Systematic patient selection criteria for face transplantation

Systemaattiset kriteerit potilasvalintaan kasvojensiirtoa varten

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Tiivistelmä – Referat – Abstract

Tiivistelmä: Systemaattiset kriteerit potilasvalintaan kasvojensiirtoa varten

Kasvoilla on useita tehtäviä vuorovaikutuksesta tärkeiden elintoimintojen ylläpitoon. Perinteisten plastiikkakirurgisten menetelmien lisäksi kasvojensiirto aivokuolleelta luovuttajalta on vakiinnuttamassa paikkaansa vaikeasti kasvoistaan vammautuneiden potilaiden hoitomuotona. Toimenpiteeseen ja elinikäiseen hyljinnänestolääkitykseen liittyvät haitat rajoittavat kasvojensiirtoon soveltuvia potilaita. Toistaiseksi potilasvalinta on tehty tapauskohtaisesti, ja systemaattiset potilasvalintakriteerit puuttuvat. Esittelemme vaikeasti kasvoiltaan vammautuneita potilaita, ja arvioimme systemaattisesti heidän soveltuvuuttaan kasvojensiirtoa varten.

Kymmenen vaikean kasvovamman vuoksi hoidetuista potilaista vuosilta 1995-2017 valittiin tutkimukseen. Tietoa kerättiin potilasasiakirjoista sekä kliinisistä tutkimuksista. Vammojen laajuus jaettiin osa-alueisiin: anatominen laajuus (10), toiminnallinen haitta, esteettinen haitta (asteikko 0-9), elämänlaatuarvio (15D-lomake) ja sosiaalinen hyvinvointi. Lisäksi arvioitiin kunkin potilaan immunologinen tila ja vasta-aiheet toimenpiteelle.

Vammojen etiologioita olivat palovammat (4), ampuma-asevammat (3), tylpän esineen aiheuttama vamma (1), räjähdysvamma (1) ja neurofibromatoosi (1). Kaikilla potilailla esiintyi keskikasvojen vaurioita, ja kuudella potilaalla oli vähintään 8/10 kasvojen osa-alueista vaurioitunut. Kaikilla potilailla ilmeni jonkin asteinen toiminnallinen vajaus. Arvioitu esteettinen vajaus oli mediaaniltaan 7/9. Elämänlaadun laskun mediaani oli -0.107. Immunologisia vasta-aineita ei havaittu, mutta viidellä potilaalla ilmeni muita vasta-aiheita toimenpiteeseen. Kuudesta vaikeasti vammautuneesta potilaasta kolme todettiin soveltuvaksi kasvojensiirtoleikkaukseen.

Vaikeasti kasvoistaan vammautuneet potilaat muodostavat monimuotoisen potilasryhmän. Aiemmin käytetyt potilasvalintakriteerit ovat epätarkkoja, eivätkä ne sisällä painotuksia eri kasvojen toimintojen välillä tai elämänlaadullista arviota. Esittelemme systemaattisen arviointimenetelmän vaikeasti kasvoiltaan vammautuneiden arvioon. Arviointimenetelmä on hyödyllinen myös toimenpiteen onnistumisen ja potilaiden toipumisen seurannassa.

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Systematic patient selection criteria for face transplantation

Short title: Patient selection for face transplantation

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Conflict of Interest statement

The Authors declare that there is no conflict of interest.

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Systematic patient selection criteria for face transplantation

Clin Transplant.

Abstract

Aim. There is a need for a systematic approach to evaluate patients for potential face transplantation (FT).

Materials and Methods. Ten patients with severe facial defects treated between 1995-2017 formed the study group. Data was collected from patient charts and examinations. Facial deficiencies were subdivided into different categories: anatomical region (10 regions), facial function, aesthetic defect (range 0-9-worst), impact on health-related quality of life (HRQoL) (15D questionnaire, range 0-1) and social well-being. Immunological status and contraindications were also evaluated.

Results. Defect aetiology consisted of burns (4), ballistic injury (3), blunt injury (1), blast injury (1), and neurofibromatosis type I (1). All patients had central facial deficiencies and 6 patients had 8 or more injured regions. All patients had at least partial loss of facial function. The median aesthetic disfigurement score was 7. The median lowering of 15D score was -0.107. None were significantly sensitized although 5 patients had significant contraindications for FT. Three of the 6 patients with a severe overall facial deficiency, were considered as potential FT candidates.

Conclusions. We herein propose a comprehensive and systematic tool to evaluate potential candidates for FT. This approach includes assessment of anatomical regions affected, facial function, aesthetics, social well-being and HRQoL.

