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A higher quality of life with cross-face-nerve-grafting as an adjunct to a hypoglossal–facial nerve jump graft in facial palsy treatment

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Summary Nerve reconstructions are the preferred technique for short-standing facial paralysis, most commonly using the contralateral facial nerve or ipsilateral hypoglossal nerve. The hypoglossal nerve provides a strong motor signal, whereas the signal of a cross-face nerve graft is weaker but spontaneous. Spontaneity in facial expression is believed to be important for psychological wellbeing. Therefore, a combination of the two procedures incorporates the best of both: a strong motor signal and a spontaneous smile. This study aimed to objectify this expected benefit. Of the 20 patients who received a hypoglossal–facial nerve anastomosis from 1995 to 2015 in our institutions, 12 patients were included in this study, 5 with and 7 without a cross-face nerve graft. The outcomes were compared using photographs, disease-specific quality of life (Facial Clinimetric Evaluation (FaCE) scale), a self-reported synkinesis scale (Synkinesis Assessment Questionnaire) and the presence of a spontaneous smile. Significant differences were found in preoperative excursion of the affected side of the mouth and the change in excursion. Median Total FaCE scores were considerably larger (18.3 points) for patients who underwent the combined procedure. A spontaneous smile was observed both with ($n = 2$) and without ($n = 1$) a cross-face nerve graft. The addition of a cross-face nerve graft to a hypoglossal–facial nerve anastomosis resulted in a positive trend in disease-specific quality of life. This benefit could also be present

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with the combination of a cross-face nerve graft with another nerve transfer such as a masseteric-facial nerve anastomosis.

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Introduction

Nerve transfers are indicated in short-standing facial nerve paralysis in the absence of a proximal facial nerve stump that provides an electrical signal. In these cases, the affected facial nerve is usually divided close to the stylo-mastoid foramen and connected to a neighbouring motor source to reinnervate the mimic muscles.¹ Various nerves have been used for this purpose since the end of the 19th century.² The contralateral facial and ipsilateral hypoglossal nerves and, more recently, the masseteric nerve, are most popular.³

In the 1970s, the idea of connecting the affected facial nerve to its contralateral counterpart by means of a cross-face nerve graft (CFNG) was introduced.⁴ In this method, the affected side of the face is reinnervated to enable facial movement of this side. A CFNG is believed to be the only source of true emotional spontaneous movement.^{1,5} The prolonged period of denervation that occurs as a consequence of the long distance the axons have to travel through the nerve graft, however, may be detrimental to the remaining facial muscles because it may lead to irreversible muscle degeneration.⁶ Therefore, functional recovery in isolated cross-face nerve grafting is generally poor.⁷ This outcome is probably also related to the low number of axons provided by this donor nerve.⁸

Hypoglossal–facial nerve anastomosis was introduced at the beginning of the 20th century.⁹ The similarities between the facial and hypoglossal nerves in axonal count and their intimate cooperation during facial function and eating are believed to make the hypoglossal–facial nerve anastomosis especially suitable for facial reanimation.¹⁰ However, a hypoglossal–facial nerve anastomosis only produces voluntary movement, and training is required to control facial movement.

One of the most common problems following facial paralysis, both before and after reconstruction, is synkinesis.^{11,12} Synkinesis is the unintentional movement of the face when voluntarily moving another part of the face, oral-ocular synkinesis being the most common.¹³ Synkinesis leads not only to physical difficulties, such as problems with speaking and eating,¹⁴ but also to difficulties in facial expression and interpersonal communication, leading to psychological problems.¹⁵ Reduction of the degree of synkinesis is therefore an important aim for both the physical and psychological wellbeing of the patient. Spontaneity of the smile is believed to be important because subtle facial movements are essential in expressing emotional information during interpersonal communication.^{16,17} The inability to smile (spontaneously) is one of the most frequently heard complaints heard from patients suffering from facial

nerve paralysis, and this inability can lead to an increase in depressive symptoms.^{18,19}

The combination of the hypoglossal–facial nerve anastomosis and CFNG was introduced by Terzis and is believed to combine the best of both: a strong motor signal for symmetry in repose and during voluntary movement and a spontaneous smile.^{20–22} The described procedure consists of an end-to-side hypoglossal to facial nerve anastomosis to 40% of the ipsilateral hypoglossal nerve and three or four CFNGs for reanimation of the mouth and eye. This study aimed to analyse the suggested benefits of a CFNG as an adjunct to another nerve transfer, in our case, a hypoglossal–facial nerve anastomosis.

