



Review

The association between health related quality of life and survival in patients with head and neck cancer: A systematic review



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SUMMARY

The aim of this study was to systematically review available evidence on the association between health-related quality of life (HRQoL) and survival in patients with head and neck cancer (HNC), adjusted for important clinical, demographic and lifestyle-related factors.

A systematic literature search in four electronic bibliographic databases was conducted in January 2014. We included studies that provided data on HRQoL, survival, and the association between HRQoL and survival among HNC patients. Two researchers independently rated the quality of the included studies. A best evidence synthesis was applied to draw conclusions.

Nineteen studies were included, of which twelve focused on all subscales of a HRQoL questionnaire and seven focused on selected subscales. The mean (SD) quality score was 72 (17)% and 11 (58)% studies were of high quality. According to the best evidence synthesis, we found strong evidence for a positive association between pre-treatment physical functioning and survival and between change in global QoL from pre-treatment to 6 months after treatment and survival. Due to inconsistent findings, we found insufficient evidence for an association with survival of other HRQoL domains, including role, emotional, cognitive and social functioning, mental health and well-being. Future high quality studies with a longitudinal design are needed to examine the complex association between HRQoL and survival.

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Introduction

Patient reported-outcomes are increasingly used in clinical trials among cancer patients in addition to traditional outcome measures such as tumor control, overall survival, morbidity and complications [1–5]. This has led to an increased understanding about the course of health-related quality of life (HRQoL) in patients with cancer. It is well known that patients have to deal with various physical and psychosocial problems related to cancer and its treatment, including reduced physical fitness and function, reduced self-esteem, increased emotional distress and fatigue, negatively affecting HRQoL [6–11]. Furthermore, there is evidence of a positive association between HRQoL and survival in patients with cancer. Previous reviews and meta-analyses in populations with different types of cancer showed that lower pre-treatment HRQoL was associated with reduced survival [12–15]. Recently, in a

pooled analysis, Quinten et al. [15] separately examined the association between pre-treatment HRQoL and survival for 11 different cancers. They concluded that for each cancer, the accuracy of survival prognosis increased by adding at least one HRQoL domain to clinical and demographic predictors such as age, performance status and metastasis [15].

Little is known about the association between HRQoL and survival in patients with head and neck cancer (HNC). Previous studies showed that HNC and its intensive treatment have a distinct impact on HRQoL. In addition to physical and psychosocial problems that patients with all cancers are facing, patients with HNC are often confronted with oral dysfunction, swallowing and speech problems [16–23]. Previous studies showed a decline in general and mental health, physical function, appearance, employment, and social functioning during and immediately after treatment for HNC [16,17,19,20,22–32]. Also, many HNC survivors continue to suffer from various disease and treatment related physical and psychosocial problems for many years after treatment [16,17,23,24]. Two prospective cohort studies reported that HRQoL ten years after diagnosis, was significantly lower than HRQoL before treatment [26,33].

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In 2008, Mehanna et al. [34] published a systematic review summarizing the available studies examining the association between a broad range of psychosocial factors and survival in patients with HNC. They reported that fewer psychosocial complaints, higher physical self-efficacy and higher physical functioning were associated with increased survival. In addition, they found that global QoL one year after diagnosis was significantly positively associated with survival, but this was not the case for global QoL at diagnosis [34]. Also the review of Montazeri et al. [13] reported significant positive associations between HRQoL and survival for most cancers, but results among HNC patients were inconsistent and based on a limited number of studies. More studies evaluating the association between HRQoL and survival in patients with HNC have been published since the two previous reviews, which warrants a new systematic review of the present evidence. Furthermore these previous reviews have not applied a best evidence synthesis to summarize the data, which hampers interpretability. Therefore, the objective of this study was to systematically review the available literature on the association between HRQoL and survival in patients with HNC, adjusted for important clinical, demographic and lifestyle-related factors, using a methodological quality assessment and best evidence synthesis.

