IMPORTANCE  Free gracilis transfer for dynamic reanimation in chronic facial paralysis is the gold standard, but there remains a need to better understand outcomes with respect to the donor nerve.

OBJECTIVE  To characterize outcomes in adults undergoing primary gracilis transfer for facial paralysis stratified by donor nerve used for neurotization.

DATA SOURCES  Search strategies were used in Ovid MEDLINE (1946-2019), Embase (1947-2019), Scopus (1823-2019), Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov (1997-2019).

STUDY SELECTION  Inclusion and exclusion criteria were designed to capture studies in adults with unilateral chronic facial paralysis undergoing single-paddle free gracilis transfer. All study types were included except case reports. Abstracts and full texts were reviewed in duplicate. Of 130 unique citations, 10 studies including 295 patients were included after applying inclusion and exclusion criteria. Data were analyzed between November 2018 and December 2019.

DATA EXTRACTION AND SYNTHESIS  PRISMA guidelines were followed. The Newcastle-Ottawa scale was used to assess study quality, and the Cochrane Risk of Bias tool was used to assess risk of bias. Independent extraction by 2 authors (P.M.V. and J.J.C.) was performed. Data were pooled using a random-effects model.

MAIN OUTCOMES AND MEASURES  Owing to heterogeneity in reporting of facial reanimation outcomes, we first performed a systematic review, and then compiled available outcomes for meta-analysis. Outcomes studied for meta-analysis were oral commissure excursion and facial symmetry.

RESULTS  Meta-analysis of masseteric nerve (MN) (n = 56) vs cross-facial nerve graft (CFNG) (n = 52) in 3 retrospective studies showed no statistical heterogeneity between these studies ($I^2 = 0\%$), and the standardized mean difference (SMD) was greater for MN (0.55; 95% CI, 0.17 to 0.94). Meta-analysis of angles of symmetry in 2 retrospective studies comparing MN (n = 51) to CFNG (n = 47) both at rest (−0.22; 95% CI, −0.63 to 0.18) and with smiling (−0.14; 95% CI, −0.73 to 0.46) were better with MN, though the difference was not statistically significant.

CONCLUSIONS AND RELEVANCE  Owing to heterogeneity in reported outcomes from facial reanimation, we were unable to make definitive conclusions regarding the optimal donor nerve. Establishing a reporting standard at peer-reviewed journals to improve results reporting is one method to allow for improved collaboration in the future. Standardizing follow-up times, assessing spontaneity in an objective and reproducible fashion, and use of consistent outcome measures would allow for future meta-analyses and better understanding of options for facial reanimation.

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Facial paralysis is a devastating condition with a cascade of downstream effects, including negative effects on quality of life. The resulting disfigurement greatly impacts patients by adversely affecting their social interactions, leading to anxiety, depression, social avoidance, and social isolation, primarily owing to the inability to express emotion. In the modern era, an increasingly common option for dynamic lower facial reanimation in chronic facial paralysis is free gracilis muscle transfer. Since its initial description by Harii et al. in 1976 using the deep temporal nerve to power the transplanted muscle, various donor nerves have been proposed, including a cross-facial nerve graft (CFNG), hypoglossal or spinal accessory nerves, masseteric nerve (MN), and most recently, using both the masseteric and a CFNG.

Recommendations from experienced centers regarding the optimal donor nerve have been mixed. Some have reported that older patients do not have as good of a result with a CFNG, but the use of the CFNG may lead to better spontaneity of smile. There is some evidence that excursion may be better with the MN, presumably because the axon count is higher compared with a CFNG, which requires 2 neurorraphies. Others have recommended using both a CFNG and the MN to provide both spontaneity and excursion.

Despite calls to standardize assessment of postoperative outcomes to allow better comparison between studies using validated measures, however, results continue to be reported in a heterogenous fashion with many different outcome measures used. Recent additions such as the FACEgram software, the FaCE instrument, and the FACIAL CLIMA system are objective, validated instruments, but because they are relatively new, they have not seen widespread use. There remains a need to better understand outcomes such as excursion, symmetry, and spontaneity of smile with respect to the various donor nerves available.

With this in mind, we performed a systematic review and meta-analysis of outcomes from gracilis muscle transfer for facial reanimation in adults, with attention to the donor nerve. The question guiding this study was: in adults undergoing primary gracilis transfer for facial paralysis, what are the outcomes stratified by donor nerve used for neurotization?

**Methods**

This systematic review and meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This study was exempt from our university institutional review board because it used data from published literature. Data were analyzed between November 2018 and December 2019.