Patients and methods

We invited all patients who were treated with a hypoglossal–facial nerve anastomosis between 1995 and 2015 at the University Medical Centre Groningen (UMCG) or Isala Clinics by the last senior author (PMNW) to participate in this cross-sectional outcome study. All patients who were willing to participate were included. Patients with a follow-up of less than 1 year were excluded. The institutional review boards of both the UMCG and Isala Clinics deemed formal approval not necessary prior to this study (METc 2015/461 and METc 16.0353 respectively), and all patients gave written consent to participate in this study.

Operative technique

For a combination of a hypoglossal–facial nerve anastomosis and a CFNG, a two-stage procedure was performed. Through a preauricular incision that was extended into the neck, the facial and hypoglossal nerves were identified and isolated. The facial nerve was cut as proximally as possible, and approximately 40% of the hypoglossal nerve was transected. On the healthy side of the face, a buccal (and in some cases, an ophthalmic) branch of the facial nerve was isolated and divided at the medial edge of the parotid gland, using a preauricular approach. One (or two) sural nerve graft(-s) was/were harvested as nerve graft(-s). The sural nerve(-s) was/were microscopically connected to the proximal end of the healthy facial nerve branch(-es) in an end-to-end manner and passed to the other side of the face using a Reverdin needle. The distal end(-s) of the CFNG(-s) was/were banked in front of the ear on the affected side awaiting the second procedure. The surplus of (one of) the sural nerve(-s) was used as a jump graft and first connected to the distal end of the divided facial nerve in an end-to-end fashion and thereafter to the 40% divided hypoglossal nerve in an end-to-side fashion. After approximately 1 year,

axonal regeneration had occurred, demonstrated by a functioning hypoglossal–facial nerve anastomosis and by a positive Tinel's sign when tapping on the banked distal end(-s) of the CFNG('s). In the second operation, the graft(-s) was/were connected to the distal end of a buccal (and a zygomatic) branch on the affected facial nerve.

For a solitary hypoglossal–facial nerve anastomosis, a one-stage procedure was performed, and the greater auricular nerve was used as a nerve graft.

Data collection

The medical charts were searched for patient and operative characteristics and preoperative photographs and videos. All patients were asked to visit our institution to obtain a recent set of photographs and a short video recording. Photographs were analysed using the FACE-gram software.²³ By measuring the distance from the midline to the corner of the mouth on the affected and healthy sides (in repose and with smile), an excursion of the corner of the mouth (difference between position of the corner of the mouth in repose and with smile) and a measurement of symmetry (difference between the position of the corner of the mouth on the healthy and affected sides) were obtained. Moreover, the photographs were graded according to the May classification into four categories: excellent (teeth-exposing smile), good (symmetrical smile without showing teeth), fair (symmetry in repose) and poor (drooping corner of the mouth on the affected side).²⁴ To test intra-rater agreement, grading was performed twice within 3 days in random order by the first author (MMvV) who did not participate in any of the reconstructions. Patients were asked to fill out the Facial Clinimetric Evaluation (FaCE) scale²⁵ and the Synkinesis Assessment Questionnaire (SAQ).²⁶ The FaCE scale is a 15-item disease specific quality of life (QoL) questionnaire, based on which a Total FaCE score and six subscores can be calculated. The scores range from 0 to 100. The SAQ is a self-reported synkinesis questionnaire consisting of nine items. SAQ scores range from 20 to 100. Both questionnaires have recently been translated and validated for use in the Netherlands.^{25,26} Additionally, questions were asked regarding the current state of their disease and smile. Finally, the videos were assessed (MMvV) for the presence of a spontaneous smile.

