Critical Review:

The Effect of Pretreatment Swallowing Exercises on Long-Term Outcomes after (Chemo) Radiation Therapy for Head and Neck Cancer.

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Introduction

Although organ-preservation approaches to cancer treatment aim to optimize functional outcomes, dysphagia is prevalent among head and neck (H&N) cancer survivors after radiation therapy (RT) (Agarwal et al., 2011; Rosenthal et al., 2006). Progressive RT-induced fibrosis and neuropathy ultimately impair the range of motion, strength, and sensitivity of the swallowing mechanism, increasing the risk for chronic or latent dysphagia (Hutcheson et al., 2012; Lazarus, 2006; Rosenthal et al., 2006; Smith et al., 2000). Potential long-term consequences include gastrostomy (G-tube) dependence, dietary limitations, and reduced quality of life (QOL) (Hutcheson et al., 2012).

Therapeutic swallowing exercises are commonly prescribed by Speech Language Pathologists (SLPs) to mitigate post-RT dysphagia. These exercises are intended to offset specific physiological swallowing deficits, such as reduced tongue-base strength, tongue-base retraction, pharyngeal strength, epiglottal deflection, and laryngeal excursion (Wall, Ward, Cartmill, & Hill, 2013). Literature shows daily swallowing exercise improves various short-term dysphagia outcomes (≤ 6 months post-RT), especially when exercise regimens are initiated prior to radiation treatment ("pretreatment exercise") versus after radiation ("post-treatment exercise") (Carnaby-Mann et al., 2012; Carroll et al., 2008; Duarte et al., 2013; van der Molen, 2011; Virani, 2013). Consequently, pretreatment exercise maintained throughout RT is becoming the standard of care across medical institutions.

Given the progressive effects of RT and potential for latent dysphagia, the long-term impact of pretreatment exercise must be explored. Unfortunately, adherence to pretreatment exercise is impeded by pain, fatigue, and nausea experienced by patients (Shinn et al., 2013). Evidence of lasting benefits would increase incentive for patients to maintain adherence despite discomfort, and provide further justification for this clinical recommendation.

Objectives

The primary objective of this paper is to critically review existing literature examining the effect of pretreatment swallowing exercise on long-term dysphagia-related outcomes in patients treated with radiation for H&N cancer.

Methods

Search Strategy

A literature search was conducted through PubMed, Medline-Ovid, and Scopus computerized databases using the following key terms: ((swallowing) OR (dysphagia)) AND ((cancer) OR (head and neck)) AND ((exercise) OR (strength*)). The search was limited to articles written in English.

Selection Criteria

Studies included in this review were required to examine the effect of pretreatment swallowing exercises on at least one long-term (≥ 1 year post-RT) dysphagia-related outcome in patients with H&N cancer who received radiation alone or in conjunction with chemotherapy.

Data Collection

The literature search yielded the following types of articles: randomized controlled trial (RCT) (2), and cohort study (3).

Results

Randomized Controlled Trials

In a study of 26 H&N cancer patients receiving chemoradiation therapy (CRT), Kotz et al. (2012) examined the effect of pretreatment swallowing exercises on oral intake and quality of life (QOL). The experimental group was prescribed the following daily exercises prior to CRT: (a) effortful swallow; (b) super-supraglottic swallow; (c) tongue hold; (d) tongue retraction; (e) Mendelsohn maneuver. The control group received swallowing intervention after concluding CRT if dysphagia symptoms were reported.

Intention-to-treat analyses were performed using appropriate statistical methods (Wilcoxon Rank Sum Test; Kruskal-Wallis Test). No significant between-group differences were found 12 months post-CRT on the Functional Oral Intake Scale (FOIS) and the Performance Status Scale for Head and Neck Cancer Patients (PSS-H&N). Poor adherence to exercise by the experimental group may account for these null findings. Only 31% of pretreatment exercisers were adherent to the regimen throughout CRT. Controlling for non-adherence may have exposed true treatment effects. Furthermore, the small sample limits the power of this study to detect statistically significant differences, and clinical measures of significance were not reported.

Additional weaknesses of this study include administration of swallowing therapy by the first author (unblind intervention; conflict of interest), and potential confounds including daily journaling and weekly follow-ups assigned to the experimental group only. These factors may have inflated between-group differences, albeit below threshold of significance. Strengths of this study include the level I design, use of validated measurement tools, and blind data collection. Overall, this study provides weak suggestive evidence that pretreatment exercise does not effect long-term outcomes.