Key words: facial allotransplantation; vascularized composite allotransplantation; candidate selection; functional outcomes

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Introduction

The human face is composed of complicated functional units that are responsible for the completion of multiple tasks, including life-sustaining actions (breathing, eating), social interactions (speaking, facial expressions, aesthetic appearance) and sensory perception (vision, olfaction, taste). In consequence to major trauma or surgical ablation, damage to these functional units is often so devastating that conventional surgical reconstructive methods fail to provide a satisfactory functional outcome. Face transplantation (FT) can offer a method of restoring near to normal facial function and aesthetics to enhance quality of life [1,2]. In contrast to lifesaving solid organ transplantations, face transplantation is considered life-enhancing, and therefore the major risks associated with obligatory lifelong immunosuppression (cancer, infections, lymphoproliferative disorders and metabolic disorders)[3,4] must be balanced with the positive outcome of regained function. [7]

Indications and contraindications for FT have evolved as knowledge increases. However, there is not yet a clear consensus regarding indications between different clinics worldwide. In practice, most centers would agree upon the indication of a large central facial defect associated with a functional deficit deemed unrepairable by conventional methods, a patient motivated for treatment, able to give informed consent and committed to lifelong follow-up and immunosuppression [6,7]. Currently, patient selection is performed on a case-by-case basis, with thus far no definite conclusion reached regarding which facial defect/deficit is severe enough to justify the significant adverse effects of immunosuppressive medication and risks of vascularized composite allotransplantation (VCA). [4,7]

Ever since the pre-FT days the issues of patient selection and psychosocial factors have been debated (8,9). However, we are still lacking structured tools for patient evaluation. Instead of evaluating each patient in isolation, the aim of this study was to systematically analyze patients with severe facial defects and to assess which patients had a sufficiently poor health-related quality of life (HRQoL), posed a significant challenge for reconstruction with conventional methods, and therefore presenting as a potential candidate for facial VCA. Our goal was to establish certain criteria in connection with facial functions and defects to enable a patient to undergo systematic evaluation as a potential candidate for facial VCA.

Patients and methods

This study was approved by the Ethics Committee, Department of Medicine, Hospital District of Helsinki and Uusimaa. Patients treated between 1995 to 2017 in the University Hospital of Helsinki, Department of Plastic Surgery, were evaluated for different types of facial defects and their reconstructions. Patients with a large facial defect deemed difficult to repair by several experienced head & neck plastic and reconstructive surgeons were selected for the study. Excluded were patients who presented with only aesthetic defects and patients not requiring additional operations following primary reconstructive surgery. Within the hospital catchment area (2.2 million), ten patients matched the inclusion criteria during the study period. These ten patients included two face transplantation recipients [10,11]

Patient evaluation was performed by clinical examination and assessment of radiological and laboratory findings. For each patient, all available medical records were analyzed. The impact of

facial deficiencies was subdivided into different categories (anatomical region affected, loss of facial function, motor and sensory status, aesthetic defect, and impact on HRQoL and social well-being)

Facial deficiency categories

Anatomical zones affected: The face was divided into 10 anatomical regions (forehead and scalp, periorbital, nasal, perioral, cheek and ears, chin, neck, intraoral, maxilla, and mandible) to evaluate the extent of the defects.

Functional deficiencies: Concerning facial function, we placed emphasis on the functions most often affected and considered most important for quality of life (breathing, mouth opening, dentition, mastication, swallowing, speaking, labial competence, eyelid function). In order to unify the data, all functions were also given a three-grade score (0 normal, 1 impaired, and 2 severely impaired or non-functional).

Mimic muscle function was tested using the Sunnybrook facial scale analysis [12,13]. The Sunnybrook facial grading system analyzes facial muscles innervated by the facial nerve by assessing muscle function in voluntary movement with respect to symmetry of each side of the face, resting asymmetry and the degree of involuntary muscle contraction during facial expressions (synkinesis), with each awarded an appropriately weighted score. The patient's total score is achieved by subtracting the involuntary synkinesis score and resting asymmetry score from the symmetrical voluntary movement score so that a greater total score would indicate better facial muscle function. In the Sunnybrook analysis (maximum of 100 points / side), evaluation consisted of resting symmetry (0 to 40 points), symmetry of voluntary movement (0 to 60 points), and synkinesis (0 to -20 points), as well as with key functional tasks (action by request: smile, grin, whistle, etc.). For the previously transplanted patients, the same analysis was performed via historical video-recorded

material prior to transplantation. Mimic muscle function was also assessed by evaluating basic facial movements such as forehead lifting, anger, smile and mouth-puckering.

