Voice rehabilitation after laryngeal cancer: Associated effects on psychological well-being

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Abstract

Purpose Psychological distress after laryngeal cancer treatment is prevalent. Although voice rehabilitation has shown to improve functional outcomes and positively affect health-related quality of life, to date, there has been limited study of the associated effect of behavioural voice intervention on psychological well-being/distress post laryngeal cancer.

Method Sixty-three patients with Tis-T4 laryngeal cancer treated with (chemo)radiotherapy were prospectively recruited and randomised to either a voice rehabilitation (VR, n = 31) or control group (n = 32). The VR group received 10 speech pathology sessions consisting of both direct and indirect voice intervention post (chemo)radiotherapy. The control group received general voice education but not specific intervention. As part of a multidisciplinary assessment battery, psychological well-being/distress was measured using the Hospital Anxiety and Depression Scale (HADS) pre, six and 12 months post VR.

Results Within-group analysis revealed a significant (p = 0.03) reduction in the proportion of patients with anxiety in the VR group between baseline and 12 months. No change over time was observed in controls. Between-group analysis revealed a trend for fewer VR cases demonstrating anxiety (p = 0.06) or depression (p = 0.08) at 6 months and significantly fewer demonstrating anxiety (p = 0.04) and depression (p = 0.04) at 12 months, compared to controls. Significant correlations were observed between patients’ voice perceptions and reduced anxiety (rpb = −0.38) and depression (rpb = −0.66) within the VR group at 12 months.

Conclusions The positive correlations and between-group analyses indicate a positive effect on psychological well-being associated with completing voice rehabilitation. Results highlight potential additional benefits of behavioural voice intervention beyond achieving direct change to voice function.

Keywords Voice therapy · Speech-language pathology · Radiotherapy

Introduction

Within head and neck cancer (HNC) research and clinical management, greater importance is now being placed on understanding the sequelae impacting patients post cancer treatment. Such information is essential to guide rehabilitation and optimise patient function, psychological health and quality of life for improved survivorship care following cancer. Within the subgroup of patients who present with laryngeal cancer managed with organ-preservation treatments, the negative impacts of (chemo)radiotherapy [(C)RT] treatment on function, health-related quality of life (HRQOL) and psychological well-being/distress have been investigated to varied extents.

Regarding impact to voice function and communication after laryngeal cancer treatment, research indicates that patients will experience vocal function changes that vary from mild to severe in nature. Often presenting as a complex dysphonia, the voice post (C)RT has been characterised as harsh, rough, strained and breathy, with glottal fry and altered pitch.
which may remain with the patient long term [1–5]. Patients themselves report poor vocal quality, hoarseness, reduced volume and vocal fatigue following laryngeal cancer treatment [6–9].

Many studies have also investigated (HRQL) and global quality of life (QOL) outcomes post laryngeal cancer. Research specific to non-surgical treatment outcomes indicates that the majority of HRQL (function and symptom scales) deteriorate 1 month post radiotherapy then improve 6–12 months to reach baseline levels (pre-radiotherapy), although these remain below normative values [1, 10]. Most HRQL function and symptom outcomes present at 12 months continue to persist long term, up to 5 years post radiotherapy [11].

However, whilst the impact on functional outcomes and quality of life has been well explored, research into patient psychological well-being/distress post laryngeal cancer has been examined to a lesser extent. Studies suggest that up to 41% of patients experience possible/probable anxiety or depression [12] which may be most prevalent either pre-radiotherapy [10] or 12 months post [13] and continues to persist years after management [14]. Johansson and colleagues (2011) also identified that patients’ mental adjustment to laryngeal cancer and their coping strategies significantly impact anxiety, depression, HRQL and survival [15].