Van der Molen et al. (2013) compared the effects of 2 pretreatment exercise regimens on multidimensional dysphagia outcomes in 29 patients with advanced H&N cancer. The experimental group performed: (a) passive mouth opening with the TheraBite™ device; (b) open-mouth swallow. The control group performed standard exercises: (a) jaw stretch; (b) tongue base stretch; (c) effortful swallow; (d) Masako maneuver; (e) super-supraglottic swallow. Change over time data was obtained using appropriate statistical methods (McNemar's test with Bonferroni correction). Grouped analysis showed significantly lower incidence of post-swallow residue, enteral feeding, and abnormal diet at 1 and 2 years compared to 10 weeks post-CRT. Weight also increased significantly between 1 and 2 years. In subgroup analyses, diet and weight changes reached significance for the experimental group exclusively.

Strengths of this study include the use of a multidimensional assessment protocol involving validated measurement tools, and confirmation of intra- and interrater reliability for videofluoroscopic observations. This study is limited by lack of control for pretreatment exercise. Since both groups performed pretreatment exercise regimens, the RCT design does not address the present research question. Relevant data resembles a weaker single group pre-posttest design. Maturation effects threaten internal validity since spontaneous recovery may account for observed findings. Moreover, attrition may systematically exclude patients who responded less well to pretreatment exercise from later follow-up. Consequently, evidence provided by this study is equivocal.

Cohort Studies

Hutcheson et al. (2013) evaluated the effects of adherence to pretreatment exercise and maintenance of oral intake throughout CRT on long-term diet status in 497 patients with pharyngeal cancer. Individualized exercise regimens included: (a) modified Shaker exercise; (b) jaw stretch; (c) supraglottic swallow; (d) Valsalva maneuver; (e) falsetto; (f) lingual protrusion/retraction; (g) yawn; (h) gargle; (i) Masako maneuver; (j) effortful swallow. Appropriate statistical methods (chi-square; *t*-test; regression analyses) were employed. Adherence to pretreatment exercise was independently associated with significantly shorter G-tube dependence and greater odds of returning to a normal diet (odds ratio, 4.0 [95% CI, 1.9-6.4]). Outcomes were optimized for patients who both adhered to exercise and maintained oral intake throughout treatment.

This study is limited by possible response bias in self-reports of adherence. Strengths include the robust sample size, statistical control of clinically relevant confounds (i.e., age, baseline diet, tumor characteristics, treatment type), and use of clinically significant descriptive statistics (i.e., odds ratios). Evidence provided by this level II study is compelling.

Kulbersh et al. (2006) investigated long-term dysphagia-specific QOL in 37 patients assigned the following swallowing exercises pre- or post-treatment: (a) Mendelsohn maneuver; (b) Shaker exercise; (c) tongue hold; (d) tongue resistance. QOL was measured an average of 15 months post-CRT with the M. D. Anderson Dysphagia Inventory (MDADI). Appropriate statistical analyses (chi-square; *t*-test) revealed significantly higher ratings of global, emotional, and physical QOL domains associated with pretreatment compared to post-treatment exercise.

Strengths of this study include use of a validated QOL measure, and control of systematic differences in patient characteristics between groups. Limitations include possible confounds caused by earlier recruitment and later assessment of the post-treatment group. Overall, the applicability of this evidence in investigating long-term outcomes is somewhat restricted by the wide variability in assessment timelines, with some evaluations completed early as 6

months post-CRT. This level II study ultimately provides suggestive evidence.

Shinn et al. (2013) examined the link between adherence to individualized pretreatment swallowing exercise and long-term dysphagia-specific QOL in 78 patients. Adherence was inferred based on clinical documentation of patients' competency with assigned exercises at follow-up appointments. Appropriate statistical analysis (*t*-test) of MDADI scores showed significantly better QOL in patients who adhered to pretreatment exercise compared to nonadherent patients.

This evidence is strengthened by the large sample size and use of a validated QOL measure. However, the validity of this study is undermined by potentially significant methodological issues. Foremost, adherence was poorly operationalized. The authors' rationale for inferring adherence through exercise competency was insufficient: they claimed regular home practice was necessary for adequate demonstration of exercises at follow-up sessions. This assertion considers the specificity of this assessment approach, but not the sensitivity. Conceivably, an adherent patient may be unable to demonstrate exercises at follow-up due to incidental factors such as acute fatigue or nausea, rather than failure to practice. Moreover, this definition of adherence does not account for variations in frequency, intensity, or duration of home practice. Patients with fewer disease-related complications may be able to demonstrate competency with less practice. Furthermore, fewer complications may translate into superior long-term QOL outcomes, irrespective of actual swallowing exercise adherence. The content validity of this study is consequently limited. Participants were also drawn from a larger-scale depression intervention study which undermines the generalizability of findings. Despite the level II design of this study, the evidence is equivocal.

Discussion

The reviewed literature provides limited suggestive evidence of improved long-term dysphagia-related outcomes for patients who perform pretreatment swallowing exercise. Control conditions employed throughout the research emphasize either intervention timing or adherence, utilizing post-treatment exercise or non-adherence for comparisons.

