Critical Review:
Post-salvage neck dissection dysphagia outcomes in head and neck cancer patients treated with radiotherapy and/or chemoradiation therapy

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Head and neck cancer (HNC) patients sometimes undergo a salvage neck dissection (SND) surgery to address recurrent or residual disease after treatment with primary radiotherapy (RT) or chemoradiotherapy (CRT). Research on this patient population thus far has been focused on survival outcomes, but to gain a full picture of the functional, participation, and social effects of this surgery, quality of life (QOL) variables must be examined. In particular, dysphagia-related variables like residue can have impacts on patients' QOL. This paper presents: i) a critical review of dysphagia-related outcomes in these HNC patients that includes a retrospective quasi-experimental between-group cohort study, a single-group repeated-measures study, and a retrospective quasi-experimental mixed cohort design (Study 1), and ii) a single group repeated measures pre-post test study comparing pharyngeal residue before and after SND across two bolus viscosities (Study 2). Findings from both studies suggest that SND does not adversely affect the QOL of these patients, though further research is needed to address this question.

Introduction

SND is a surgical intervention performed in HNC patients who have already undergone definitive RT or combined CRT treatment (Liauw et al., 2006). Specifically, a neck dissection is considered salvage if it takes place a) after cessation of primary treatment, and b) in order to address residual or recurrent disease.

When looking at outcomes of a salvage neck dissection in the specific population of HNC patients treated with primary RT/CRT, research tends to demonstrate that SND is associated with acceptable survival and mortality rates (Chung et al., 2014; Robbins, 2005), regardless of whether the patient received primary RT or CRT (Mukhija et al., 2009). While there is not a large body of research surrounding this specific treatment combination for HNC patients, in the studies that are focused on this group survival and mortality rates are the most common outcomes investigated.

When we think about outcomes for this surgery, survival and mortality are both important pieces of information about what life is like for these patients. However, is this information enough for us to make accurate and full descriptions of what life is like post-surgery? I would argue that survival is not enough to be able to describe fully the effects of post-treatment SND, especially in functional and social parameters. We must look at another outcomes measure: QOL. QOL is a multi-domain measure that aims to capture the functional, emotional, and social well being of individuals (Park, 1988). Although QOL can be a global measure, there is evidence to support a direct link between dysphagia-related variables and QOL. These variables could include saliva management, chewing, residue, penetration, and aspiration (Høxbroe et al., 2017), and all can contribute to a patient's QOL. For example, Nguyen et al., (2005) demonstrate that swallowing function (i.e., dysphagia) is associated with overall QOL, as well as anxiety and depression scores in HNC patients.

There is also a link between dysphagia-related QOL and HNC treatment: Høxbroe et al. (2017) summarize in a meta-analysis that reductions in dysphagia-related QOL domains like saliva management, chewing, and swallowing were all significantly related to treatment of HNC, though there was no mention of neck dissection as part of this analysis. It would appear that the post-RT/CRT SND population is not adequately represented in HNC research, particularly as it pertains to dysphagia-related QOL outcomes.

In summary, there is a link between QOL decreases and treatment of HNC, as well as a link between HNC-related dysphagia and decreases in QOL in HNC patients. However, as yet there has been little research examining these relationships more specifically in the population of HNC patients who have undergone treatment of primary RT/CRT followed by SND.

Objectives

Given the lack of evidence around QOL outcomes following SND in this particular patient population, the objectives of this study are threefold. First, a critical appraisal of the available literature on dysphagia-related QOL outcomes in this population will be presented (Study 1). Second, Modified Barium Swallow Study (MBS) data will be analyzed to assess the change in a specific dysphagia parameter before SND, and at 1 and

3 months post-SND surgery (Study 2). Thirdly, clinical recommendations will be provided based on the findings from this critical review and analysis.

Study 1: Critical Review

SND can be expected to impact QOL given that this surgery, as well as the preceding RT/CRT, can alter form and function of facial and swallowing features. Study 1 reviewed the existing literature examining this relationship.