Statistical analysis

Descriptive statistics were given using medians, interquartile range (IQR) and numbers for nominal data. A squared weighted Cohen's kappa was calculated to determine intra-rater agreement of the May classifications. A kappa of 0.80 or higher was considered good.²⁷ Spearman's ρ was calculated for the association between age, denervation time and follow-up time on the Total FaCE score and May classification score in the total group. Mann–Whitney *U* tests were performed to assess the difference between men and women in Total FaCE score and May classification score. Additionally, Spearman's ρ was calculated for the association between the Total FaCE score and the observed and self-reported spontaneity of the smile. Mann–Whitney

U tests were computed to analyse differences in excursion on the affected side, symmetry with smile, May classification, SAQ score, spontaneity of the smile and FaCE (sub) scores between groups. Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 22 (Chicago, IL). The level of significance was set at 0.05.

Results

Initially, 20 patients who were treated with a hypoglossal–facial nerve anastomosis were identified. One patient had a follow-up time lesser than 1 year. One patient had passed away. The remaining six patients could not be traced, despite extensive effort (Figure 1). These eight lost for follow-up patients did not differ from the included patients regarding sex, age, denervation time and procedure performed. Twelve patients, eight men and four women with a median age of 57.8 years, who were treated with a hypoglossal–facial nerve anastomosis, five with and seven without an additional CFNG, after a median denervation time of 12.6 months, were included in this study (Table 1). Of the patients treated with a CFNG, four patients were treated with one CFNG for mouth reanimation. One patient was treated with two CFNGs, one for reanimation of the mouth and one for reanimation of the eye. All patients presented with complete facial nerve paralysis preoperatively. All patients filled out the questionnaires after a median follow-up time of 3.4 years. Ten patients were willing to visit our institution for a new set of photographs and a short video. One patient had sent us a set of recent photographs. In one patient, the most recent photographs from the medical files were used (Figure 1).

Figure 1 Schematic representation of patient inclusion.

Table 1 Characteristics of hypoglossal–facial nerve anastomosis patients with and without CFNG.^a

Patient	Gender	Age ^b (years)	Cause of facial paralysis	Side	Preoperative FP ^c grade	DT ^d (months)	Follow-up (years)	CFNG
1	M	51	Vestibular schwannoma	L	Complete	13	2.7	CFNG × 1
2	F	68	Vestibular schwannoma	R	Complete	24	11.7	CFNG × 1
3	M	53	Vestibular schwannoma	L	Complete	7	4.1	CFNG × 2
4	M	59	Facial nerve neurofibroma	R	Complete	8	2.2	CFNG × 1
5	M	11	Facial nerve schwannoma	R	Complete	34	1.3	CFNG × 1
6	F	46	Vestibular schwannoma	L	Complete	12	15.1	—
7	M	58	Vestibular schwannoma	R	Complete	13	1.1	—
8	M	58	Vestibular schwannoma	R	Complete	20	1.3	—
9	F	60	Vestibular schwannoma	L	Complete	48	21.4	—
10	M	24	Astrocytoma	R	Complete	23	7.5	—
11	M	72	Cholesteatoma	L	Complete	12	6.5	—
12	F	73	Parotidectomy	L	Complete	0	2.2	—
Median (IQR ^e)		57.8 (47.5; 66.3)				12.6 (9.2; 23.8)	3.4 (1.5; 10.7)	

^a Cross-face-nerve-graft.^b Age at the time of investigation.^c Facial paralysis.^d Denervation time.^e Interquartile range.**Table 2** Pre- and postoperative outcomes.

