Data analytics for predicting quality of life changes in head and neck cancer survivors: a scoping review

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Abstract—Head and neck cancer is the seventh most common cancer worldwide. The incidence of this cancer is increasing, but at the same time, the cancer-related mortality rate has decreased over time, leaving more head and neck cancer survivors. More emphasis is needed on quality-of-life research in the head and neck cancer field to improve their daily lives and reduce the disease and treatment response burden. To achieve this, we conducted a scoping review to find and learn which predictors and data analysis techniques have been used in previous studies. This work is undertaken in the context of the BD4QoL EU Research project.

I. INTRODUCTION

Head and Neck cancer (HNC) is the seventh most common cancer worldwide [1], affecting 833,000 new patients in 2020 [2]. In the last five years, the cancer survival rate has increased due to several causes, including increased knowledge about the causes of cancer, the availability of new treatments and the decrease in smoking [3]. More emphasis on health-related quality of life (HRQoL) is needed to deal with the physical and psychosocial side effect of the disease on HNC survivors. This will optimise patients' health and well-being and improve cancer survivorship care [4].

Previous QoL literature reviews in HNC survivors have been focused on evaluating the QoL status in these patients instead of the questionnaires, techniques, and predictors used in the individual studies [5]. This scoping review aims to understand the most suitable features and data analysis techniques for designing and implementing a data analysis model to study the Quality of Life (QoL) change in HNC survivors. Within this aim, five specific objectives have been identified: 1) to detect the most used QoL questionnaires; 2) to review the applied data analysis techniques approaches in the field; 3) to identify the sociodemographic and clinical characteristics that are used as model input parameters; 4) to study the evolution of patients' QoL over time; 5) to identify the parameters that are predictors or are associated with a worse HRQoL in patients with HNC.

This work is developed in the BD4QoL, a research project funded by the European Commission that aims to improve HNC survivors' QoL through person-centered monitoring and follow-up plan using artificial intelligence and big data. The study does not employed experimental procedures involving human subjects or animals.

II. MATERIALS AND METHODS

The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) is a 22-item checklist commonly used to report a model study [6]. The items are grouped into six different sections: *Title and abstract, Introduction, Methods, Results, Discussion, and Other information*. In this work, we elaborate the items of the prediction model that belong to the *Introduction*, including the identification of the clinical context (3a) and the *objectives* (3b); and to the *Methods* sections, the predictors that may be used as input variables (7a).

A scoping review was performed to identify these items, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations and guidelines [7]. PubMed and Scopus search engines were consulted (last search conducted on 01-09-2020), filtering by title and abstract these search terms: "quality of life" AND "head and neck cancer survivors". No filter was applied on the date of publication of the articles to collect as much information as possible.

As inclusion criteria, studies performing QoL analysis, through QoL questionnaire, from HNC patients who have completed their primary treatment were included. Exclusion criteria considered: articles that did not assess QoL through questionnaires or did not perform any data analysis, opinion articles or clinical guidelines/recommendations. Only articles addressing head and neck cancer were included.

Once the records were identified and the duplicates were excluded, we conducted a three-level analysis. In the *screening*, the articles were assessed only by title and abstract, including those that satisfied the inclusion criteria. A full-text assessment of the records included after the screening analysis was carried out following the same criteria in the *eligibility and data extraction*. The following data were extracted for a *qualitative synthesis*: QoL questionnaires used, the data analysis techniques conducted, the sociodemographic and clinical characteristics used as input parameters, and studies outcomes related to symptoms, side effects, predictors, and factors associated with worse QoL.

III. RESULTS

A total of 191 articles were retrieved through PubMed and Scopus. After removing duplicates (n=82), 109 records resulted. In the screening analysis, 31 articles were excluded, 78 full-text articles were included to be assessed for eligibility, and 67 articles were included for data extraction and qualitative synthesis. The publication dates of these articles are between 1995 and 2020. The workflow followed during the studies selected is shown in Fig. 1.

Figure 1. PRISMA flow chart

Figure 2. Statistical analysis and machine learning techniques.