Materials and methods

Selection of studies

A literature search was conducted in four electronic bibliographic databases (PubMed, EMBASE, PsychINFO and CINAHL) in collaboration with a librarian (earliest to January 2014). In order to identify all relevant papers, we used keywords, MeSH terms and free terms for the following search terms: “Head and neck neoplasm”, “Quality of life” or “patient reported outcome” and “survival” or “prognostic”. The complete search strategy of the literature search is available upon request. The reference lists of all selected papers were screened for additional relevant papers.

Study inclusion criteria

Studies were included if they (1) included patients with HNC, (2) had a prospective study design, (3) assessed HRQoL with a standardized questionnaire, (4) measured mortality and/or survival, (5) analyzed the association between HRQoL and mortality or survival, and (6) were full text articles written in English, German or Dutch. Studies focusing on patients with cancer of the thyroid, esophagus, skin or skull base were excluded. We also excluded studies that were part of a supportive care intervention aiming to improve the HRQoL of patients.

Selection procedure and quality assessment

Titles and abstracts of the references were reviewed to exclude articles out of scope (first author). Full texts of potentially relevant articles were assessed for eligibility by two independent reviewers (first and second author). Two authors (first and second author) independently assessed the methodological quality of the included studies. Disagreements were discussed and resolved. The methodological quality of the included studies was scored using a methodological criteria list based on the criteria list suggested by Hayden et al. [35], who developed their list after an extensive review and critical appraisal of systematic reviews of prognostic studies supplemented by recent methodological studies. The list comprises 6 potential biases for prognostic studies i.e. study participation, study attrition, prognostic factors, outcome measurement, confounding measurements and account and analysis. Because most

of the included studies focused on HRQoL assessed at only one time point, we excluded the item study attrition. Table 1 presents the methodological quality scoring list used in the present study. We defined clinical variables (tumor location and stage), demographic variables (age, gender), and comorbidity and lifestyle factors (smoking and alcohol intake) as important confounders that should be accounted for in the analysis, since they are important predictors for survival. The list contained 11 criteria which could be scored positively (1) or negatively (0). A positive score was given when sufficient and adequate information on the criterion was available, and a negative score when the paper provided no or insufficient information about the criterion. For the last item in the methodological quality assessment (i.e., presentation of point estimates and measures of variability) 0.5 points were given when the article presented all data from the univariate analyses but not from the multivariate analyses. If the study referred to another article containing relevant information of the study, we retrieved this article to score the criterion of concern. The total score was calculated by the sum of all criteria that were scored positively, with a maximum score of 11 points. In addition, for each study we calculated the percentage of items scored positively on the methodological quality list. A study was considered of ‘high quality’ if the quality score was $\geq 75\%$ [36].

Data extraction

The following data were extracted (first author): first author, year of publication, number of patients included, cancer location and stage, assessment of HRQoL, subscales included in the analysis, assessment and period of survival, univariate and multivariate association between HRQoL and overall survival (including hazard ratios with 95% confidence intervals (CI) and *p*-values), and covariates.

Level of scientific evidence

To synthesize the methodological quality of the studies and to be able to draw conclusions on the association between HRQoL and survival, we applied a best-evidence synthesis [36,37]. This rating system consists of three levels and takes into account the number, methodological quality and consistency of outcomes of the studies as follows: (A) strong evidence, provided by generally consistent findings in multiple (≥ 2) high quality studies, (B) moderate evidence, provided by generally consistent findings in one high quality study and ≥ 1 low quality studies, (C) insufficient evidence, when only one study was available or when findings were inconsistent in multiple (≥ 2) studies. We considered results to be consistent when $\geq 75\%$ of the studies showed results in the same direction, which was defined according to significance ($p < 0.05$). If two or more studies were of high methodological quality, we disregarded the studies of low methodological quality in the best evidence synthesis. In addition, in our best evidence synthesis, the results of the multivariate analyses were included and it was separately applied for each time point of HRQoL measurement (e.g. pre-treatment, post-treatment), and for each HRQoL domain (e.g. global QoL, functioning, well-being).

Results

Identification and selection of the literature

After removing duplicates, the literature search yielded 2481 unique articles. For 82 potentially relevant articles, we checked full text (Fig. 1). The majority of the studies ($n = 29$) were excluded because they lacked information on survival or they did not assess

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