Given the extent of functional impairments and reduced quality of life outcomes after laryngeal cancer treatment, recent research has explored potential benefits of behavioural voice rehabilitation for this clinical group. Studies indicate that voice rehabilitation post laryngeal cancer significantly improves voice (acoustic and perceptual qualities), patient perceptions, communication and several HRQL outcomes when compared to a laryngeal cancer cohort who did not receive voice rehabilitation [9, 16–19]. Furthermore, there is a known interrelationship between function, quality of life and patient well-being. Rinkel and colleagues (2014) highlighted that, specifically within the laryngeal cancer population, the prevalence of voice, communication (and swallowing) problems after laryngeal cancer treatment is high and clearly related to quality of life and emotional distress [20]. Consequently, it could be hypothesised that patients who receive rehabilitation for their voice deficits following laryngeal cancer, and experience positive functional and HRQL effects, may also experience positive benefits for their psychological well-being.

However, whilst results from rehabilitation trials have demonstrated improved voice function and positive impacts to HRQL outcomes, to date, any potential impact on psychological well-being has not been examined. Given the interrelationship between function, HRQL and psychological well-being, this study aims to determine if there is also an associated effect on patient well-being/distress, specifically experiences of anxiety and/or depression for patients who receive behavioural voice intervention following (chemo)radiotherapy for laryngeal cancer.

Methodology

Study population

The current data were collected as part of a larger, prospective randomised control trial at Sahlgrenska University Hospital, Gothenburg, Sweden [18, 19]. Ethical approval was granted and the study was conducted in accordance with the Declaration of Helsinki. Patients diagnosed with laryngeal cancer (Tis–T4) in the Västra Götaland Region were referred to a weekly tumour conference at the Otorhinolaryngology Department and invited to be part of the study. Inclusion criteria for the study were laryngeal cancer patients planned for curative (chemo)radiotherapy, who had sufficient Swedish language competency to independently answer questionnaires and partake in voice rehabilitation. Exclusion criteria were tracheostomy and severe cognitive impairment limiting participation in voice rehabilitative exercises. A total of 163 patients were available for inclusion, of which 89 agreed to participate or remained eligible for study participation (CONSORT flow diagram, Fig. 1). Randomisation occurred electronically using Pocock’s sequential randomisation method [21] considering patient’s age, smoking status, tumour site, size and self-evaluation of communication pre (C)RT. Twenty-six patients were lost to follow-up, leaving a total of 63 patients available for analyses. Comparisons of the demographics between the two groups confirmed there were no significant differences between the voice rehabilitation (VR) and control groups when compared for gender, mean age, tumour location, radiotherapy regime, comorbidity or working status (Table 1).

Oncologic treatment

The radiotherapy regime, as determined by regional guidelines, was either (1) conventional, once daily radiotherapy at 2–2.4 Gy fractions to a total of 62.4–68 Gy, or (2) hyperfractionated, twice daily radiotherapy at 1.7 Gy fractions to a total of 64.6 Gy. Patients with T2–T4 tumours generally received radiation to lymph nodes (n = 24) and three patients with T3–T4 tumours also received induction chemotherapy.

Procedure

Outcome assessments occurred at baseline, i.e., 1 month post (chemo)radiotherapy cessation (pre–voice rehabilitation), and post voice rehabilitation at 6 and at 12 months post (C)RT. At each time point, all patients completed an assessment battery including voice recording and analyses, self-reported communication experiences and health-related quality of life measures. These results have been previously reported [9, 18, 19]. For the current study, only the data relating to patient perceptions of their voice acceptability and the data relating to patient well-being, as
reported by the Hospital Anxiety and Depression Scale [22], is examined. The Hospital Anxiety and Depression Scale (HADS) was developed for the general medical patient population and has been used extensively both clinically and within research [23]. It consists of the two scales, anxiety and depression, each with seven questions answered on a 0–3 scale, where a larger number represents greater symptoms of anxiety/depression. Within each scale, summed scores of <8 indicate no case of anxiety/depression, scores of 8–10 indicate possible anxiety/depression and scores ≥11 indicate probable anxiety/depression [22]. Patient’s voice perceptions were examined using a study-specific questionnaire, reported in earlier studies [9, 24, 25]. However, from this, only the question examining whether the patient believed their voice to be acceptable in a social environment, answered on a Likert scale with 0 = never, 1 = sometimes, 2 = often and 3 = always, was included in this study.