PRISMA 2009 Flow Diagram
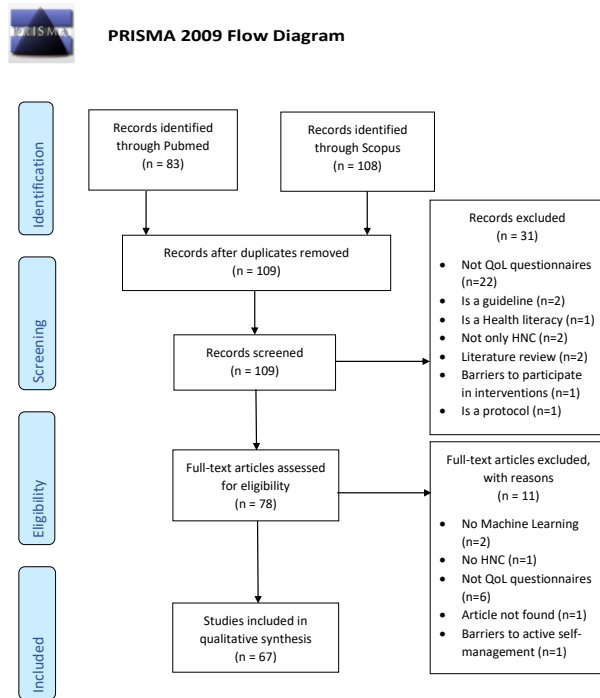
A. Quality of life assessments

In the studies analysed, several questionnaires were used. The most used questionnaires (58,21%) were the cancer-specific QoL instruments, where 22 articles used the Functional Assessment of Cancer Treatment (FACT) questionnaire and 17 used the European Organisation for Research and Treatment for Cancer Quality-of-Life Questionnaires (EORTC QLQ-C30). The next most used (40.3%) questionnaires were site-specific QoL instruments, of which 14 used the Treatment for Head and Neck Cancer Quality-of-Life (EORTC QLQ-H&N35) questionnaire, and 13 used the University of Washington Quality-of-Life (UW-QOL) questionnaire. Other articles also used other questionnaires, such as The Short Form Health Survey or the European Quality of Life Questionnaire. Nevertheless, those appear in few studies where a specific questionnaire is needed or accompanying the previous ones.

B. Data Analysis Techniques

In Fig. 2, the different techniques used in the studies are shown, categorised by the main task conducted. A vast amount of the studies (49%) conducted parametric tests to assess differences between patient subgroups, for instance, comparing the scores change. These 33 studies used mainly t-test, chi-squared test, Pearson's correlation, and others such as ANOVA test, Wilcoxon test, Mann-Whitney or Kruskal-Wallis test. Almost the same number of studies (48%) applied regression models to find predictors of QoL changes. The most common methods used are linear or logistic univariate and multivariate regression, but also hierarchical regression analysis or stepwise regression analysis have been conducted. As concerns the 3% remaining, one paper applied a cox model for survival analysis and another run a non-linear classification technique named Breiman recursive partitioning analysis.
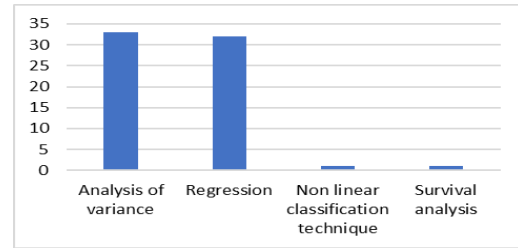
C. Sociodemographic and clinical characteristics

According to the articles that have specified which variables were included in their model, the most used features, due to their influence on the QoL results, were: age (n=26), sex (n=25), tumour site (24), treatment modality (n=22), stage (n=18), marital status (n=12), comorbidity (n=10), education level (n=9), tobacco use (n=9), time since treatment (n=8) and alcohol use (n=7). Other variables have also been used, although the number of articles that included them was lower.

D. Changes of QoL and side effects

The QoL questionnaires' scores at the end of the treatment are significantly lower than at the beginning [8] since the QoL usually deteriorates due to the side effects of the treatment and the disease's development. In general, at the end of the treatment, these problems progressively decrease up to a month later. The patients' QoL begins to improve over the next 12 months; however, after these months, some of the symptoms remain, making the symptoms survivors scores lower than the normal population [9]. Within 12 months after treatment, HNC survivors present several symptoms: speech and swallowing problems, deficits in general physical function and social attitude, problems falling asleep, weight loss, xerostomia, depressive symptoms, anxiety, fatigue, and pain [10][11][12]. The origins of these dysfunctions can be diverse but are vital since they affect survivors' HRQoL and can be related to a cancer recurrence or second malignancies. Therefore, follow-up in long term is essential to prevent the appearance of new symptoms or the worsening of them [12].