Sensory function was assessed with light touch discrimination using a static monofilament and well-localized 10mm two-point touch discrimination. Sensation was graded: 0 normal, 1 impaired, and 2 severely affected or numb in six facial regions: forehead and scalp, periorbital, perioral, cheek and ears, chin and neck.

Aesthetic evaluation: A survey among 20 board certificated plastic surgeons was conducted showing pictures of the patients in the study. For the evaluation, a score from 1 to 9 was used, with 1 being normal and 9 the most severe aesthetic defect (14). The score was also transformed to a 3-step score: 0 near normal, 1 impaired, 2 severely disfigured.

Health-Related Quality of life: At the time of clinical evaluation, the patient's HRQoL was also measured using the generic 15D and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck Module (EORTC QLQ-HN35)(15,16). The single index score (15D score) represents the overall HRQoL on a 0-1 scale (1=full health, 0=being dead). Each patient's 15D score was compared to the mean score of patient's gender- and age-group in the general population. The minimum clinically important change or difference in the 15D score has been estimated to be ±0.015 on the basis that patients can on average feel such a difference. The changes or differences in the 15D scores can be classified as follows: >0.035 for much better, 0.015-0.035 for slightly better, >-0.015 and <0.015 for no change, -0.035- -0.015 for slightly worse and <-0.035 for much worse (17).

Social impairment: The effect on social well-being of the facial disfigurement and functional deficit was estimated from the patient charts. All patients had been evaluated by a psychiatrist or psychologist and most patients had visited a social worker. The Sheehan Disability Scale (SDS), a patient-rated measure of functional disability in work, social and family life was used. These 3 items added together provide a global impairment score that ranges from 0 (unimpaired) to 30 (highly impaired). (18) This score was also transformed to a 3-step score: 0 near normal, 1 impaired, 2 severely impaired.

Comorbidities and immunological status: In addition, potential contraindications for face transplant and comorbidities were recorded from the patient charts. Contraindications included any relevant comorbidities for organ transplantation in general, such as malignancies, progressive chronic medical disease, neurological diseases and psychiatric disorders. In order to predict the immunological suitability of a potential donor, human leukocyte antigen antibodies (HLA-ab) were measured from a routine venous blood sample and cPRA (calculated panel reactive antibodies) were estimated by comparing the patients' HLA-ab findings to HLA antigen frequencies in the Finnish reference population. One Lambda Labscreen® mixed and single antigen beads with Luminex® were used for HLA antibody screening and identification with the use of HLA Fusion software (One Lambda Inc., Canoga Park, CA). A normalized Mean Fluorescence Intensity (MFI) cut-off point of 1000 was used for positivity in single antigen analyses.

Results

Demographic data

The patients included in the study are summarized in Table 1. Two patients presented with incomplete medical records. Patients consisted of three females and seven males. The median age was 41 years (range 26-66), the median age at the time of injury was 29 years (range 22-57, not including one patient with a congenital defect and one patient with missing age at injury). Facial defect aetiology consisted of burn injury (n=4), ballistic injury (n=3), blunt injury (n=1), congenital neurofibromatosis type 1 (NF1) (n=1) and blast injury (n=1). The median number of reconstructive operations was 10 (range 4-34, two patients had incomplete medical records) and microvascular flaps were used in five patients (median number of flaps 3, range 1-6). (Table 1).

Table 1: Demographic data

Patient	1	2	3	4	5	6	7	8	9	10
Gender (M/F)	M	M	F	M	M	F	M	M	F	M
Age (years)	34	60	47	52	66	31	26	36	59	32
Age at injury (years)	18	41	29	N/A	26	22	NA	26	57	38
Mechanism of injury	Ballistic	Ballistic	Burn	NF1	Ballistic	Burn	Blunt	Burn	Burn	Burn
No of reconstructions	25	>20	20	7	34	N/A	N/A	10	4	9
No. of microvascular flaps	5	6	2	1	3	N/A	N/A	0	0	0