Voice rehabilitation occurred between pre-voice rehabilitation (1 month post treatment) and the 6-month post (C)RT time point. Voice rehabilitation consisted of 10 speech pathology intervention sessions over 10 weeks using a structured protocol consisting of both direct and indirect voice intervention, including tasks such as breathing, relaxing, posture and specific physiology-targeted phonation exercises [9]. The final sessions focused on transferability of skills and generalisation into conversation and holistic communication. The control group received general voice education such as vocal hygiene advice, but not specific intervention.

Statistical methods

Descriptive statistics were used to calculate the proportion of HADS ‘no case’ versus ‘possible/probable’ anxiety and
Table 1  Patient inclusion demographics

|                    | Control group n (%) | Voice rehabilitation n (%) | Difference p value |
|--------------------|----------------------|----------------------------|-------------------|
| Patients           | 32                   | 31                         | 0.96              |
| Gender             |                      |                            |                   |
| Male               | 28 (87)              | 27 (87)                    |                   |
| Female             | 4 (13)               | 4 (13)                     |                   |
| Mean age (years)   | 62.1                 | 65.8                       | 0.19              |
| Range              | 41–82                | 41–86                      |                   |
| Tumour location    |                      |                            | 0.59              |
| Glottic (78%)      | 24 (75)              | 25 (81)                    |                   |
| Tis                | 1                    | 0                          |                   |
| T1                 | 15                   | 19                         |                   |
| T2                 | 7                    | 6                          |                   |
| T3                 | 1                    | 0                          |                   |
| Supraglottic (22%) | 8 (25)               | 6 (19)                     |                   |
| T1                 | 1                    | 2                          |                   |
| T2                 | 3                    | 2                          |                   |
| T3                 | 4                    | 1                          |                   |
| T4                 | 0                    | 1                          |                   |
| Radiotherapy       |                      |                            | 0.46              |
| Conventional       | 23 (72)              | 19 (61)                    |                   |
| Hyperfractionated  | 9 (28)               | 12 (39)                    |                   |
| Comorbidity (ACE-27)* | (n = 31)            |                            | 0.22              |
| None               | 13 (42)              | 13 (42)                    |                   |
| Mild               | 14 (45)              | 9 (29)                     |                   |
| Moderate           | 4 (13)               | 9 (29)                     |                   |
| Severe             | 0                    | 0                          |                   |
| Working status—employed | 14 (44)        | 12 (39)                    | 0.69              |
| Vocally demanding workc | 7/14 (50)       | 7/12 (58)                  | 0.95              |

*Adult Comorbidity Evaluation (ACE-27) [35]

b One patient with missing data

c As determined by patient report

depression. Within- and between-group statistical analyses were conducted using SPSS statistics software, version 22, with a significance set at p < 0.05. Within-group analysis (across time points) was calculated using the McNemar chi-square test for categorical data. Difference between groups was calculated using the chi-square statistic. Correlation between possible/probable anxiety or depression (dichotomous variable) and patient voice perceptions (ordinal data) was calculated using point-biserial correlation coefficient (rpb) using VassarStats: Website for Statistical Computation [26]. Correlation strength was interpreted using the following criteria: 0.00–0.30 = negligible correlation, 0.30–0.50 = low correlation, 0.50–0.70 = moderate correlation, 0.70–0.90 = high correlation and 0.90–1.00 = very high correlation [27].

Results

Within- and between-group comparisons are displayed in Table 2. Within-group analysis showed a trend (p = 0.06), in the VR group, towards a reduction in number of possible/probable anxiety cases at 6 months, and by 12 months, the number of possible/probable anxiety cases was significantly lower (p = 0.03) than pre-voice rehabilitation. No significant change in cases of depression, in the VR group, was observed over time. For the control group, no changes were observed in the proportion of patients reporting anxiety or depression across any of the time points.