**Search Strategy and Study Selection**

No review protocol was published for this study. Using the PICOS framework for this systematic review, the population of interest was adults aged 18 years or older with chronic facial paralysis, the intervention was free gracilis transfer for facial reanimation, the comparator was the nerve(s) used to neurotize the gracilis, the outcome was the measure used to report postoperative results, and the study design was all study types except case reports.

A medical librarian created search strategies for the concepts of facial paralysis, gracilis muscle transfer, and facial reanimation in multiple electronic databases including Ovid MEDLINE (1946-2019), Embase (1947-2019), Scopus (1823-2019), Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov (1997-2019). All search strategies were completed November 8, 2018, and resulted in 116 unique citations. An updated literature search was completed on December 23, 2019, and identified 14 additional unique citations. Fully reproducible search strategies for each database can be found in eTable 1 in the Supplement. Abstracts and full texts were reviewed independently in duplicate (P.M.V. and J.J.C.), and disagreements were resolved by consensus. At the abstract review stage, we excluded studies for the following reasons: (1) review article and not original research, (2) did not use the gracilis flap for reanimation, (3) pediatric study, (4) duplicate publication, (5) cadaver study, (6) revision surgery, (7) bilateral facial paralysis, (8) used a double paddle gracilis flap, and (9) non-English language. At the full text review stage, we excluded studies for the following reasons: (1) pediatric studies, (2) did not report objective outcome measures, (3) revision surgery, (4) full text was not available, (5) did not separate adult and pediatric data, (6) case report, (7) duplicate publication, (8) incomplete paralysis, and (9) review article (Figure 1). Studies that did not report objective outcome measures were excluded owing to the inherent heterogeneity in reporting the result.

**Data Extraction and Quality Assessment**

The primary outcomes of interest were the postoperative smile outcomes reported in the study, and the nerve(s) used to neurotize the gracilis free flap. Study design, location, and length of follow-up were also assessed. If data were not available in the published article, authors were contacted via e-mail. A modified version of the Cochrane Collaboration's Risk of Bias Tool was used. Because none of the included studies were randomized clinical trials, the domains specific to randomized trials (sequence generation, allocation concealment) were marked as not applicable. The Newcastle-Ottawa scale was validated.

**Key Points**

**Question** In adults undergoing primary gracilis transfer for facial paralysis, what are the outcomes, stratified by donor nerve used for neurotization?

**Findings** In this systematic review and meta-analysis, we found that use of the masseteric nerve may be associated with improved oral commissure excursion compared with the cross-facial nerve graft, but many incompatible outcomes were reported in the included studies.

**Meaning** The masseteric nerve may be associated with the best excursion in facial reanimation with gracilis free transfer, but reporting of results from facial reanimation surgery must be standardized.
used to assess study quality, graded independently by 2 authors (P.M.V. and J.J.C.).

**Statistical Analysis**

Descriptive statistics were used for studies included in the systematic review that were unable to be summarized in meta-analysis owing to heterogeneity of outcome measures. Random effects meta-analyses were performed to quantify mean excursion and symmetry with smiling and at rest with the MN vs CFNG in studies that used the FACEgram. The effect size was calculated using the standardized mean differences in centimeters. All analyses were performed in Stata statistical software (version 14.1, StataCorp) and Microsoft Excel (version 15.2, Microsoft).

**Results**

The search strategy resulted in 130 unique citations. After applying inclusion and exclusion criteria, 10 studies were included in our systematic review (Figure 1).

The Table describes the characteristics of the included studies. Eight were retrospective cohort studies, and 2 were case series. The studies came from all over the world, including Italy, Germany, Spain, Taiwan, South Korea, Japan, Boston, Massachusetts, and Baltimore, Maryland. Eight studies scored 8 of 9 on the Newcastle-Ottawa scale, and 2 studies scored 7 of 9 on the scale, indicating all studies were of good quality. All studies lost a point in the comparability category because there were no controls and the studies were all retrospective, and 2 studies\(^{11,24}\) lost another point in the selection category due to including both flaccid and nonflaccid paralysis patients in their study. Follow-up time ranged from 6 months for patients reanimated with MN, and 12 months for CFNG, to over 40 months. One study\(^{23}\) did not explicitly state length of follow-up. Six studies\(^{7,12,23,25,26,28}\) were rated as having an unclear risk of bias, 2 studies\(^{1,27}\) had a low risk of bias, and 1 study\(^{24}\) had a high risk of bias. The only study\(^{24}\) with a high risk of bias was rated as such because the outcome assessment was unblinded and relied entirely on assessment from the surgeon. Because the data used in the meta-analysis came from studies with either low or unclear risk of bias, we do not believe the risk of bias is sufficient to affect the interpretation of the results (eTable 2 in the Supplement).