Methods

Search Strategy

An exhaustive literature search was conducted using online scholarly search engines PubMed, Web of Science, ProQuest, and Google Scholar using the following search strategy: [(salvage neck dissection) OR (neck dissection)] AND [(curative radiotherapy) OR (curative chemoradiotherapy) OR (head and neck cancer)] AND [(dysphagia) OR (quality of life) OR (functional outcomes)].

Selection Criteria

Papers selected are works that examine variables of quality of life and/or dysphagia in the HNC population who have undergone a SND after primary RT/CRT.

Data Collection

The literature search resulted in three studies that directly or indirectly assessed swallow function/dysphagia and QOL effects of SND on HNC patients after definitive RT/CRT. One paper (Hutcheson et al., 2016) is a level 3 retrospective quasi-experimental between-group cohort study; one (Wang, Amdur et al., 2016) is a level 3 single-group repeated-measures study; the final paper (Wang, Moon et al., 2019) uses a level 2b retrospective quasi-experimental mixed cohort design. Levels of evidence used to describe are derived from Archibald (2015).

Results

Hutcheson et al. (2016) used a retrospective cohort design to evaluate the impact of neck dissection on chronic dysphagia in 75 HNC (35 women, mean age = 56 years) patients treated with primary RT and/or CT with and without SND. The functional impact of the surgery was examined through a gold standard measure of dysphagia evaluation (Caudell, 2009) based on MBS/Fiberoptic endoscopic evaluation of swallowing (FEES) imaging. Feeding tube dependence was also a variable of interest. These variables as well as patient demographic information were gathered from patient charts.

Appropriate statistical analyses revealed that development of chronic dysphagia was not associated with SND dissection itself or level of dissection. As well, neck dissection was not associated with the dysphagia-related variables of chronic aspiration, stricture, or feeding tube dependence.

Strengths of the study include well-controlled statistical procedures, inclusion of relevant predictor variables, well-specified participant inclusion criteria, sound procedures to capture physiological data, and long-term data capture period. Limitations include the use of a binary system for classifying dysphagia, the retrospective nature of the study itself, and the lack of a specific measure of QOL.

Overall, this study provides highly suggestive evidence that SND specifically that SND surgery is not associated with any higher risk of development of chronic dysphagia and dysphagia-related sequelae (which we know are related to QOL) as measured by mechanical swallowing events.

Wang, Amdur et al. (2016) used a within-subjects repeated measures study to examine temporal changes in QOL in 37 well-described patients (82% male, median age = 61 years) with squamous cell carcinoma treated with primary CRT followed by a SND. Several published QOL measures were completed to measure general QOL, head and neck specific QOL, severity of dysphagia, and the specific impact of neck dissection on QOL. These measures were compared across 4 time points: baseline (pre-CRT treatment), pre-SND (6 weeks post-CRT), early post-SND (as the first QOL assessment after surgery), and late post-SND (closest QOL assessment to 1.5 years after neck dissection). Clinical parameters examined included unilateral vs. bilateral neck dissection and radiation, number of levels dissected, and number of nodes dissected.

Multiple statistical analyses were completed, revealing significant decreases in all measures of QOL after CRT and improvements over time after SND “almost to baseline.”

Strengths of this work lie in the design (specifically in the timeline of data collection), and inclusion of multiple measures of QOL. One limitation is that the time points of the early post-SND did not include information regarding how much time since the SND had passed when the data were collected. Another limitation is the lack an omnibus statistical test and control for multiple comparisons.

Ultimately, this paper provides highly suggestive evidence that while CRT tends to have a negative impact on quality of life outcomes, SND tends to be associated with QOL improvement over time.

Wang, Mood et al. (2019) conducted a retrospective post-hoc analysis of pooled data from 147 well-described HNC patients (21 females, median age = 63) who had undergone primary CRT with and without SND. Multiple measures of QOL were completed to assess severity of dysphagia and head and neck specific QOL. These measures were compared across five time points: baseline (pre-RT), and 6, 12, 18, and 24 months, and between SND and non-SND groups.

Multiple statistical analyses revealed that there were no differences in measures of QOL between groups and across time points, save for greater reported pain exacerbations and mouth opening at 6 months in the SND group.