Between-group analyses revealed no significant difference between groups at baseline; however, at 6 months, the VR group reported less cases of possible/probable anxiety and depression, a difference approaching significance (p = 0.06 and p = 0.08, respectively). By 12 months, however, the two groups were statistically significantly different (p = 0.04) with the VR group reporting significantly less cases of anxiety and depression than the controls. Within the VR group at 12 months, significant correlations were found between positive patient perceptions of voice acceptability and the reduction in cases of anxiety (p = 0.03, rpb = −0.38) and depression (p < 0.001, rpb = −0.66).

Discussion

Results from the current study suggest associated positive effects on psychological well-being following voice rehabilitation. At baseline (post radiotherapy/pre-voice rehabilitation), both the control and VR groups were statistically similar in their reported cases of anxiety/depression, and results from this study are largely comparable to prior research which indicates that 15 and 23% of patients report anxiety and depression (respectively), immediately post radiotherapy [13]. Following voice rehabilitation, our results demonstrate that there was a continued reduction in the proportion of patients with anxiety between baseline—6 months—and between 6 and 12 months within the VR group only. By 12 months, the proportion of anxiety (6%) and depression (6%) cases in the VR group were significantly lower than the control group where 25% continued to report ongoing anxiety or depression. The control group data in the current study is largely comparable to previous literature. Hammerlid et al. (1998) found 26 and 24% of their patients indicated anxiety and depression (respectively) at 12 months [13].

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A number of possible theories could be proposed for why there were improved cases of anxiety and depression following voice rehabilitation. One possible reason could be the improved functional outcomes achieved by voice

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Table 2  Between- and within-group analysis of the proportion of patients with no, possible or probable anxiety and depression at each time point

|                     | Pre-VR number (%) | 6 months number (%) | 12 months number (%) | Within-group analysis |
|---------------------|-------------------|---------------------|----------------------|-----------------------|
|                     |                   |                     |                      | Pre-VR to 6 months p value | 6 to 12 months p value | Pre-VR to 12 months p value |
| Control group       |                   |                     |                      |                        |                        |                           |
| Anxiety             |                   |                     |                      |                        |                        |                           |
| No case             | 21 (66)           | 23 (72)             | 24 (75)              | 0.73                   | 1.00                   | 0.38                       |
| Possible/probable   | 11 (34)           | 9 (28)              | 8 (25)               |                         |                        |                           |
| Depression          |                   |                     |                      |                        |                        |                           |
| No case             | 20 (63)           | 25 (78)             | 24 (75)              | 0.18                   | 1.00                   | 0.22                       |
| Possible/probable   | 12 (37)           | 7 (22)              | 8 (25)               |                         |                        |                           |
| VR group            |                   |                     |                      |                        |                        |                           |
| Anxiety             |                   |                     |                      |                        |                        |                           |
| No case             | 23 (74)           | 28 (90)             | 29 (94)              | 0.06                   | 1.00                   | 0.03                       |
| Possible/probable   | 8 (26)            | 3 (10)              | 2 (6)                |                         |                        |                           |
| Depression          |                   |                     |                      |                        |                        |                           |
| No case             | 25 (81)           | 29 (94)             | 29 (94)              | 0.29                   | 1.00                   | 0.22                       |
| Possible/probable   | 6 (19)            | 2 (6)               | 2 (6)                |                         |                        |                           |
| Between-group analysis |           |                     |                      |                        |                        |                           |
| Anxiety             | p = 0.50          | p = 0.06            | p = 0.04             |                        |                        |                           |
| Depression          | p = 0.11          | p = 0.08            | p = 0.04             |                        |                        |                           |

Statistical significance (p < 0.05) indicated by italic font

VR voice rehabilitation
rehabilitation. Prior studies have reported positive voice function (acoustic and perceptual) outcomes following voice rehabilitation compared to no voice rehabilitation [9, 16]. Furthermore, Karlsson and colleagues (2015) demonstrated that voice rehabilitation significantly improved communication, social function, social contact and quality of life at 6 months post rehabilitation when compared to a control group [19]. Indeed, in the current study, positive perceptions of voice acceptability were significantly correlated with fewer cases of anxiety and depression. This interrelationship and impact of function on quality of life and psychological well-being/distress is not a new phenomenon and has been reported both in the laryngeal cancer population [20] in the larger HNC population [28, 29].

