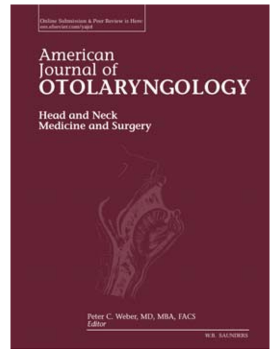
Accepted Manuscript



Facial Nerve Repair After Operative Injury: Impact of Timing on Hypoglossal-Facial Nerve Graft Outcomes

Robert J. Yawn MD, Harry V. Wright MD, David O. Francis MD, MS, Scott Stephan MD, Marc L. Bennett MD, MMHC

PII: S0196-0709(16)30024-2
DOI: doi: 10.1016/j.amjoto.2016.05.001
Reference: YAJOT 1711

To appear in: *American Journal of Otolaryngology–Head and Neck Medicine and Surgery*

Received date: 14 March 2016

Please cite this article as: Yawn Robert J., Wright Harry V., Francis David O., Stephan Scott, Bennett Marc L., Facial Nerve Repair After Operative Injury: Impact of Timing on Hypoglossal-Facial Nerve Graft Outcomes, *American Journal of Otolaryngology–Head and Neck Medicine and Surgery* (2016), doi: 10.1016/j.amjoto.2016.05.001

TITLE: Facial Nerve Repair After Operative Injury: Impact of Timing on Hypoglossal-Facial Nerve Graft Outcomes

AUTHORS: Robert J. Yawn, MD, Harry V. Wright, MD, David O. Francis, MD MS, Scott Stephan, MD, Marc L. Bennett, MD MMHC

ORIGINATING INSTITUTIONS: Department of Otolaryngology-Head and Neck Surgery, Vanderbilt University, Nashville, TN 37232

CORRESPONDING AUTHOR:
Marc L. Bennett, MD MMHC
Department of Otolaryngology-Head and Neck Surgery
The Bill Wilkerson Center for Otolaryngology & Communication Sciences 7209 Medical Center East
South Tower 1215 21st Avenue South
Nashville, Tennessee 37232-8605

Phone: (615) 875-1262
Fax: (615) 936-2887
E-mail: marc.bennett@vanderbilt.edu

FINANCIAL MATERIAL & SUPPORT: Salary support for DOF from National Institute for Deafness and other Communication Disorders (K23DC013559, L30DC012687)

CONFLICT(S) OF INTEREST TO DECLARE: There are no relevant conflicts of interest to disclose.

INSTITUTIONAL REVIEW BOARD APPROVAL: Vanderbilt University Institutional Review Board Number

KEYWORDS: facial reanimation, hypoglossal-facial nerve graft, facial paralysis, skull base, facial nerve trauma

RUNNING HEAD: Hypoglossal-Facial Nerve Grafting

ABSTRACT

PURPOSE: Reanimation of facial paralysis is a complex problem with multiple treatment options. One option is hypoglossal-facial nerve grafting, which can be performed in the immediate postoperative period after nerve transection, or in a delayed setting after skull base surgery when the nerve is anatomically intact but function is poor. The purpose of this study is to investigate the effect of timing of hypoglossal-facial grafting on functional outcome.

MATERIALS AND METHODS: A retrospective case series from a single tertiary otologic referral center was performed identifying 60 patients with facial nerve injury following cerebellopontine angle tumor extirpation. Patients underwent hypoglossal-facial nerve anastomosis following facial nerve injury. Facial nerve function measured using the House-Brackmann facial nerve grading system at a median follow-up interval of 18-months. Multivariate logistic regression analysis was used determine how time to hypoglossal-facial nerve grafting affected odds of achieving House-Brackmann grade of ≤3.

RESULTS: Patients who underwent acute hypoglossal-facial anastomotic repair (0-14 days from injury) were more likely to achieve House-Brackmann grade ≤3 compared to those that had delayed repair (OR 4.97, 95% CI 1.5-16.9, *p*=0.01).