Strengths of this study include the use of multiple QOL measures, a well-described inclusion criteria, the mixed design, and, although this was a retrospective post-hoc study, selection of relevant variables. Limitations include the lack of omnibus test and control for multiple comparisons, as well as lack of informative details about post-surgery time periods.

Overall, this study provides highly suggestive evidence that SND surgery does not influence QOL over time, nor does it change QOL significantly compared to not receiving surgery.

Discussion

There were only three published studies that directly or indirectly examined QOL outcomes in HNC patients undergoing SND after primary RT/CRT. Outcomes examined included functional dysphagia parameters (e.g., penetration and aspiration), general QOL measures, as well as head and neck specific measures. Though lack of statistical control for multiple comparisons makes it difficult to make definitive statements about specific time lines, the available literature strongly suggests that SND is not associated with detriments to QOL on this population.

Study 2: Data Analysis

Though the above three papers focus specifically on dysphagia-related outcomes and QOL in HNC patients who have undergone primary RT/CRT, as yet there is no research focusing specifically on residue-based outcomes in this particular population. For these patients, there are several important factors to consider when thinking about residue. First, post-swallow residue is associated with aspiration (Molfenter & Steele, 2013). Second, aspiration has negative impacts on patient treatment response and survival (Shirasu et al., 2020). Most importantly, residue itself is associated with different swallowing-related quality of life outcomes independent of penetration and aspiration: Meyer et al. (2017) demonstrate that while penetration and/or aspiration and residue were significantly related to functional status of HNC patients treated with RT/CRT, only residue was significantly related to QOL measures, such that patient QOL decreased with increased residue. These patients were all rated as having at least moderate dysphagia, meaning that the lack of association between penetration/aspiration and QOL is not a function of lack of swallowing difficulties. Ultimately, this means we cannot assume that using perceptual and instrumental assessments of penetration and aspiration fully captures the impact of this treatment on patient quality of life. As Meyer et al. (2017) demonstrate, dysphagia cannot be inferred from aspiration alone.

Additionally, as Wang, Amdur et al. (2017) demonstrate, we know that the impact of SND may change over time. The best way to examine the affect of this surgery on residue (and therefore on dysphagia-related outcomes) is having multiple timelines. Pretest-postest design is best-practice to facilitate better understanding of outcomes for these individuals. The purpose of Study 2 was to examine how SND changes residue management in HNC patients after CRT. Specifically, pharyngeal residue after swallows of 1 tsp thin liquid and 1 tsp pudding boluses was measured pre-SND, and 1- and 3-months post-SND.

Methods

Participants

Patient data was drawn from an existing database of MBS studies performed in southwestern Ontario and included HNC patients (N = 4: 3 males, mean age = 62.75 ± 5.73 years) who had all undergone CRT. After cessation of treatment, all patients underwent a SND (all unilateral). The surgery was performed between 1-7 months (mean = 3.25 ± 0.95 months) after primary treatment had ended. Participants were included in the study if they had data from all three time points.

Apparatus and Stimuli

All participants completed a MBS study where they swallowed sips, ½ teaspoon (tsp), and 1 tsp of thin liquid, as well as ½ tsp, and 1tsp of puree and pudding. They were also given fruit and a cookie to masticate and swallow. MBS studies were performed at baseline

(before CRT), and 1-, 3-, and 6-months post-CRT treatment. Since not every patient performed swallows with all bolus volumes and viscosities, only 1 tsp volumes of thin liquid and pudding were selected for analysis.

Images from these MBS tapes were captured with VLC (VideoLan, 2006) software and imported into ImageJ (Rasband, 2018) for analysis. Scaled pixel measurements for calibration of images were calculated using pixels/mm to simulate best-practice taping of a quarter to the neck during the MBS.

Measures

The Normalized Residue Ratio Scale (NRRS) (Pearson et al., 2013) is a quantitative method validated for describing residue present in the pharynx. This method gives residue outcomes in terms of percentage of pharynx filled with residue. For each 1 tsp swallow of thin liquid and pudding at each time point, a percentage of pharyngeal space taken up by residue (i.e., pharyngeal residue %) was calculated.