	XII-VII anastomosis (<i>n</i> = 7)	XII-VII anastomosis with CFNG (<i>n</i> = 5)	<i>p</i> -Value ^a
Excursion on the affected side (mm, median (IQR))			
Preoperative ^b	−1.0 (−1.2; −0.5)	−2.4 (−3.5; −1.5)	0.03
Postoperative	0.8 (−0.1; 2.3)	2.3 (0.7; 5.3)	0.25
ΔExcursion ^b	0.8 (0.7; 2.1)	3.7 (3.4; 4.8)	0.03
Symmetry with smile (mm, median (IQR))			
Preoperative ^b	15.5 (12.8; 17.7)	13.8 (11.4; 16.5)	0.49
Postoperative	5.2 (2.6; 8.4)	3.4 (1.5; 10.2)	0.79
ΔSymmetry ^b	−11.2 (−14.1; −8.2)	−7.1 (−10.1; −4.8)	0.06
May score			
Preoperative ^b (<i>n</i>)			1.00
Excellent	0	0	
Good	0	0	
Fair	0	0	
Poor	5	4	
Postoperative (<i>n</i>)			0.41
Excellent	0	1	
Good	2	2	
Fair	5	2	
Poor	0	0	
ΔMay score ^b (median (IQR))	1.0 (1.0; 1.5)	1.5 (1.0; 2.0)	0.52
SAQ score (median (IQR))	28.9 (8.9)	28.9 (6.7)	0.74
Spontaneous smile ^b (<i>n</i>)			
Yes	1	2	1.00
No	4	3	
Conscious smile ^c (<i>n</i>)			
Always	3	2	1.00
Most times	0	0	
Sometimes	1	1	
Seldom	2	1	
Never	1	1	

^a Computed by Mann–Whitney *U* test, *p*-level set at *p* = 0.05.^b Missing values.^c Answer to the question: 'Do you consciously have to think about smiling?'.

Figure 2 Total FaCE scores and FaCE scale subscores. Blue bars represent the hypoglossal-facial nerve anastomoses without a CFNG, and green bars represent the hypoglossal-facial nerve anastomoses with CFNG. No statistically significant differences were found between both groups in any of the FaCE scores as determined by Mann-Whitney *U* tests.

Intra-rater agreement of the May classification was 0.90. A smaller preoperative median excursion on the affected side and larger median difference in excursion was found in patients treated with an additional CFNG (Table 2). No statistically significant differences were seen in all other outcomes, including spontaneity of the smile, between patients treated with and without a CFNG (Table 2). A large difference in median Total FaCE scores for patients with a CFNG (68.3, IQR: 34.2; 75.0) compared to patients without a CFNG (50.0, IQR: 40.0; 65.0) was found (Figure 2). Median oral function scores were the same (50.0) for both groups; a large difference was found in median social function scores for patients with a CFNG (87.5, IQR: 34.4; 96.9) compared to those without a CFNG (56.3, IQR: 43.8; 93.8) (Figure 2). No statistically significant differences were found between both groups in any of the FaCE (sub)scores (Figure 2). An example of patients' photographs with the corresponding May classification scores and Total FaCE scores is presented (Figures 3–5).

A significant positive association was found between follow-up time and the May classification score (Table 3). No other associations were significant. No statistically significant differences were found between men and women in Total FaCE score (median (IQR); 65.8 (43.8; 68.3) and 45.0 (36.3; 56.3) respectively; $p = 0.18$) and May

Figure 3 A 45-year-old patient presented with complete left-sided paralysis after vestibular schwannoma resection and was treated with a XII-VII jump anastomosis with concurrent CFNG (3A: preoperative). At 2.7 years follow-up, the postoperative result was graded as 'moderate' (May classification 2), and the patient had a total FaCE score of 18.3 points (3B: postoperative).