**Excursion and Symmetry**

All 10 studies examined excursion and symmetry as an outcome measure. Reported measures included the distance from the midline lower lip to the oral commissure as calculated with FACEgram\(^{17}\) software (4 studies\(^{1,11,25-27}\)); Terzis and Noah grade,\(^{29}\) a combined aesthetic and functional scale ranging from 1 (poor) to 5 (excellent) based on standard photographic analysis by an observer (4 studies\(^{7,24,26,28}\)); FACIAL CLIMA,\(^{10}\) an automated measurement software program based on infrared photographic analysis (1 study\(^{26}\)); distance between the tragion and oral commissure on lateral photography (1 study\(^{10}\)); and the Sunnybrook Facial Grading System,\(^{10}\) a validated scoring system used to evaluate symmetry at rest and with movement, as well as synkinesis (1 study\(^{27}\)).

Because 4 studies\(^{11,25-27}\) reported outcomes using the FACEgram, we chose to use this measure for meta-analysis. Of the 4 studies reporting results, only FACEgram results for MN and CFNG were reported. Unfortunately, 1 study\(^{26}\) reported combined results for patients who underwent either MN or MN combined with the CFNG, and was thus excluded from the meta-analysis. Thus, meta-analysis of MN (n = 56) vs CFNG (n = 52) showed no heterogeneity between the 3 studies\(^{1,25,27}\) (I\(^2\) = 0%), and excursion was greater with the masseteric nerve (0.55 mm; 95% CI, 0.17–0.94) (Figure 2). Angles of symmetry were only reported in 2 of these studies,\(^{1,25}\) and thus a meta-analysis was performed for these 2 studies with MN (n = 51) vs CFNG (n = 47). Heterogeneity was low (I\(^2\) = 37.5% at rest, 0% with smiling). Angles of symmetry at rest (−0.14; 95% CI, −0.73 to 0.46) and with smiling (−0.22; 95% CI, −0.62 to 0.18) were better with MN, though the differences were not statistically significant (Figure 3).
Spontaneity

Four studies, including 56 patients examined the rate of achieving a spontaneous smile. Three studies showed patients a funny movie, and observed them for spontaneity, graded as yes vs no. One study also asked family members to fill out a questionnaire to determine whether they observed spontaneous smiling. One study did not use any objective measures, and reported the results of physician observation during follow-up visits. Two retrospective studies found that 1 of 10 (10%) and 20 of 36 patients (56%)...
achieved spontaneity with the masseteric nerve. In 2 case series, including 4 and 6 patients with masseteric nerve plus CFNG, 4 of 4 (100%) and 6 of 6 patients (100%) achieved spontaneous smile.

Additional Outcome Measures
Four studies examined other outcome measures. These measures included secondary revision rates for thinning of the gracilis for flap bulkiness (2 studies); the FaCE scale, a validated patient-reported outcome measure focused on facial impairment and disability (1 study); and the compound motor action potential (CMAP), an electromyographic measure that allows for quantitative assessment of muscle strength (1 study). Though several studies excluded patients who underwent secondary revision of the gracilis flap, the 2 studies that did report cited a rate ranging from 23% to 29%. Postoperative thinning of the flap, while decreasing excursion, may help improve symmetry in patients with excessive pull. Of the 7 studies (29, 30, 31, 24, 27, 28) that reported flap survival, 213 of 218 flaps survived (97.7%). One study reported 2 infections in 14 flaps, 1 in the face, and 1 in the donor site.

Discussion
This systematic review and meta-analysis included 295 adults undergoing free gracilis muscle transfer for facial reanimation from 10 studies done around the world. It is encouraging that all studies included in this systematic review and meta-analysis were of high quality. Unfortunately, the meta-analysis was limited owing to the heterogeneity of reporting, which precluded our ability to make definitive conclusions regarding the optimal choice of donor nerve. However, our meta-analysis of 3 studies with 108 patients showed that excursion may be superior with masseteric nerve compared with CFNG. Symmetry was not found to be different between the 2 groups in the 2 studies reporting angle data from the FACEgram. Though we were unable to perform a meta-analysis on studies reporting results on smile spontaneity owing to heterogeneity in reported outcome measures, 100% of the 10 patients included in this systematic review achieved spontaneity with masseteric nerve plus CFNG, whereas fewer than half of the 46 patients who underwent masseteric nerve alone achieved spontaneity. Roughly one quarter of patients underwent thinning of the flap postoperatively in the 2 studies that reported revision rates. Given that our study included case series and retrospective cohort studies, this constitutes level 3 evidence.