Procedure

Screenshots were taken of MBS swallows for 1 tsp thin liquid and pudding swallows for each patient at each time point. These images were imported into ImageJ. Calculation of the NRRS was done according to the procedure set forth by Curtis (2018). The measurements used for this calculation are pharyngeal area at hold (while patient holds 1 tsp thin liquid in oral cavity before any posterior oral transport has begun), and pharyngeal residue after swallow (after majority of bolus has passed through the upper esophageal sphincter. Screenshots were taken at both time points and imported into ImageJ software. Patient identities were blinded and order randomized during screenshot collection and NRRS calculation.

Patient time-points (i.e., baseline, post-SND) were un-blinded at this point for analysis.

Statistical Analysis

In cases where patients had multiple swallows for the same bolus volume and/or viscosity, the first swallow of the duplicate pair was accepted and all repeating swallows were excluded. RStudio (version 3.2.1, 2015) was used for all analyses. Participants with any missing data were removed from the analysis in a case-wise fashion.

A 2-viscosity (thin vs. pudding) x 3 time (baseline vs. 1 month vs. 3 months post surgery) two-way repeated measures analysis of variance (ANOVA) was conducted to assess the effects of bolus type and time since surgery on pharyngeal residue, with post-hoc t-tests if needed where appropriate.

Results

A 2-viscosity x 3-time repeated measures ANOVA revealed no significant main effects of bolus viscosity or time (*p*s > 0.05). The viscosity x time interaction was also not significant ($p > 0.05$). SND did not influence residue management across time, regardless of bolus viscosity.

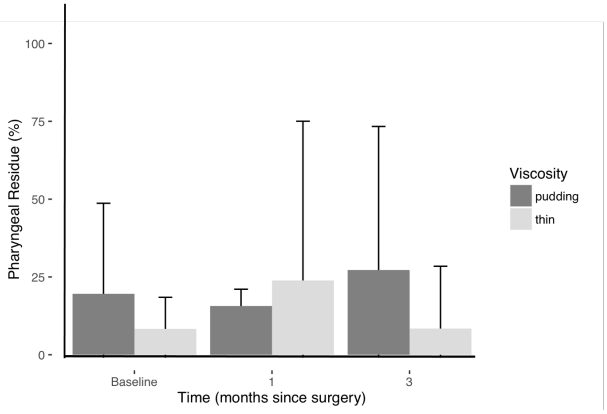

Figure 1. Percent pharynx filled with residue after swallow of 1 tsp pudding and thin liquid bolus, pre-SND surgery, and 1- and 3-months post-SND surgery.

Discussion

Findings from Study 2 reveal that residue management (as indicated by % pharynx filled with residue) abilities in HNC patients treated with CRT and SND do not vary from pre-surgery to post-surgery, regardless of bolus viscosity. Though no research on residue has been conducted using SND patients, Barbon et al. (2020) also found that in oropharyngeal cancer patients treated with RT only, treatment was not associated with increased residue on thin liquids (though these patients were not treated with SND). Since residue has been shown to be a significant predictor of QOL (Meyer et al., 2017), the results from this small study are consistent with available literature that SND does not adversely affect patient dysphagia-related QOL.

Visually, it appears that there may potentially be an effect of thin liquid at the 1-month time period, though it may be masked by the large amount of variability. Another approach for analyzing this data might have been to ditchotomize residue (e.g., Barbon et al., 2020) based on healthy swallow reference values for thin liquids (Steele et al., 2019). Especially in cases where

data is skewed with a large number of 0% responses (as was somewhat the case here), this method may be another valid way of capturing statistical differences. Intuitively, this may also provide more clinically digestible results if clinicians are used to thinking in a categorical way about it (i.e., is residue a concern for this person or not?).

Aside from its small sample size, this study was limited by the use of a less-than-optimal measurement calibration. Because the data used came from clinical records that were not taken with a study purpose in mind, a measurement anchor (usually a quarter taped to the neck while in the MBS) was not used. Calibration was estimated from pixel size, and while this does provide enough information to calculate relative pharynx size for each individual, it is not gold-standard practice.