Figure 4 A 47-year-old patient presented with complete right-sided paralysis after vestibular schwannoma resection and was treated with a XII-VII jump anastomosis (4A: preoperative). At 1.1 years follow-up, the postoperative result was graded as 'moderate' (May classification 2), and the patient had a total FaCE score of 41.7 points (4B: postoperative).

classification scores (median (IQR); 2.0 (2.0; 2.8) and 3.0 (2.3; 3.8) respectively; $p = 0.17$).

Discussion

The addition of a CFNG resulted in a substantially higher Total FaCE score and social function score, but no significant differences were found between both groups of patients. Preoperatively, all patients had a complete facial nerve paralysis. Postoperatively, no significant difference was observed in excursion on the affected side of the face, symmetry with smile or May classification scores. Most of our patients achieved either symmetry of the mouth in repose or could produce a symmetrical smile without showing teeth, irrespective of the addition of a CFNG. Several studies showed either symmetry in repose^{28–31} or a symmetrical smile^{20,32,33} as the achieved result after hypoglossal–facial nerve anastomosis. When comparing published series of hypoglossal–facial anastomoses with the addition of a CFNG to studies without a CFNG, the results do not seem to differ.^{20,28–33} However, this comparison is hampered by the different grading systems applied^{20,31} or the use of no standardised grading system at all.^{28–30,32,33} Moreover, many studies are case reports, and most authors report the addition of a CFNG for reanimation

of the eye and not for the mouth.^{31,32} In a case series of four patients, a nerve transfer combined with a CFNG for reanimation of the mouth was evaluated.³⁰ Postoperative symmetry in repose was found, but no spontaneous movement was observed on the affected side of the face. Another study describing two cases with the addition of a CFNG reported the presence of a spontaneous symmetrical smile after 1 year.³³

A study with the largest series of patients ($n = 20$) with the combination of a hypoglossal–facial nerve anastomosis with a CFNG for reanimation of the mouth reported 15 patients with 'good' to 'excellent' results according to the Terzis' Grading system.²⁰ This result indicates that patients either achieved symmetry and almost full contraction during smile ('good') or a symmetrical and teeth showing smile ('excellent').³⁴ In a study including 53 patients who were treated with one of five different types of facial nerve reconstructions, postoperative clinical and electrophysiological outcomes were reported.³¹ After hypoglossal–facial nerve jump graft, mean postoperative scores were 3.0, corresponding to symmetry in repose (scale range 1 (superb) to 5 (failure)).³⁵

To the best of our knowledge, we are the first to compare the hypoglossal–facial nerve anastomosis and the combination of a hypoglossal–facial nerve anastomosis with a CFNG for reanimation of the mouth. The exact

Figure 5 A 54-year-old patient presented with complete right-sided paralysis after facial nerve neurofibroma resection and was treated with a XII-VII jump anastomosis with concurrent CFNG (5A: preoperative). At 2.2 years follow-up, the postoperative result was graded as 'good' (May classification 3), and the patient had a total FaCE score of 68.3 points (5B: postoperative).

interrelationship between the May classification and the Terzis' Grading is not clear. The 'good' to 'excellent' scores according to the Terzis' Grading system correspond to a symmetrical smile with (near) full contraction.²⁰ At first sight, our results may seem less favourable than the results of other studies,^{20,33} with symmetry in repose as the most commonly achieved result; however, our patients had a median age of 58 years. A higher age has been shown to be associated with a poorer postoperative outcome.³¹ In our sample, age was not associated with postoperative outcomes; however, follow-up time was associated with better May classification scores. Because we did not perform multiple follow-up measurements, however, we could not determine a time point for the optimum postoperative result in our sample.

The median Total FaCE score was substantially better for the patients who had been treated with a CFNG in addition to a hypoglossal–facial nerve anastomosis; however, the difference was not statistically significantly different. Disease-specific QoL was measured because an improvement of QoL should always be the primary aim of facial reanimation surgery. We believe that the presence of a spontaneous smile would lead to a higher QoL, although we were not able to find a significant association between spontaneity of the smile and quality of life. The clinical relevance of the 18-point difference in Total FaCE scores we found is unclear. A difference in means of 39.6 points was found between patients with a facial paralysis and healthy controls.³⁶ Total FaCE score increased by 3.8 points after patients received botulinum toxin type A treatment

Table 3 Association between Total FaCE and May classification scores and age, denervation time, follow-up time, and the observed and self-reported spontaneity of the smile as expressed by Spearman's ρ and p -values.