CONCLUSIONS: Early hypoglossal-facial anastomotic repair after acute facial nerve injury is associated with better long-term facial function outcomes and should be considered in the management algorithm.

1. INTRODUCTION

Facial nerve paralysis is a well-recognized complication of skull base surgery, with documented rates of transection as high as 6%[1]. It continues to represent a significant operative morbidity despite improved surgical technique and the routine use of nerve monitors. Consequences of this injury can be devastating and include exposure keratosis and blindness, disfigurement, poor nasal airflow, oral incompetence, synkinesis, and psychological stress [2].

Management largely depends on nerve integrity. An injured, but intact facial nerve presents a unique prognostic dilemma, as it is difficult to predict the ultimate degree of recovery. In contrast, a transected nerve results in predictably severe sequelae. Several types of procedures have been devised in an attempt to rehabilitate patients with this complication[3]. One approach, first described by Korte in 1904 [4], is transposition of cranial nerve XII (hypoglossal) to the distal stump of VII (facial) (i.e., XII-VII transposition). Its primary indication is situations when the proximal portion of VII is inaccessible or nonfunctional. A second indication is complete paralysis persisting greater than one year[5]. In both instances, the goal is to provide alternate cortical input to the mimetic musculature.

Previous investigations reported that nearly all patients treated with hypoglossal-facial nerve anastomosis have some functional improvement, and that 65% achieve a House-Brackmann 3 or better [6]. However, controversy surrounds whether timing of repair affects the ultimate degree of facial mimetic recovery. The challenge exists to identify patients that will not spontaneously recover nerve function and would benefit from earlier intervention. One report failed to show an outcome association related to the interval between acoustic neuroma surgery (i.e., injury) and rehabilitation with XII-VII transposition [6]. In contrast, other studies suggest that delayed repair (greater than 1-2 years from injury) is associated with less favorable outcomes [7, 8]. The purpose of this retrospective case series is to investigate whether early rehabilitation with XII-VII transposition (0 – 14 days from injury) resulted in better outcomes (House-Brackmann (HB) grade ≤3) than patients treated in a more delayed manner.

2. MATERIALS AND METHODS

The study was performed in accordance with the Declaration of Helsinki, Good Clinical Practice, and approved by the Vanderbilt Institutional Review Board (IRB# 120693).

2.1 Subject selection. All cerebellopontine angle (CPA) surgeries for presumed vestibular schwannoma (VS) performed between 1979 and 2007 were identified. Medical records were reviewed to identify patients who: i) underwent resection of a histopathologically confirmed CPA vestibular schwannoma, ii) had postoperative facial paresis (HB 4 or greater) either by nerve transection or poor function in the setting of anatomically intact nerve, iii) underwent postoperative reanimation surgery by XII-VII nerve anastomosis, and iv) had follow-up data available postoperatively with last documented facial nerve function being used in the final analysis. Patients with known intraoperative transection of the nerve underwent early reanimation, while those with anatomically intact nerves after resection but poor function underwent delayed nerve transfer. Patients with pathology other than vestibular schwannoma (meningioma, astrocytoma, facial schwannoma) were excluded from analysis.

2.2 Variables Collected. Patient characteristics (age, gender, tobacco use, comorbid conditions [e.g., diabetes mellitus, peripheral vascular disease, hypertension, hypercholesterolemia]), initial data on the surgical resection of skull base tumor (extent of resection, nerve status at time of surgery) timing of XII-VII surgery, and outcomes were extracted from medical records. The primary outcome was facial nerve function one year after XII-VII surgery, which was graded using the House-Brackmann (HB) classification[9]. Function was evaluated and recorded pre-operatively, immediately post-operatively, and at each subsequent follow-up clinic visit. A successful outcome was defined *a priori* as HB ≤3, as patients with HB ≤3 have symmetry at rest and are able to completely close the eye.