The 3 major categories of outcome measures reported in the included studies were excursion, symmetry, and spontaneity. Unfortunately, despite calls to standardize reporting of results after facial reanimation surgery, there continue to be disparate outcome measures reported in the literature. Otologists faced a similar problem in the reporting of hearing outcomes after surgery, limiting the ability to perform meta-analyses on published data. They addressed that barrier by creating a minimum reporting standard, put forth by the Hearing Committee of the American Academy of Otolaryngology–Head and Neck Surgery, and recommended that researchers publish results in whatever format they desired, as long as the minimum standard was included. This reporting standard was subsequently endorsed by other major peer-reviewed journals, but not without generating some controversy from the American Academy of Audiology, for example. An analogous standard could be developed for reporting outcomes of facial reanimation surgery, to allow for better collaboration and meta-analysis of future studies. This reporting standard could include agreed-on measures of these 3 categories—excursion, symmetry, and spontaneity.
Consistent with prior studies, our results support the use of the masseteric nerve and CFNG together, rather than either alone, as the best option for neuromating the gracilis flap for facial reanimation in adults. Several experienced facial reanimation surgeons have postulated that achieving spontaneity is only likely with use of the CFNG.9,27,38,39 Unfortunately, as noted in the past by several independent groups, the limitation of CFNG may be the decreased axon count that reaches the transplanted muscle after multiple anastomoses.40,41 Thus, the added robust axonal input from the masseteric nerve may help augment the excursion beyond what the CFNG can achieve alone.10,11,41,42 Though the mechanism for this phenomenon is not known, the previously described “babysitter” procedure is one possible explanation.43 As with the originally described “minihypoglossal” graft during the first stage of a CFNG, the masseteric nerve may serve this purpose by providing neural input while the CFNG is maturing.

Though our meta-analysis was limited to the masseteric nerve and CFNG, there is some compelling evidence that the masseteric nerve may be the best nonfacial nerve to use for this purpose. Researchers have theorized that, owing to the premotor and primary motor area, it may be easier for patients to achieve spontaneity after reinnervation with the masseteric nerve.44,45 In addition, there is normal activation of the masseteric nerve during smiling,46 which further supports the case for the masseteric nerve because this is the gesture used to trigger a smile by patients after reanimation with this nerve.

Opportunities for Future Research
It is clear from our systematic review that spontaneity is the most heterogeneously reported measure in facial reanimation. Unfortunately, no existing patient-reported outcome measure addresses this specific issue of standardizing how spontaneity is measured. A standard protocol for measuring spontaneity postoperatively would likely require a video assessment with independent, blinded raters, and would require a patient to fall within a defined upper limit for the amount of time allowed to elapse after exposure to a smile stimulus to be called spontaneous. Hadlock’s group has proposed a smile spontaneity assay to address this problem, and recently showed that the correlation between the assay and clinician-graded spontaneity was unfortunately quite low (R = 0.35).47,48

A related issue is that of preoperative patient factors such as age and severity of paralysis. Though facial reanimation surgeons would likely agree that younger age is a positive prognostic factor for subsequent spontaneity, and a nonflaccid paralysis will likely have a better result than a flaccid paralysis owing to better postoperative resting tone, neither of these factors are well-controlled for in published studies. As reporting standards improve over time, we expect that the impact of age, flaccidity, and other patient factors will become better understood in a more quantitative fashion.

Limitations
Despite a thorough systematic search, our study is somewhat limited in that there were a small number of donor nerve options to use for our meta-analysis, which precluded our ability to make definitive conclusions. Unfortunately, we were limited to previously published studies, which do not capture all the possible donor nerves that have been used in facial reanimation with alternative techniques. For example, others have obtained successful outcomes with a hypoglossal nerve transfer.9,49,50 Because those studies did not use a gracilis free flap, however, they were excluded from this study. In addition, our meta-analyses were largely driven by the study by Bhama et al11 because it was the largest of the included studies. Furthermore, all of the studies included in our meta-analyses were done in the United States at 1 of 2 centers. Though this does limit the generalizability of our findings, this helps to highlight the need for compatible outcome measures and improved results reporting in facial reanimation.

Conclusions
Owing to the heterogeneity in reported outcomes from facial reanimation, we were unable to make definitive conclusions regarding the optimal donor nerve for this purpose. Establishing a reporting standard at peer reviewed journals to improve results reporting is one method to allow for improved collaboration in the future. Standardizing follow-up times, assessing spontaneity in an objective and reproducible fashion, and use of consistent outcome measures would allow for future meta-analyses and better understanding of options for facial reanimation for this challenging patient population.

Statistical analysis: Vila, Kallogjeri. Administrative, technical, or material support: Chi. Study supervision: Vila, Chi.

Conflict of Interest Disclosures: Dr Kallogjeri reported grants from Potentia Metrics outside the submitted work. No other disclosures were reported.

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Powering the Gracilis for Facial Reanimation

Original Investigation Research

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