However, it should be noted that the correlations between voice acceptability (the patient perceptions of voice function) and anxiety/depression were small to moderate in size. As such, additional factors contributing to the positive benefits observed for the VR group, such as broader impacts of behavioural intervention, should be considered. Within HNC trials, it has been observed that those trials which focus on improving function, as well as effective communication, problem-solving, and distress, result in reduced social impairment, psychological distress and improved HRQL [30]. Given that our study’s intervention arm focused on improving voice function, facilitating effective communication and transferring skills into the patient specific communication/social environment, it is possible that an improvement in these functional skills positively affected quality of life and patient well-being outcomes, secondary to the interrelation between these parameters.

The current data raises some important clinical implications. Function rehabilitation post laryngeal cancer treatment has shown to improve communication and HRQL outcomes [9, 16, 18, 19] and, now, the current data supports potential positive benefits for patient well-being/distress. Furthermore, it is recognised more broadly in the literature that survivorship care should incorporate both function rehabilitation and psychosocial intervention [28, 31–33]. Recent research within HNC literature, investigating behavioural and psychosocial intervention post treatment, suggests that structured, theoretically based interventions which address functional, HRQL and psychosocial impairments and incorporate problem-focused, self-management, collaborative goal-setting, action-planning, shared care and linkage to health-care supports are key elements for survivorship care [31–33]. Although the current voice rehabilitation program used in this RCT was not developed with this specific focus, it has achieved some of these desired benefits. Future development of behavioural interventions for the laryngeal cancer population need to ensure that rehabilitation is sufficiently holistic to support the patient in their recovery, focusing on both function rehabilitation and psychosocial management.

Limitations of this study include the heterogeneous laryngeal cancer cohort used within this study, including both glottic and supraglottic tumours and stage I–stage IV cancers. However, the focus on voice rehabilitation within the laryngeal cancer population specifically versus the larger HNC population is also considered to be a strength of this study. Furthermore, our study’s cohort is reflective of the usual laryngeal cancer demographics [34]; therefore, results from this study may be generalisable to the larger laryngeal cancer patient population. It is acknowledged that no data on patient coping skills, adjustment, or other reasons for the observed levels of anxiety or depression were examined. As such, it is possible that other factors, unrelated to the voice rehabilitation, could account for the current findings. Investigation and incorporation of these factors are recommended for future trials.

Conclusion

Although voice rehabilitation has shown to improve functional outcomes and positively impact HRQL, the current data suggests positive associated effects of behavioural voice intervention on psychological distress/well-being. This study found lower rates of possible/probable anxiety and depression being reported at 6 and 12 months in the VR group compared to controls, and this improvement in anxiety/depression correlated moderately with patient perceptions of voice acceptability. Results highlight potential additional benefits of behavioural voice intervention beyond achieving direct change to voice function.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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References

1. Karlsson T, Bergström L, Ward E, Finizia C (2016) A prospective longitudinal study of voice characteristics and health-related quality of life outcomes following laryngeal cancer treatment with radiotherapy. Acta Oncol 55(6):693–699. doi:10.3109/0284186X.2016.1150604

2. Morgan DAL, Robinson HF, Marsh L, Bradley PJ (1988) Vocal quality 10 years after radiotherapy for early glottic cancer. Clin Radiol 39(5):295–296. doi:10.1016/S0009-9260(88)805415

3. Bibby JR, Cotton SM, Perry A, Corry JF (2008) Voice outcomes after radiotherapy treatment for early glottic cancer: assessment using multidimensional tools. Head & neck 30(5):600–610. doi:10.1002/hed.20750

4. van der Molen L, van Rossum MA, Jacobi I, van Son RJ, Smeele LE, Rasch CR, Hilgers FJ (2012) Pre- and posttreatment voice and speech outcomes in patients with advanced head and neck cancer treated with chemoradiotherapy: expert listeners’ and patients perception. J Voice 26(5):e625–e633. doi:10.1016/j.jvoice.2011.08.016