2.3 Statistical analysis. Analyses were performed to determine whether timing of XII-VII transposition was associated with ultimate facial nerve functional outcome. The dependent variable was facial nerve function one year following XII-VII transposition defined by HB grade. For analysis, HB grades were dichotomized into ≤3 (i.e., success) or >3. Multivariate logistic regression analysis was used to estimate adjusted odds (95%

CI) of HB ≤3 at follow-up. Parametric and non-parametric tests were used as appropriate and all analyses performed using STATA 12MP (College Station, TX).

3. RESULTS

Patient and tumor characteristics are summarized in **Table 1**. The 60 patients meeting inclusion criteria were mostly female (60%) and had median age of 49.3 years (interquartile range (IQR) 37.5-60.6). Surgical approaches were translabyrinthine (66.7%), combined translabyrinthine/retrosigmoid (30.0%), middle fossa (1.7%), and retrolabyrinthine decompression (1.7%).

House-Brackmann grade 6 facial paralysis was noted in 98.3% of patients prior to XII-VII anastomosis, with the remainder demonstrating HB grade 5 paralysis. Median time interval between facial nerve injury and repair was 14 days (IQR 8-365 days). The majority of patients underwent end-to-end anastomosis of the entire hypoglossal nerve (97%) with the remainder having a partial hypoglossal nerve procedure. Facial nerve function was HB≤3 in 71.6% of patients at 374 days (IQR 352-1693) median postoperative follow-up. Thirty-four patients with nerve transection (57%) underwent hypoglossal-facial nerve anastomosis within 14 days of facial nerve injury, while 26 patients (43%) with anatomically intact facial nerves but poor function underwent hypoglossal-facial anastomosis after fourteen days of injury.

Results of multivariate analysis are shown in **Table 2**. Acute XII-VII anastomosis repair (within 14 days of facial nerve insult) showed a significant association with HB of ≤3 at last follow-up. When adjusted for patient age, repair with 14 days of facial nerve injury was associated with 4.97-fold greater odds of achieving HB of ≤3 (95% CI 1.5-16.9, p=0.01). Patient age at reanimation surgery was not associated with improved outcomes (p=0.28).

4. DISCUSSION

Facial reanimation following acute injury to the facial nerve during skull base surgery is an important aspect of postoperative rehabilitation. A variety of reanimation techniques have been advocated (primary anastomosis, cable graft, nerve-transfer), with success usually being defined as achieving a House-Brackmann grade 3 or lower, as this is associated with symmetry at rest and complete eye closure. There have been numerous case series in the literature that have shown the utility of hypoglossal-facial anastomosis in a variety of timeframes, but because of the relative infrequency of this problem, the optimal timeframe for repair is unknown[8, 10]. In these studies, shorter length of paralysis was associated with improved outcomes, and patients that had longer length of paralysis had slower onset of clinical benefit. These findings are supported by the current study, which represents the largest case-series to date assessing the results of XII-VII anastomosis for treatment of post-operative facial paralysis.

As surgical techniques of tumor resection have improved, rates of intraoperative transection of the nerves have greatly decreased. This presents a particular challenge in evaluating patients with an anatomically intact nerve but poor postoperative facial nerve function as a wide range of functional outcomes are possible. Traditionally, waiting one year has been recommended in this situation to allow spontaneous improvements in facial nerve function, as surgeons are hesitant to intervene on a nerve that may improve without further operative intervention[11]. Intraoperative stimulation of the proximal facial nerve has been used to predict patients that will have HB 1 or 2 with 98% probability if intraoperative minimal stimulus intensity was 0.05 mA or less and response amplitude was 240 mV or greater with 98%. Other algorithms have been developed to predict patients with poor outcomes, suggesting that patients with HB 6 that improve to HB 5 seven months or later have a 90% chance of a poor outcome (defined as HB 4 or greater) and that patients with HB 5 or 6 that improve to HB 4 within 10 months have an extremely low chance of poor long-term outcome[12]. These rules are largely experiential and further investigation is needed to understand which patients would benefit from earlier intervention.

