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Postoperative Radiotherapy and Facial Nerve Outcomes Following Nerve Repair: A Systematic Review

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Abstract

Objective. To compare outcomes of facial nerve repair or grafting following facial nerve-sacrificing procedures among patients treated with and without postoperative radiotherapy (RT).

Data Sources. PubMed, OVID, Conference Papers Index, Cochrane Library, ClinicalTrials.gov.

Review Methods. Databases were searched using terms including "facial nerve," "graft," "repair," and "radiotherapy." Abstracts mentioning facial nerve repair and evaluation of facial nerve function were included for full-text review. Studies that utilized the House-Brackmann or similar validated scale for evaluation of postoperative facial nerve function were selected for review. All identified studies were included in a pooled *t* test analysis.

Results. Twelve studies with 142 patients were included in the systematic review. All 12 studies individually demonstrated no significant difference in facial nerve outcomes between patients who received postoperative radiation and patients who did not. A pooled *t* test of data from all studies also demonstrated no significant difference in postoperative facial nerve function between the postoperative RT and non-RT groups (t stat = 0.92, $p = .36$).

Conclusion. This analysis, including 12 studies, demonstrated that among patients undergoing facial nerve grafting or repair, there was no significant difference in postoperative facial nerve function between postoperative RT and non-RT patients. Due to the small sample size and variability in study methods, further studies directly comparing outcomes between patients with and without postoperative RT would be beneficial.

Keywords

facial nerve sacrifice, House-Brackmann, parotidectomy, radiation, radiotherapy, repair graft, temporal

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Facial nerve injury can result in functional deficits and deformities that negatively impact patients' quality of life and cause emotional distress.[1] Resection within the parotid gland or temporal bone risks injury to the facial nerve.[2] Furthermore, based on the pathology, postoperative radiation therapy (RT) may be required to improve local disease control and the potential for long-term survival.[3,4] When tumor resection requires facial nerve sacrifice, direct facial nerve repair or nerve grafts have been successful in restoring the function of the nerve.[5,6]

The effects of postoperative RT on functional outcomes after facial nerve repair or grafting are debated. Historical studies evaluating the impact of postoperative RT on functional outcomes after facial nerve repair demonstrated worse outcomes among patients receiving RT.[7-9]

More recent studies utilizing standardized Facial Nerve Grading Scales (FNGS), however, have demonstrated that facial nerve outcomes are not significantly worse in patients receiving postoperative RT. This evidence consists of mostly small, individual retrospective studies, which may have been inadequately powered to detect small differences between outcomes and carry a higher risk of type 2 error. Aggregation of results increases power, allowing for the potential detection of differences not detected by smaller studies. We, therefore, sought to systematically review the existing literature and consolidate the available data on facial nerve outcomes to better answer this clinical question. The objective of this systematic review is to compare facial nerve function in patients who underwent direct facial nerve repair or

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grafting following facial nerve sacrifice during tumor resection, based on the presence or absence of postoperative RT.

Methods

The study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines as well as Cochrane Handbook recommendations[10,11] (see Supplemental Item 1, available online, for the PRISMA checklist. Institutional review board approval was not required).

Information Sources and Search Strategy

Two authors (H.L.K. and R.H.J.) searched PubMed, OVID Medline, and Conference Papers Index using terms including "facial nerve," "graft," "repair," "radiotherapy," as well as associated MeSH terms. This search was adapted for Cochrane Database and Clinicaltrials.gov to search for any unpublished data. Reference lists from all resulting papers were also searched for additional eligible studies. No limits were applied for language, publication date, or publication status. The last search was run in November 2021. The authors were contacted to obtain additional information, if applicable (see Supplemental Item 2, available online, for a sample search strategy).

In reviewing full texts, inclusion criteria consisted of randomized clinical trials, prospective clinical trials, or retrospective chart reviews studying facial nerve function following nerve repair procedures. Any participant who underwent facial nerve sacrifice with subsequent facial nerve repair, via direct repair or interposition graft, and postoperative evaluation of facial nerve function, accompanied by an indication of postoperative RT administration, was considered. Primary outcome measures included a postoperative or postradiation measurement of facial nerve function using a standardized facial nerve gradings scale, such as the House-Brackmann (HB) scale, or a scale that can be directly converted to a validated grading scale.[12] All identified studies (including studies with only a postoperative RT cohort), were included in a pooled *t* test.