5. Meleca RJ, Dworkin JP, Kewson DT, Stachler RJ, Hill SL (2003) Functional outcomes following nonsurgical treatment for advanced-stage laryngeal carcinoma. Laryngoscope 113(7):720–728. doi:10.1097/00005537-200304000-00025

6. Peeters AJGE, van Gogh CDL, Goor K, Verdonck-de Leeuw IM, Langendijk JA, Mahieu HF (2004) Health status and voice outcome after treatment for T1a glottic carcinoma. European Archives of Oto-Rhino-Laryngology and Head & Neck 261(10):534–540. doi:10.1007/s00405-003-0697-5

7. Szuecs M, Kuhnt T, Punke C, Witt G, Klautke G, Kramp B, Hildebrandt G (2015) Subjective voice quality, communicative ability and swallowing after definitive radio (chemo)therapy, laryngectomy plus radio (chemo)therapy, or organ conservation surgery plus radio (chemo) therapy for laryngeal and hypopharyngeal cancer. J R Radiat Res. doi:10.1093/jrr/rmu093

8. Hocevar-Boltezar I, Zargi M, Strojan P (2009) Risk factors for voice quality after radiotherapy for early glottic cancer. Radiother Oncol 93(3):524–529. doi:10.1016/j.radonc.2009.09.014

9. Bergström L, Ward EC, Finizia C (2016) Voice rehabilitation for laryngeal cancer patients: functional outcomes and patient perceptions. The Laryngoscope:n/a-n/a. doi:10.1002/lary.25919

10. Johansson M, Ryden A, Finizia C (2008) Self evaluation of communicative experiences after laryngeal cancer—a longitudinal questionnaire study in patients with laryngeal cancer. BMC Cancer 8:80. doi:10.1186/1471-2407-8-80

11. Nordgren M, Abendstein H, Jannert M, Boysen M, Ahlner-Elmqvist M, Silander E, Bjordal K, Hammerlid E (2003) Health-related quality of life five years after diagnosis of laryngeal carcinoma. International Journal of Radiation Oncology Biology Physics 56(5):1333–1343: DOI: 10.1016/S0360-3016(03)00292-X

12. Siipinsikiene N, Vaitkus S, Grebliukauskiene M, Engelmanaita L, Sunksiene J (2008) Quality of life and voice in patients treated for early laryngeal cancer. Medicina Kaunas, Lithuania 44(4):288–295

13. Hammerlid E, Mercke C, Sullivan M, Westin T (1998) A prospective quality of life study of patients with laryngeal carcinoma by tumor stage and different radiation therapy schedules. Laryngoscope 108(5):747–759

14. Singer S, Danker H, Dietz A, Homemann B, Koscienly S, Oeken J, Matthaus C, Vogel H, Krauss O (2008) Screening for mental disorders in laryngeal cancer patients: a comparison of 6 methods. Psychooncology 17(3):280–286

15. Johansson M, Ryden A, Finizia C (2011) Mental adjustment to cancer and its relation to anxiety, depression, HRQL and survival in patients with laryngeal cancer. A longitudinal study. BMC Cancer 11(1):283

16. van Gogh CD, Verdonck-de Leeuw IM, Boon-Kamma BA, Rinkel RN, de Bruin MD, Langendijk JA, Kuik DJ, Mahieu HF (2006) The efficacy of voice therapy in patients after treatment for early glottic carcinoma. Cancer 106(1):95–105. doi:10.1002/cncr.21578

17. van Gogh CDL, Verdonck-de Leeuw IM, Langendijk JA, Kuik DJ, Mahieu HF (2012) Long-term efficacy of voice therapy in patients with voice problems after treatment of early glottic cancer. J Voice 26(3):398–401. doi:10.1016/j.jvoice.2011.06.002