E. Predictors and factors associated with QoL

A summary of the QoL predictors or factors associated with QoL is shown in Table I. As *sociodemographic predictors*, several studies have seen a significant association between the age and sex of the HNC patients with their HRQoL. Patients with a younger age reported a higher survival rate [10] and physical activity scores [13][14][15][16], better physical health [14] and functional well-being [16][13]. However, younger age was also related to worse scores in fear of recurrence (FoR) [17], posttraumatic growth (PTG) [18], sense impairments [11], aesthetics, social disruption, mental health outcomes [14], depressive symptoms [14][16] and anxiety/mood [17]. Regarding patients' sex, being female was related to more PTG [18], lower emotional [15] and mental health domain scores [9] and a higher number of unmet needs [19]. Other sociodemographic factors that are related to a worse HRQOL are not being married [15][20][21] and the presence of medical comorbidity at diagnosis. Patients who were married

were positively associated with social and functional domains [15] and less likely to report neck disability [21] and financial toxicity [20]. The presence of medical comorbidity at diagnosis was related to worse scores in physical activity [16], physical health [14], QoL and cancer-specific QoL [22].

While studying *clinical predictors*, it was found that disease and treatment-related aspects also affect the HNC patients' QoL. Among them, tumour stage, tumour site and treatment modality are the most representative. Early stages were associated with significantly better outcomes on aesthetics, mental health [14], social disruption, eating [14][23], speech, overall QoL [14][24], work status [25], symptoms sum score [26][24], depression [14][38], role functioning [24] and higher survival rate [10]. Regarding tumour site, depending on the cancer location, the scores vary in the scales of mental health, speech [9][14], eating [14], swallowing, and social eating [11]. The treatment modality selected can affect patients' neck disability, physical, social and symptoms subscale scores [21][24].

Due to symptoms and side effects suffered by patients, *social support* perceived at this period is associated with the HRQoL reported by HNC survivors one year after diagnosis, specifically in the domains of speech, aesthetics, and social disruption [27]. Patients with social support from family and friends, who could help them through their difficulties were more likely to improve HNC specific HRQoL,with better mental and physical health, respectively [28].

Concerning *psychological variables*, the presence of depression can predict a lower HRQoL during the first year of follow-up, specifically in the scales related to the factors of speech, eating, aesthetics, and social disruption [29]. Regarding the long-term survivors' QoL, the psychosocial variables are also strongly associated with cancer-specific additional concerns, physical well-being [30], and FoR [31].

TABLE I. SUMMARY OF QoL PREDICTORS

Variables	Associated factors
Sociodemographic characteristics	
Age, years	Physical activity, functional well-being, survival, fear of recurrence, anxiety/mood, posttraumatic growth, mental health, aesthetics, social disruption, physical health, depressive symptoms
Sex	Posttraumatic growth, emotional, mental health, unmet needs
Marital status	Financial toxicity, social and functional domains, neck disability, financial toxicity
Comorbidity	Physical activity, physical health, generic and cancer-specific QoL
Clinical characteristics	
Tumour state	Survival, aesthetic, mental health, social disruption, eating, speech, overall QoL, work status, symptom sum score, depression, role functioning
Tumour site	Mental health, speech, swallowing, social eating
Treatment	Physical and social subscales, symptoms
Social support	
	Speech, aesthetics, social disruption, physical health, mental health
Psychological variables	
	Speech, aesthetics, social disruption, additional concerns, physical well-being, fear of recurrence
Physical activity	
	Global QoL, pain, physical, social, emotional, functional well-being, additional concerns, fatigue, patient empowerment, mental health

High levels of *physical activity* are significantly associated with higher global QoL [13] and a better HRQoL in the domains of physical well-being, social well-being, emotional well-being, functional well-being and FACT additional concerns related to HNC [16][32]. A higher physical activity level was also associated with less fatigue [13] [16] and pain [13]. Furthermore, apart from improving physical condition, sports' participation can increase patients' empowerment and enhance their mental health [32].

E. Model definition - TRIPOD statement

The TRIPOD items results covered in this work are summarised in Table II. Regarding the medical context, it has been found that the number of cancer survivors has increased, necessitating a greater emphasis on the study of HRQoL (3a). Moreover, QoL scores vary over time; because of that, its research may be interesting. For these reasons, we have decided to carry out a study focused on QoL changes of HNC survivors for early detection of significant deterioration (3b). To predict the change of HNC survivors QoL, the predictors identified from the results of this literature can be used (7a).