Adherence to pretreatment exercise is supported by compelling evidence of superior diet outcomes (Hutcheson et al., 2013). Research demonstrating improved QOL is equivocal due to major methodological limitations (Shinn et al., 2013). Overall, adherence to pretreatment exercise appears to be advantageous. This evidence does not address intervention timing, and consequently, cannot directly support clinical decisions to implement exercises before cancer treatment.

Literature demonstrating the relative long-term benefit of pretreatment versus post-treatment exercise is contradictory. Suggestive evidence reveals superior QOL (Kulbersh et al., 2006), as well as unaffected QOL and oral intake (Kotz et al., 2012). However, null findings are undermined by lack of control for poor rates of exercise adherence. Evidence suggesting superior outcomes after pretreatment exercise compared to post-treatment exercise is tentative.

Interpretation of overall results is limited by differences in design and methodology among the 5 reviewed studies. Heterogeneous patient characteristics, disease/treatment factors, exercise regimens, control conditions, assessment timelines, and outcome measures restrict direct comparisons of findings.

Crucially, many disease and treatment factors that differ between studies are independent predictors of dysphagia after RT (Langendijk et al., 2009). Between-study differences in tumor characteristics are particularly important since degree of dysphagia risk depends on tumor size, tumor site, and the associated dose distribution of radiation (Langendijk et al., 2009). Oropharyngeal cancer was most often examined in the literature, however, 2 studies also incorporated laryngeal cancer (Kulbersh et al., 2006; van der Molen et al., 2013), and 1 study examined pharyngeal cancer exclusively (Hutcheson et al., 2013).

Vast differences in pretreatment exercise regimens between studies also limits synthesis of the findings. Prescribed exercise varied widely in type, dose, and intensity. Regimens consisted of 2 to 11 exercises, with 18 distinct exercises utilized across the research. Overall, exercises targeted tongue-base strength and retraction, pharyngeal strength, laryngeal excursion, and upper esophageal sphincter opening. It is impossible to determine the impact of specific exercise factors due to diversity within and between studies.

Several gaps in the literature remain. Firstly, the duration of exercise practice after concluding RT was not addressed by the research. Continued practice would likely prolong exercise benefits, affecting long-term outcomes. Given the risk of latent dysphagia, exercise duration is an important consideration.

Secondly, only a single study evaluated swallowing function directly (van der Molen, 2013). The goal of

pretreatment exercise is to improve physiological function, therefore, direct measures of swallowing ability provide fundamental insight into their effectiveness. Unfortunately, limited availability, expense, and inherent risk to participants may preclude the use of instrumental assessment in many research studies (Agarwal et al., 2011).

Finally, clinically relevant descriptive statistics were conspicuously absent from all but one study (Hutcheson et al., 2013). Effect size measures are necessary to identify the magnitude of treatment outcomes and illuminate the clinical importance of findings. This information facilitates clinical decision-making and justifies practical applications of research.

Conclusion

Research investigating the long-term effects of pretreatment exercise remains immature. Collectively, this literature review presents early suggestive evidence of improved long-term diet and QOL outcomes associated with pretreatment exercise. The research employed moderately strong designs, appropriate statistical methods, and validated outcome measures. Careful interpretation is necessary due to some methodological limitations and heterogeneity within and between studies.

Additional research is necessary to address the limitations discussed. Recommendations for future research include:

- Investigate pretreatment versus post-treatment exercise with control for adherence to clarify long-term effects.
- Examine long-term outcomes in large RCT studies.
- Determine the optimal type, dose, and intensity of pretreatment exercise.
- Explore effects of exercise duration after RT.
- Investigate the influence of disease/treatment factors on pretreatment exercise outcomes.
- Employ direct measures of swallowing function.
- Report clinically relevant results.

Clinical Implications

Pretreatment swallowing exercises are commonly used to mitigate acute dysphagia after radiation-based treatments for H&N cancer. This practice is becoming standard of care as evidence of short-term benefits accumulates. Since dysphagia can develop years after RT, it is important for SLPs to consider the long-term impact. Overall, early suggestive evidence of improved long-term outcomes must be interpreted cautiously. Without effect size measures, the clinical relevance of findings remains uncertain. Moreover, previously discussed limitations present challenges to clinical application. Due to diversity among the studies, the research cannot clearly inform appropriate selection of pretreatment exercises or outcome expectations for specific patients in the H&N population.

Despite merely tentative long-term evidence supporting the use of pre- versus post-treatment exercise, established short-term benefits justify the early initiation of exercise programs targeting strength and range of motion (Carnaby-Mann et al., 2012; Carroll et al., 2008; Duarte et al., 2013; van der Molen, 2011; Virani, 2013). Stronger long-term evidence provided by adherence studies can be used to substantiate this clinical recommendation, and to counsel patients on the importance of maintaining practice throughout cancer treatment.

Further research is needed to explore the long-term impact of pretreatment exercise, and to determine the type, dose, intensity, and duration of exercise required to maximize feasibility and optimize outcomes.

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