To the authors' knowledge, the affect of acute repair with hypoglossal-facial nerve anastomosis (less than 14 days from injury) has not been investigated. Recent reports using split hypoglossal nerve grafts showed 92% of patients achieving HB≤3 when reanimation surgery was performed early (average time from injury to reanimation was 6 months)[13]. Our results indicate that patients who undergo hypoglossal-facial anastomosis within 14 days of injury are associated with 4.97-fold improved odds of having HB≤3 compared to those treated in a delayed manner (95% CI 1.5-16.9; p=0.01). This was independent of the original size of CPA tumor, tumor pathology, extent of resection, or patient age. Interestingly, only two patients in the series failed to reach HB 4 with treatment, one of which had XII-VII repair 10 days after initial injury and the other at three months. An important consideration is that the patients in the early reanimation group were known to have surgically disrupted nerves whereas the patients in the late reanimation group had anatomically intact but non-functioning nerves.

Variations of the original end-to-end repair technique have been described, including side-to-end grafting, partial end-to-end with interposition jump grafting, partial end to end without grafting, but all of the variations appear to have similar outcomes[14]. Facial nerve outcomes are similar in patients that undergo partial hypoglossal grafting, but when one-half of the hypoglossal nerve is left intact, patients retain tongue function and only suffer mild muscular atrophy, thus avoiding the morbidity of total hemiparesis of the intrinsic tongue musculature[15]. The majority of patients in this series underwent anastomosis of the entire hypoglossal nerve (97%) prior to the advent of partial procedures, with the remainder receiving a partial hypoglossal nerve procedure, and overall rates of success were similar to other smaller series in the literature[6].

Our study has several limitations. Some are inherent to its retrospective nature, which limits the ability to confirm data accuracy and to add further potentially useful data on these patients, including electromyographic studies. Additionally, the majority of patients received total hypoglossal anastomoses as this was the preferred method of repair during the timeframe of facial nerve injury. Currently, the authors' prefer a custom approach based on injury pattern that may include primary anastomosis, cable graft, split hypoglossal-facial anastomosis, or static reanimation techniques. There is selection and treatment bias, in that patients with known transection were treated with acute reanimation (≤14 days) and those with anatomically intact nerves were treated in a delayed fashion (>14 days). The decision to intervene is simplified with a known facial nerve transection. The challenge remains how to predict outcomes and manage patients with an intact facial nerve with poor function. Data herein suggest that earlier time to intervention may be associated with improved outcomes, but identifying patients with intact nerves that will not improve over time is a complex task that this study was not designed to accomplish. Currently in management, the authors consider electromyographic studies at approximately 6 months post-injury in patients that have shown minimal improvement to consider reanimation in patients with minimal response based on clinical observation and the aforementioned predictive study by Rivas et al[12].

5. CONCLUSION

Hypoglossal-facial anastomosis is a reliable option for rehabilitation of patients with acute facial nerve injury. Patients may benefit from early hypoglossal-facial nerve anastomosis reanimation surgery, but further investigation is needed to confirm this association. Better predictors are needed in the immediate postoperative period to understand which patients would benefit from acute intervention.