Exclusion criteria consisted of individual case reports, patients who additionally underwent brachytherapy, and studies lacking postoperative facial nerve evaluation utilizing a validated scale. Patients undergoing nerve transposition reanimation procedures, as well as studies incorporating dynamic reanimation with free flap reconstruction (with a nerve source intended to reanimate the face), or a dynamic regional flap with the same intent, were excluded to reduce additional sources of heterogeneity. Notably, free flaps utilized for purely soft tissue reconstruction were included.

Data Collection Process and Data Items

Two authors (H.L.K. and R.H.J.) extracted data from eligible studies. Extracted data were compared, with any discrepancies being resolved through discussion with the third author (S.L.O.). When information regarding any of the above was unclear, the authors of the studies were contacted for further details.

Measures of facial nerve function at any postoperative time point using a standardized FNGS were collected. Preoperative facial nerve function data were also collected if reported. Data were also sought for the type of procedure performed requiring facial nerve sacrifice, the type of facial nerve repair, and information pertaining to RT administration.

Effect Measures and Synthesis of Results

Rstudio was used for statistical analysis. A pooled 2-tailed *t* test, including all studies, both with and without non-RT cohorts, was performed. The level of significance was defined as a $p < .05$.

Assessment of Risk of Bias

To ascertain the validity of the 12 eligible nonrandomized trials, 2 reviewers worked independently using the Risk of Bias in Non-Randomized Studies-of Interventions (ROBINS-I) tool, a tool recommended by Cochrane Reviews to assess for bias in nonrandomized studies.

Additional Analyses

Individual preoperative HB scores were extracted when available. A secondary analysis was performed with the objective of comparing the difference in preoperative and postoperative HB scores based on the presence of RT, using a pooled *t* test. Additionally, a Wilcoxon-Mann-Whitney *U* test was performed comparing the change in average pre- to postoperative scores among the RT cohort to that of the non-RT cohort.

Results

Study Selection

The search of PubMed, OVID MedLine, Conference Papers Index, Cochrane Library, and ClinicalTrials.gov provided a total of 479 citations. Reference searches of the resulting citations provided an additional 479 citations. After adjusting for duplicates, 758 remained. Of these, 545 studies were discarded based on abstract reviews. Two hundred thirteen remaining studies were examined through full-text review. After a full-text review, 201 studies were excluded, as they did not meet the inclusion criteria.

Authors from 5 studies were contacted to obtain a subset of data that would meet eligibility criteria. Four authors no longer had access to their data, whereas 1 author provided data that was eligible for inclusion.

Twelve studies met the inclusion criteria and were included in the systematic review.[2,9,13-22] All 12 studies were included in a pooled *t* test. The search process and results of the study selection are summarized in **Figure 1**.