IV. DISCUSSION

With recent advances in treatment and supportive care of HNC, overall survival has increased, and more emphasis is needed in the study of patients' QoL. With this scoping review, the most used QoL questionnaires and data analysis techniques have been extracted to understand the interpretation of QoL and side effects and identify the predictors of changes in QoL.

This research has analysed how during and after treatment, the symptoms and the QoL of patients significantly worsen due to disease and treatment-related effects. Generally, this QoL improves one year after treatment; however, some symptoms persist and do not return to normal. These results are consistent with previous research findings [16].

According to these results, survivors' QoL use to vary over time; therefore, developing a model to predict the change in QoL during this period can be of great importance for early detection of QoL deterioration.

These deteriorations could be associated with malignancies, so predicting it can help clinicians make decisions to improve patient's future well-being. Regarding sociodemographic and clinical parameters, it has been observed how the most used as input parameters in the data analysis models coincide with the predictors identified in the literature review. The sociodemographic and clinical characteristics, social support, psychological variables, and physical activity have also been identified as QoL predictors.

The most common analysis conducted so far for comparing the answers of the QoL questionnaires and other patients' characteristics is the analysis of variance. The most used prediction methods were linear and logistic regression. The main limitation of these methods is that they cannot model complex relationships and are sensitive to outliers. The most common questionnaires identified were FACT and EORCT-C30. Analysis of variance methods was strictly followed by the regression techniques to identify associations and relevant predictor factors of QoL change.

Item summary results	
Introduction – Background and objectives	
3a	- The number of cancer survivors has increased. - More emphasis is needed in HRQoL. - QoL scores of HNC patients vary over time.
3b	- The main objective is to develop a predictive model to study the change of the QoL.
Methods – Outcome and Predictors	
7a	- Demographic characteristics: age, sex, marital status, education level, tobacco and alcohol use. - Clinical characteristics: Tumour site, treatment modality, stage, comorbidity and time since treatment. - Social support, psychological variables and physical activity are also relevant.

V. CONCLUSION

This literature review has observed that symptoms remain relatively high in the post-treatment period up to one year later. Monitoring the survivors' QoL during this time is very important as these symptoms may worsen due to a cancer recurrence or second malignancies. Therefore, the creation of this prediction model is of great importance to detect and prevent patients' QoL early deterioration during post-treatment follow-up. With the results obtained, we understood the research problems and identified the data analysis techniques and features of the predictive model.

ACKNOWLEDGMENT

REFERENCES

[1] Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893-2917.

[2] Boscolo-Rizzo P, Zorzi M, Del Mistro A, et al. The evolution of the epidemiological landscape of head and neck cancer in Italy: Is there evidence for an increase in the incidence of potentially HPV-related carcinomas?. PLoS One. 2018;13(2):e0192621. Published 2018 Feb 7.

[3] Cancer Facts & Figures 2016. American Cancer Society. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2016.html. Accessed April 28, 2021.

[4] Taylor K, Monterosso L. Survivorship Care Plans and Treatment Summaries in Adult Patients With Hematologic Cancer: An Integrative Literature Review. Oncol Nurs Forum. 2015;42(3):283-291.

[5] So WK, Chan RJ, Chan DN, et al. Quality-of-life among head and neck cancer survivors at one year after treatment--a systematic review. Eur J Cancer. 2012;48(15):2391-2408. doi:10.1016/j.ejca.2012.04.005

[6] Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ. 2015;350:g7594. Published 2015 Jan 7.

[7] Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62(10):1006-1012.

[8] Sandstrom SK, Mazanec SR, Gittleman H, Barnholtz-Sloan JS, Tamburro N, Daly BJ. A Descriptive, Longitudinal Study of Quality of Life and Perceived Health Needs in Patients With Head and Neck Cancer. J Adv Pract Oncol. 2016;7(6):640-651.

[9] Hammerlid E, Taft C. Health-related quality of life in long-term head and neck cancer survivors: a comparison with general population norms. Br J Cancer. 2001;84(2):149-156.

[10] Oskam IM, Verdonck-de Leeuw IM, Aaronson NK, et al. Prospective evaluation of health-related quality of life in long-term oral and oropharyngeal cancer survivors and the perceived need for supportive care. Oral Oncol. 2013;49(5):443-448.