REFERENCES

[1] Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve--preservation and restitution of function. Neurosurgery 1997; 40: 684-694; discussion 694-685.
[2] Melvin TA, Limb CJ. Overview of facial paralysis: current concepts. Facial Plast Surg 2008; 24: 155-163.
[3] Gordin E, Lee TS, Ducic Y, Arnaoutakis D. Facial nerve trauma: evaluation and considerations in management. Craniomaxillofac Trauma Reconstr 2015; 8: 1-13.
[4] W K. Ein Fall van Nerventropfung. Des Nervus facialis auf den Nervus hypoglossus. Deutch Wochenschr; 17.
[5] Gavron JP, Clemis JD. Hypoglossal-facial nerve anastomosis: a review of forty cases caused by facial nerve injuries in the posterior fossa. Laryngoscope 1984; 94: 1447-1450.
[6] Sood S, Anthony R, Homer JJ, Van Hille P, Fenwick JD. Hypoglossal-facial nerve anastomosis: assessment of clinical results and patient benefit for facial nerve palsy following acoustic neuroma excision. Clin Otolaryngol Allied Sci 2000; 25: 219-226.
[7] Yetiser S, Karapinar U. Hypoglossal-facial nerve anastomosis: a meta-analytic study. Ann Otol Rhinol Laryngol 2007; 116: 542-549.
[8] Samii M, Alimohamadi M, Khouzani RK, Rashid MR, Gerganov V. Comparison of Direct Side-to-End and End-to-End Hypoglossal-Facial Anastomosis for Facial Nerve Repair. World Neurosurg 2015.
[9] House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg 1985; 93: 146-147.
[10] Dalla Toffola E, Pavese C, Cecini M, Petrucci L, Ricotti S, Bejor M, Salimbeni G, Biglioli F, Klersy C. Hypoglossal-facial nerve anastomosis and rehabilitation in patients with complete facial palsy: cohort study of 30 patients followed up for three years. Funct Neurol 2014; 29: 183-187.
[11] Boahene K. Facial reanimation after acoustic neuroma resection: options and timing of intervention. Facial Plast Surg 2015; 31: 103-109.
[12] Rivas A, Boahene KD, Bravo HC, Tan M, Tamargo RJ, Francis HW. A model for early prediction of facial nerve recovery after vestibular schwannoma surgery. Otol Neurotol 2011; 32: 826-833.
[13] Hayashi A, Nishida M, Seno H, Inoue M, Iwata H, Shirasawa T, Arai H, Kayamori R, Komuro Y, Yanai A. Hemihypoglossal nerve transfer for acute facial paralysis. J Neurosurg 2013; 118: 160-166.
[14] Le Clerc N, Herman P, Kania R, Tran H, Altabaa K, Tran Ba Huy P, Sauvaget E. Comparison of 3 procedures for hypoglossal-facial anastomosis. Otol Neurotol 2013; 34: 1483-1488.
[15] Cusimano MD, Sekhar L. Partial hypoglossal to facial nerve anastomosis for reinnervation of the paralyzed face in patients with lower cranial nerve palsies: technical note. Neurosurgery 1994; 35: 532-533; discussion 533-534.

TABLES

TABLE 1

Characteristics and Outcomes		Percent (n=60)
Gender	Male	40%
	Female	60%
Age at surgery, median years (IQR)		49.3 (37.5 – 60.6)
Resection Approach	Translabyrinthine	66.6%
	Combined*	30.0%
	Retrolabyrinthine	1.7%
	Middle Fossa	1.7%
Extent of resection	Total	97%
	Subtotal	3%
Pre-repair HB	5	1.7%
	6	98.3%
Time to repair, median days (range, IQR)		14 (0-987, 8 – 365)
Type of XII-VII	Total 12**	97%
	Partial 12**	3%
Post-repair HB	>3	28.4%
	≤3	71.6%
Follow-up time, days (median, IQR)		374 (352 – 1693)

*IQR=Interquartile range, *translabyrinthine and retrosigmoid*

*** Total 12- Total hypoglossal-facial nerve anastomosis, Partial 12- Partial use of the hypoglossal nerve leaving half of the nerve intact to supply intrinsic tongue musculature.*

TABLE 2

Covariates		**Odds of HB≤3 (95% CI)**	**P-value**
Female		1.35 (0.44 – 4.12)	0.60
Age		0.98 (0.95 – 1.02)	0.28
Time to nerve graft			
	≤14 days	4.97 (1.5 – 16.9)	0.01*

*P-value < 0.05 considered significant

TABLE LEGENDS

Table 1: Characteristics and surgical outcomes of patients that underwent hypoglossal-facial nerve anastomosis

Table 2: Multivariate analyses of facial nerve outcomes adjusted for gender, age, and time to hypoglossal-facial nerve anastomosis