al.[12]	2006	Germany	Prospective cohort study	146	S, RT	RT has more impact on QoL than surgical treatment. Global QL was not affected by any treatment
Nordgren et al.[13]	2006	Sweden	Prospective cohort study	89		Problems with dry mouth and teeth became worse between diagnosis and the 5-year follow-up. Problems with thick secretions and teeth increased between 1 and 5 years
Fang et al.[14]	2008	Taiwan	Longitudinal	203	RT	Patients treated by IMRT had a both statistically and clinically significant in QoL 3 months after RT
Nordgren et al.[15]	2008	Sweden	Prospective cohort study	122		Treatment of cancer result in long time side effects such as dry mouth, problems with teeth, and sticky saliva
Guibert et al.[16]	2011	France	Cross-sectional	70	S, CT, RT	QoL is impaired in all patients. The type of treatment, surgical or conservative, affects differently various aspect of QoL
Silveira et al.[17]	2011	Portugal	Cross-sectional	289	S, RT	Age (geriatrics), gender (female), tumor site (larynx) had worse QoL score
Akkas et al.[18]	2013	Turkey	Longitudinal	82	RT	QoL was affected negatively during and after the RT
Singer et al.[19]	2014	Germany	Prospective cohort study	174	S	QoL decreases initially after laryngectomy; some QoL areas recover slowly over the course of year after surgery and some remain significantly worse than at baseline

HNC=Head and neck cancer, S=Surgery, RT=Radiotherapy, CT=Chemotherapy, QoL=Quality-of-life, IMRT=Intensity modulated radiation therapy, HRQL=Health-related quality-of-life

with HNC. Study conducted by Mehanna *et al*.<sup>[22]</sup> and two systemic reviews<sup>[23,24]</sup> strongly suggest the strong influence of psychological copying on QoL among the patients suffering from HNC thus if one wishes to have a better understanding on the topic it is necessary to review these papers as well.

## **Conclusion**

The studies reported in this review provide evidence for a positive relationship between patients suffering from HNC and QoL. It is recommended that future studies should be reviewed especially to methodology related to randomized control trial as this is the best-known methodology to evaluate treatments outcomes related to QoL among cancer patients which was the shortcoming of this review as only observational studies has included. Though there is advancement in the treatment of HNC in recent past, the QoL had significantly affected, so a protocol has to be set up to assess the QoL at the time of diagnosis, during and after treatment. Hence, there is a need to conduct good epidemiological studies aiming to assess QoL among HNC patients using well-validated and accepted health-related QoL questionnaire.

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