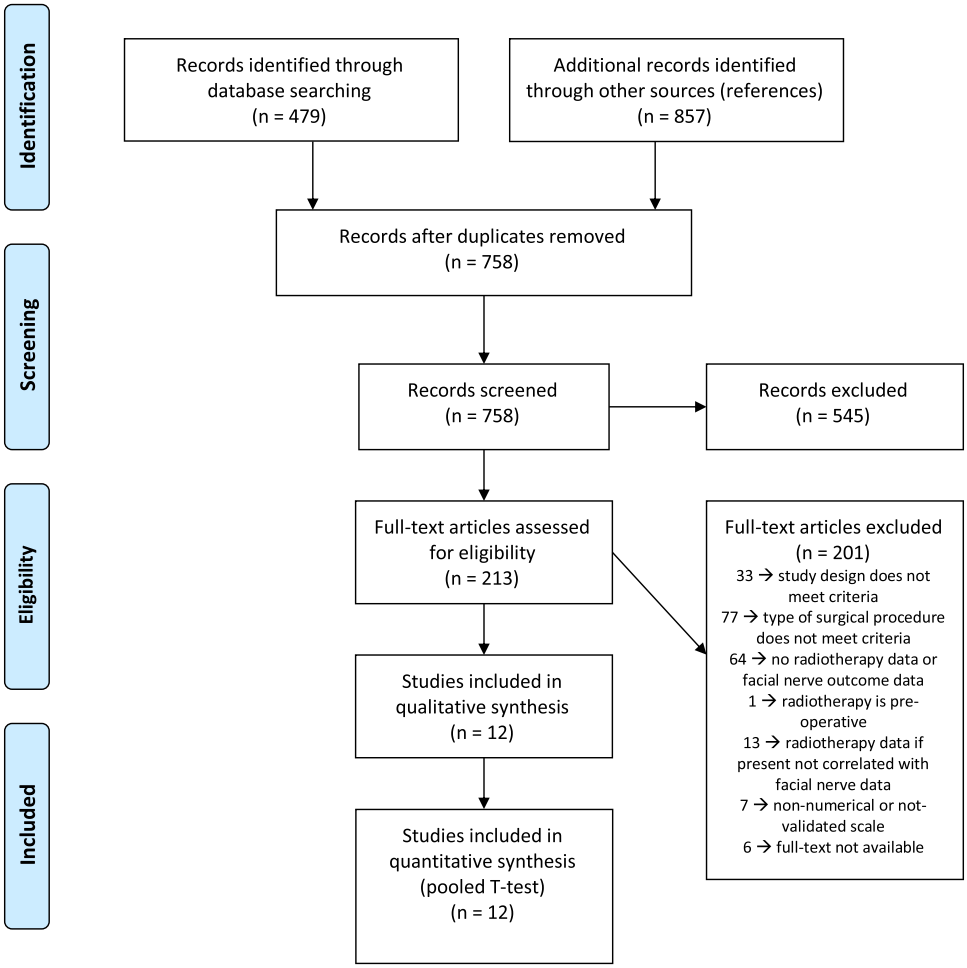

Figure 1. Flow diagram of study selection.

Study Characteristics

All 12 included studies were retrospective reviews, published in English. There was a total of 142 participants. Ninety-eight of these participants underwent postoperative RT, whereas 44 participants did not. Six of the 12 studies[2,9,18,20-22] reported preoperative and postoperative scores for secondary analyses comparing the mean preoperative scores of the RT cohort and non-RT cohort as well as the pre- to postoperative change among the 2 cohorts.

Surgical ablative procedures included parotidectomy of various degrees (ranging from radical to superficial), temporal bone procedures, or mandibulectomy. The facial nerve repairs included end-to-end repair or cable nerve grafting utilizing the sural, great auricular, cervical plexus, lateral femoral cutaneous, motor nerve to vastus lateralis, or ansa cervicalis nerves. Three studies utilized free flaps for soft tissue reconstruction, without dynamic reinnervation.[2,13,17] Postoperative radiation doses ranged from 3000 to 7630 cGy. The duration of follow-up ranged from 3 to 117 months among studies that reported follow-up timing.

The Gidley et al[9] study utilized a modified Repaired Facial Nerve Recovery Scale using similar scoring (ranging from A to F, with F being the worst outcome). The Lee et al[15] study utilized the FNGS 2.0, a 2009 revision of the HB grading system, with grading using similar scoring (from I to VI, with VI being the worst outcome). All other studies utilized the HB scale.

A summary of information regarding surgical procedures and postoperative measurements can be viewed in **Table 1**.

Risk of Bias in Studies

Based on the ROBINS-I assessment, none of the included studies were at high risk of bias. Two studies[14,21] were considered to be at moderate risk of bias due to bias in the measurement of outcomes; in these studies, measurements could have been influenced by knowledge of the intervention received (see Supplemental Item 3, available online, for the summary of bias assessments).

Results of Individual Studies

The results of individual studies are summarized in **Table 2**.