18. Tuomi L, Andrell P, Finizia C (2014) Effects of voice rehabilitation after radiation therapy for laryngeal cancer: a randomized controlled study. International Journal of Radiation Oncology Biology Physics 89(5):964–972. doi:10.1016/j.ijrobp.2014.04.030

19. Karlsson T, Johansson M, Andrèll P, Finizia C (2015) Effects of voice rehabilitation on health-related quality of life, communication and voice in laryngeal cancer patients treated with radiotherapy: a randomised controlled trial. Acta Oncol 54(7):110171024. doi:10.3109/0284186X.2014.995773

20. Rinkel RNPM, Verdonck-de Leeuw IM, van den Brakel N, de Bree R, Eerenstein SEJ, Aaronsen N, Leemans CR (2014) Patient-reported symptom questionnaires in laryngeal cancer: voice, speech and swallowing. Oral Oncol 50(8):759–764. doi:10.1016/j.oraloncology.2014.05.009

21. Pocock SJ, Simon R (1975) Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biometrics 31(3):103–115. doi:10.2307/2529712

22. Zigmond A, Snaith R (1983) The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 67:361–370

23. Stern AF (2014) The Hospital Anxiety and Depression Scale. Occup Med 64(5):393–394. doi:10.1093/occmed/kqu024

24. Finizia C, Hammerlid E, Westin T, Lindström J (1998) Quality of life and voice in patients with laryngeal carcinoma, a posttreatment comparison of laryngectomy (salvage surgery) versus radiotherapy. Laryngoscope 108(10):1566–1573. doi:10.1002/00005537-199810000-00027

25. Finizia C, Lindström J, Dottevall H (1998) Intelligibility and perceptual ratings for treatment after laryngectomy versus radiotherapy. Laryngoscope 108(1):138–143. doi:10.1097/00005537-199801000-00027

26. Lowry R (2016) VassarStats: Website for Stastical Computation. Retrieved from http://vassarstats.net/pbcorr.html. Accessed August 8, 2016.

27. Flinck D, Wiersma W, Jurs S (2003) Applied statistics for the behavioral sciences. Houghton Mifflin, Boston, Massachusetts

28. Ringash J (2015) Survivorship and quality of life in head and neck cancer. J Clin Oncol 33(29):3322–3327. doi:10.1200/jco.2015.61.4115

29. Aarstad HJ, Osthus AA, Olofsson J, Aarstad AKH (2014) Level of distress predicts subsequent survival in successfully treated head and neck cancer patients a prospective cohort study. Acta Otolaryngol 134(2):211–219. doi:10.3109/00016489.2013.841989

30. Howren MB, Christensen AJ, Kornell LH, Funk GF (2013) Psychological factors associated with head and neck cancer treatment and survivorship, evidence and opportunities for behavioral medicine. J Consult Clin Psychol 81(2):299–317. doi:10.1002/hed.10174

31. McEwen SE, Davis AM, Jones JM, Martino R, Poon I, Rodriguez AM, Ringash J (2015) Development and preliminary evaluation of a rehabilitation consult for survivors of head and neck cancer: an intervention mapping protocol. Implement Sci 10(1):9. doi:10.1186/s12913-014-0191-z

32. Turner J, Yates P, Kenny L, Gordon LG, Burmeister B, Thomson D, Batstone M, Carswell K (2014) The ENHANCES study—enhancing head and neck cancer patients experiences of survivorship:
33. van der Meulen IC, May AM, de Leeuw JR, Koole R, Oosterom M, Hordijk GJ, Ros WJG (2014) Long-term effect of a nurse-led psychosocial intervention on health-related quality of life in patients with head and neck cancer a randomised controlled trial. Br J Cancer 110(3):593–601. doi:10.1038/bjc.2013.733

34. Statistikdatabas för cancer (2014) Socialstyrelsen, Stockholm. http://www.socialstyrelsen.se/statistik/statistikdatabas/cancer. Accessed 20 September, 2016

35. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr (2004) Prognostic importance of comorbidity in a hospital-based cancer registry. JAMA 291(20):2441–2447. doi:10.1001/jama.291.20.2441