	Age	Denervation time	Follow-up time	Spontaneous smile	Conscious smile ^a
Total FaCE score, ρ (p -value)	−0.06 (0.85)	0.14 (0.66)	−0.24 (0.46)	0.19 (0.60)	0.18 (0.58)
May classification score, ρ (p -value)	0.18 (0.58)	0.00 (0.99)	0.62 (0.03)	—	—

^a Answer to the question: 'Do you consciously have to think about smiling?'.

for synkinesis.²⁵ We believe that the difference in median scores reflects a substantial difference and justifies adding a CFNG to a hypoglossal–facial nerve anastomosis.

Most median FaCE scale subscores did not differ much. Most relevant in our study are the oral function and social function scores. The median oral function scores were exactly the same. A 31-point difference in median social function scores was, however, found in favour of the addition of a CFNG to a hypoglossal–facial nerve anastomosis. We believe that this indicates that the CFNG is of limited importance in oral function, perhaps because of its limited functional abilities. The higher median social function score, however, might suggest a more natural and spontaneous facial expression with the addition of a CFNG.

Synkinesis was assessed because of its effect on physical and emotional wellbeing of the patient^{14,15} and the possible benefit of the CFNG in reducing synkinesis. However, our median SAQ scores did not differ between the groups.

Disappointingly, a spontaneous smile was observed in only two of five patients treated with a CFNG. Surprisingly, we even saw a spontaneous smile in one of our patients without a CFNG. We did not have a research setup, however, in which it was possible to properly elicit and observe spontaneous movement. The one spontaneous smile in the patient not treated with a CFNG could further very well have been an automatic smile instead of an emotional smile because we were not able to differentiate the two.

A limitation of this study is the small sample size and the non-participation of patients. Despite several efforts, we were not able to trace those patients. In a post hoc analysis based on our findings, we determined the sample size needed for a significant result: in total, 74 patients in both groups would need to be included.

Another limitation is the cross-sectional design of this study. Standardised collection of QoL or synkinesis measurements has not been a common practice at our department yet, and thus, we were not able to evaluate quality of life and synkinesis longitudinally. Further, the decision whether to perform a CFNG was not randomised. It was a joint decision between surgeon and patient, considering general health, age and motivation of the patient to undergo a more extensive treatment. Although the age and health between our two groups did not differ and the group of patients that was treated with a CFNG generally had a more severe form of facial nerve paralysis, this group might have been more motivated to undergo more extensive treatment and rehabilitation; hence, confounding by indication may be present in our study results.

Finally, one of the limitations of our study is that we have only included hypoglossal–facial nerve transfers, given our retrospective cohort and our previous preference of hypoglossal–facial nerve transfers. Some might argue that the hypoglossal–facial nerve transfer is relatively out of date and may favour a masseteric-facial nerve transfer.³⁷ Clinical and animal studies have demonstrated similar results in hypoglossal–facial and masseteric-facial nerve transfers, however.^{38,39} Preference for the masseteric nerve is mainly based on the minimal donor-site morbidity.⁴⁰ Therefore, we believe our results with hypoglossal–facial nerve transfers can quite possibly be conveyed to other nerve transfers such as masseteric-facial nerve transfers.

Conclusions

We believe that the large difference in median quality of life scores could indicate a benefit for the addition of a CFNG to a hypoglossal–facial nerve anastomosis. Future research should aim at a larger sample, a prospective evaluation and preferably include masseteric-facial nerve transfers. The sample size needed would probably require multiple centres to participate.

Conflict of interest

The authors have no personal or financial relationships to disclose as a conflict of interest.

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