Results of Syntheses

Among the 12 studies included in the pooled *t* test, using HB or similar scales ranging from 1, indicating normal

Table 1. Results of Individual Studies

Author	Cohorts	Patient N (RT/non-RT)	Procedure	Repair method	RT dosing (Gy)	Follow-up length (months)	Outcome measure
Biglioli et al[2]	RT/non-RT	7/1	RP	CG (TD), LD flap	NR	>12	HB
Ciolek et al[13]	RT/non-RT	12/1	RP	CG (MNVL), ALT flap	NR	11.38 (3-28)	HB
Gidley et al[9]	RT/non-RT	1/24	Temporal bone	CG (GA or sural)	NR	21.04 (4-60)	HB modification
Gidley et al[14,a]	RT only	12/—	Parotidectomy, temporal bone, or mandibulectomy	CG (varying donor sites), or direct repair	60 (30-66)	37.8 (3-117)[b]	HB
Lee et al[15]	RT/non-RT	7/5	Parotidectomy or schwannoma resection	CG (sural)	NR	21.75 (8-61)	FNGS 2.0, HB revision
McGuirtet al[16]	RT only	9/—	Parotidectomy	CG (GA or sural)	59.4 (33.75-76.3)	NR	House scale
Motomura et al[17]	RT/non-RT	2/2	Parotidectomy	CG (sural), SCM, or pectoralis flap	46-50	70.5 (59-76)	HB
Park et al[18]	RT only	11/—	Parotidectomy	CG (sural)	NR	6-12	HB
Preis et al[19]	RT only	14/—	Parotidectomy	CG (GA or cervical plexus), or direct repair	NR	12	HB
Reddy et al[20]	RT/non-RT	6/4	RP	CG (cervical sensory plexus)	49.87 (40-59.4)	24	HB
Sanchez-Burgos et al[21,a]	RT only	3/—	RP + petrosectomy	CG (GA or sural)	50-66	14 (6-24)	HB
Yi et al[22]	RT/non-RT	(14/7)	Parotidectomy, transmastoid, or cholesteatoma	CG (sural)	58.24 (50-64.4)	NR	HB

Abbreviations: ALT, anterolateral thigh; CG, cable graft; FNGS, Facial Nerve Grading Scale; GA, great auricular; HB, House-Brackmann scale; LD, latissimus dorsi; MNVL, motor nerve to vastus lateralis; NR, not reported; ROBINS-I, Risk of Bias in Non-Randomized Studies-of Interventions; RP, radical parotidectomy; RT, radiation therapy; SCM, sternocleidomastoid; TD, thoracodorsal.

[a]Risk of moderate bias according to the ROBINS-I scale.

[b]Most results were reported from a 12-month postoperative visit.

Table 2. Postoperative Facial Nerve Outcomes Using the House-Brackmann or Similar Scale

Author	RT group mean (SD), N 1 = best, 6 = worst	Non-RT group mean (SD), N 1 = best, 6 = worst
Biglioli et al[2]	2.00 (0.82), n = 7	1.00 (0.00), n = 1
Ciolek et al[13]	4.33 (1.37), n = 12	6.00 (0.00), n = 1
Gidley et al[9]	6.00 (0.00), n = 1	3.33 (0.82), n = 24
Gidley et a.l[14]	3.58 (1.68), n = 12	NA
Lee et al[15]	3.42 (0.53), n = 7	3.80 (1.10), n = 5
McGuirt et al[16]	2.88 (0.93), n = 9	NA
Motomura et al[17]	2.50 (0.71), n = 2	3.00 (0.00), n = 2
Park et al[18]	4.55 (0.67), n = 11	NA
Preis et al[19]	3.64 (1.08), n = 14	NA
Reddy et al[20]	3.33 (0.82), n = 6	3.00 (0.00), n = 4
Sanchez-Burgos et al[21]	4.00 (1.00), n = 3	NA
Yi et al[22]	4.14 (1.29), n = 14	4.14 (1.35), n = 7

Abbreviations: NA, not applicable; RT, radiation therapy; SD, standard deviation.

facial function, to 6, indicating total paralysis, the mean postoperative facial nerve score was 3.68 (standard deviation [SD] 1.30, range 1-6) among the RT cohort and 3.48 (SD 1.07, range 1-6) among the non-RT cohort. Among the 98 patients in the RT cohort, 87 achieved at least some visible movement (88.8%), defined as a score between 1 and 5. Among the 44 patients in the non-RT cohort, 41 achieved at least some visible movement (93.2%).