[11] Bower WF, Vlantis AC, Chung TM, Van Hasselt CA. Mode of treatment affects quality of life in head and neck cancer survivors: Implications for holistic care. Acta Otol. 2010;130(10):1185-1192.

[12] Cramer JD, Johnson JT, Nilsen ML. Pain in Head and Neck Cancer Survivors: Prevalence, Predictors, and Quality-of-Life Impact. Otolaryngol Head Neck Surg. 2018;159(5):853-858.

[13] van Nieuwenhuizen AJ, Buffart LM, van Uden-Kraan CF, et al. Patient-reported physical activity and the association with health-related quality of life in head and neck cancer survivors. Support Care Cancer. 2018;26(4):1087-1095.

[14] Funk GF, Karnell LH, Christensen AJ. Long-term health-related quality of life in survivors of head and neck cancer. Arch Otolaryngol Head Neck Surg. 2012;138(2):123-133.

[15] Thomas AA, Timmons A, Molcho M, et al. Quality of life in urban and rural settings: a study of head and neck cancer survivors. Oral Oncol. 2014;50(7):676-682.

[16] Rogers LQ, Courneya KS, Robbins KT, et al. Physical activity and quality of life in head and neck cancer survivors. Support Care Cancer. 2006;14(10):1012-1019.

[17] Ghazali N, Cadwallader E, Lowe D, Humphris G, Ozakinci G, Rogers SN. Fear of recurrence among head and neck cancer survivors: longitudinal trends. Psychooncology. 2013;22(4):807-813.

[18] Sharp L, Redfearn D, Timmons A, Balfe M, Patterson J. Posttraumatic growth in head and neck cancer survivors: Is it possible and what are the correlates?. Psychooncology. 2018;27(6):1517-1523.

[19] O'Brien KM, Timmons A, Butow P, et al. Associations between neighbourhood support and financial burden with unmet needs of head and neck cancer survivors. Oral Oncol. 2017;65:57-64.

[20] Mady LJ, Lyu L, Owoc MS, et al. Understanding financial toxicity in head and neck cancer survivors. Oral Oncol. 2019;95:187-193.

[21] Nilsen ML, Lyu L, Belsky MA, et al. Impact of Neck Disability on Health-Related Quality of Life among Head and Neck Cancer Survivors. Otolaryngol Head Neck Surg. 2020;162(1):64-72.

[22] Wells M, Swartzman S, Lang H, et al. Predictors of quality of life in head and neck cancer survivors up to 5 years after end of treatment: a cross-sectional survey. Support Care Cancer. 2016;24(6):2463-2472.

[23] Van Liew JR, Christensen AJ, Howren MB, Hynds Karnell L, Funk GF. Fear of recurrence impacts health-related quality of life and continued tobacco use in head and neck cancer survivors. Health Psychol. 2014;33(4):373-381.

[24] Chaukar DA, Walvekar RR, Das AK, et al. Quality of life in head and neck cancer survivors: a cross-sectional survey. Am J Otolaryngol. 2009;30(3):176-180.

[25] 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;46(1):56-60.

[26] Chaukar DA, Walvekar RR, Das AK, et al. Quality of life in head and neck cancer survivors: a cross-sectional survey. Am J Otolaryngol. 2009;30(3):176-180.

[27] Howren MB, Christensen AJ, Karnell LH, Funk GF. Health-related quality of life in head and neck cancer survivors: impact of pretreatment depressive symptoms. Health Psychol. 2010;29(1):65-71.

[28] Agarwal M, Hamilton JB, Crandell JL, Moore CE. Coping strategies of African American head and neck cancer survivors. J Psychosoc Oncol. 2010;28(5):526-538.

[29] Howren MB, Christensen AJ, Karnell LH, Funk GF. Health-related quality of life in head and neck cancer survivors: impact of pretreatment depressive symptoms. Health Psychol. 2010;29(1):65-71.

[30] Holloway RL, Hellewell JL, Marbella AM, Layde PM, Myers KB, Campbell BH. Psychosocial effects in long-term head and neck cancer survivors. Head Neck. 2005;27(4):281-288.

[31] Moschopoulou E, Hutchison I, Bhui K, Korszun A. Post-traumatic stress in head and neck cancer survivors and their partners. Support Care Cancer. 2018;26(9):3003-3011.

[32] Sammut L, Fraser LR, Ward MJ, Singh T, Patel NN. Participation in sport and physical activity in head and neck cancer survivors: associations with quality of life. Clin Otolaryngol.