General Discussion

This study aimed to examine dysphagia-related QOL outcomes research in HNC patients who have undergone RT/CRT followed by SND. Study 1 focused on critically evaluating available literature surrounding functional, participation, social, and dysphagia-related domains of QOL of these patients, demonstrating that SND does not decrease QOL scores across many domains.

There is not research currently published that examines residue as a specific outcome variable in this population. Study 2 was a small sample repeated measures study examining the effect of SND on pharyngeal residue – showing that SND did not adversely affect patients' residue management across time or bolus viscosity. In the context of work by Meyer et al. (2017), which shows that residue is an independent predictor of QOL, results from this paper suggest that SND does not influence QOL of HNC patients after SND as far as residue is concerned.

Though results from Study 1 and Study 2 are consistent in QOL outcomes, it is essential that more research be conducted to fully capture what QOL looks like for these patients.

Because QOL is such a broad measure, even when narrowing focus to dyaphagia-related QOL, it is essential that further research use multiple QOL measures. Having physiological measures such as dysphagia-related variables like residue, penetration, and aspiration will capture functional aspects of QOL (e.g., Meyer et al., 2017; Hutcheson et al., 2016). On the other hand, in order to fully capture participation and social dimensions of QOL, one must use validated patient report measures that capture these domains. For example, Wang, Amdur et al. (2016) include multiple questionnaire measures of QOL. While this may at first appear redundant, the authors make a case for each measure capturing different aspect of QOL (e.g., general vs. head and neck vs. neck dissection specific). This, I believe, contributes to a broader understanding of the impact of this surgery, especially given that there is not a vast body of research for this population. Had there been differences in results between the measures, this would also open avenues for further research to improve outcomes for these patients. The research reviewed in Study 1 as a whole broadly captures several QOL domains, and future research should follow this precedent.

Another important factor to consider when thinking about outcomes – and especially long-term outcomes – for HNC patients is the HPV status of their cancer. Patients tend to have better prognosis (Klozar et al., 2007) and QOL (Broglie et al., 2012) outcomes if their cancer is HPV-positive. Importantly, with these patients having significantly longer survival rates, this means that they tend to live long enough to develop long-term sequelae of treatment that could affect QOL. A limitation of both Study 2 and Study 1, save for Wang, Mood et al. (2019) is the lack of reporting of HPV status. Otherwise, it can be difficult to parse out the moderating effects of this variable.

Other factors that can potentially confound the relationship between SND and QOL include characteristics of the SND itself, such as the number of levels dissected or unilateral vs. bilateral dissection. This is important because level of neck dissection differentially affects QOL: Kuntz and Ernest (1999) demonstrate that scores on multiple measures of QOL decrease with increasingly involved neck dissection. All three appraised papers in Study 1 as well as the data analysis presented in Study 2 at least report neck dissection characteristics; although Wang, Amdur et al. (2016) is the only work that statistically accounts for this variable. In Study 2, all patients had unilateral neck dissection. For further research, these variables should be collected and accounted for when making conclusions about QOL.

Given the known acceptable survival and mortality rates associated with SND after RT/CRT (e.g., Chung et al., 2014; Robbins, 2005), we can now begin to add a QOL piece to discussions about SND outcomes. Ultimately, there are still variables that need to be accounted for and explored in researching QOL for these patients. Results from Study 1 and Study 2 indicate that SND as a treatment option to increase survival outcomes for HNC patients does not decrease QOL even as an additional invasive procedure.

Clinical Implications

Clinically, it is important for clinicians working with HNC patient population to be aware of dysphagia-related outcomes associated with the SND procedure. When examining these types of variables, clinicians must expand their frame of thinking beyond complications associated with penetration and aspiration in the context of aspiration pneumonia. They must be able to counsel patients about *all* risks and benefits of the SND procedure, and these include QOL parameters. For speech-language pathologists, the results from this study are highly suggestive that SND will not lower patient QOL in terms of functional, participation, and social aspects. Though more research is needed, patients apprehensive about the development of swallowing difficulties as a direct result of this additional surgery can be comforted by the that idea SND is not associated with decreases in dysphagia-related QOL.

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