The pooled *t* test, including all 12 studies, detected no significant association between treatment with RT and facial nerve outcomes (t stat = 0.92, $p = .36$).

A secondary analysis was performed using individual preoperative and postoperative scores available from 6 of the 12 studies. The preoperative mean HB score was 2.84 in the non-RT group and 2.26 in the RT group, which was not significantly different in a pooled *T* test (t stat = −1.42; $p = .16$). Among these 6 studies, the average pre- to postoperative score increase was 0.62 points (SD 1.36) in the non-RT group and 1.93 points (SD 1.97) in the RT group, with increasing scores indicating less desirable results based on the HB or similar scales utilized. A Wilcoxon-Mann-Whitney *U* test demonstrated no significant difference in the average pre- to postoperative score change between the non-RT and RT groups (W stat = 6, $p = .24$).

Discussion

The purpose of this study was to determine whether the aggregated literature demonstrates a difference in postoperative facial nerve outcomes between patients who did or did not receive postoperative RT following facial nerve repair. The results of the pooled *t* test suggest that facial nerve outcomes following nerve grafting or repair do not significantly differ based on the administration of postoperative RT. In both RT and non-RT cohorts, almost all patients achieved some visible movement following facial nerve direct repair or grafting, suggesting that patients can usually derive some level of benefit from reanimation regardless of postoperative RT administration. The outcomes of these analyses build upon the limited evidence that exists in individual studies pertaining to outcomes following facial nerve repair and the role of postoperative RT.

Secondary analyses suggest that there was no significant difference in preoperative scores, further validating our findings. A secondary analysis also did not detect a significant difference in change from preoperative to postoperative scores between RT and non-RT cohorts.

While the results of this analysis suggest that postoperative facial nerve outcomes following nerve repair do not differ with the administration of postoperative RT, the results are limited by the small number of studies and patients included. We sought uniformity among studies through the exclusion of dynamic flap repairs and brachytherapy administration as well as the inclusion of only standardized FNGS; however, variability in methodology still remains among the included studies, with differences in terms of surgical procedure, method of nerve repair, length of follow-up, and RT dosing. Notably, 2 studies included postoperative evaluation beginning at 3 months,[13,14] which may not have accounted for the full extent of recovery among these patients. Additional surgical information such as the number of neurorrhaphies, duration of preoperative facial weakness, branch-specific involvement of the facial nerve, and length of cable graft would be beneficial but were not universally available. Patient's past medical history and preoperative nutritional status may impact outcomes, and this was not accounted for within the study. Thus, the ability to control for extraneous variables in this analysis was limited. Additionally, the pooled analysis measured facial nerve outcomes using the HB grading scale or similar scales, which may not be able to detect more

granular yet clinically significant differences in facial nerve outcomes, as well as more contemporary FNGS such as the Sunnybrook Facial Grading scale, or eFACE.[23,24] It is possible that a true difference in facial nerve outcomes does exist based on the use of adjuvant radiation that could not be detected based on the limitations of these studies.

This area of study would benefit from further research, especially in the form of prospective trials with larger sample sizes and more robust data collection. A greater evidence base could better delineate the impact of postoperative RT on facial nerve outcomes following nerve repair, and how that impact varies based on the type of repair performed or based on the method of nerve repair. Further evidence could also help to understand the impact of postoperative RT based on dose or the effects on nerve transpositions that may be performed concurrently with direct grafting. In all, this information could help to better tailor care and preoperative counseling for patients who require facial nerve resection.

Conclusion

Adjuvant RT is an important aspect of treatment for some malignancies to improve local-regional control and survival.[3,4] While successful treatment of the malignancy is of paramount importance, the impact of facial paralysis on patients' quality of life can be profound,[25] and the importance of facial reanimation should not be overlooked. The results of this systematic review, though limited by several factors, provide some evidence that facial nerve reconstruction outcomes are not negatively impacted by adjuvant RT, and physicians should embrace facial nerve reconstruction at the time of nerve sacrifice whenever possible.

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Author Contributions

Hannah L. Kenny, design, analysis, manuscript preparation, critical editing; **Rachel H. Jonas**, design, manuscript preparation, critical editing, presentation; **Samuel L. Oyer**, design, manuscript preparation, critical editing.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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