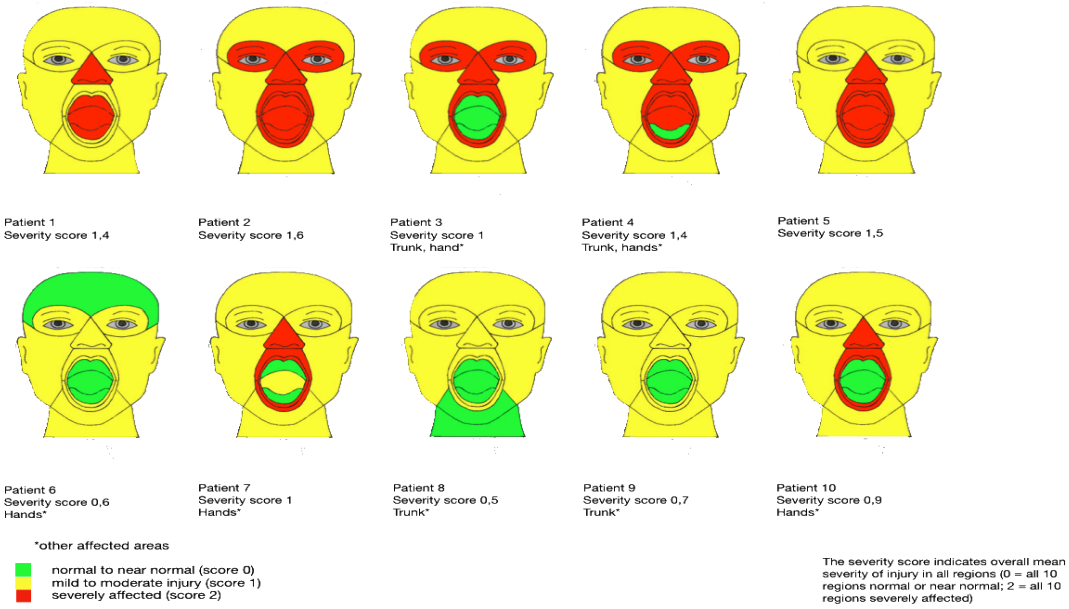
NF1:Neurofibromatosis1
N/A: Data not available

Anatomical defects in different facial regions

The regional defects for each patient are presented in Figure 1. Four patients had injuries involving their maxilla and of these, three also had a mandible deformity. All bony injuries were graded

severe. Nine out of 10 patients had injuries to their forehead, and all were graded mild to moderate. The periorbital, nasal, perioral, and cheek regions were affected in all 10 patients (graded severe in the perioral region in six patients, severe in the nasal region in seven patients and severe in the periorbital region in three patients). Nine out of 10 patients had at least mild to moderate injury to their chin and neck. Intraoral injuries were present in five patients (four were graded as severe) (Figure 1).

Figure 1. Affected facial regions.



Functional facial defects

Mouth opening was affected in seven patients (severe in one). The most common cause was scar adhesions restricting movement. Labial competence was affected in all patients (severe in two patients with ballistic injuries). The reason for labial incompetence was scarring in six patients and a tissue defect in four patients. Three ballistic injury patients had lost their teeth and the NF1 patient had incomplete dentition. Eating was compromised in four patients due to poor masticatory

function. Swallowing was impaired in all three of the ballistic injury patients. None of the patients had a permanent gastrostomy (Table 2).

Air conduction was scored as normal airway, loss of nasal breathing, and loss of upper airway requiring a permanent tracheostomy. Breathing was impaired in seven patients with loss of the nasal airway. Patient 2 required a permanent tracheostomy. Speech was scored subjectively as normal, partly impaired, and unintelligible. Speech was partly impaired in two patients and unintelligible in three patients. In the three patients with a ballistic injury, speech was affected due to impaired mobility of the tongue and abnormal anatomy of the oral cavity (Table 2).

Periorbital function was analyzed with regard to eyelid function and visual acuity. One patient was blind, and one patient had only monocular vision. Seven patients had suffered an injury that impaired their lid function. The most commonly encountered problem was ectropium secondary to lid scarring (Table 2).

Impaired sensation most commonly affected the midface in comparison to the forehead and neck. Sensation was impaired in the forehead in 5 patients (absent in 1), periorbitally in 8 patients (absent in 1), periorally in all patients (absent in 3), in the cheeks and ears in all 10 patients (absent in 1 unilaterally), and in the chin and neck in 8 patients (partially absent in 4 patients). (Table 2).

Forehead movement was absent in two, and impaired in one patient due to the use of a previous forehead flap. The expression used for snarl was impaired in two and missing in five patients. Smile was impaired in seven patients and missing in two. Lip pucker was impaired in six and missing in two patients. Applying the Sunnybrook scores (data available from 7 patients) there was severe bilateral

Table 2. Functional impairment evaluation

	Patient	1	2	3	4	5	6	7	8	9	10
Oral	Mouth opening	Impaired	Impaired	Normal	Impaired	Restricted	Normal	Impaired	Normal	Impaired	Impaired
	Labial competence	Impaired	Incompetent	Impaired	Impaired	Incompetent	Impaired	Impaired	Impaired	Impaired	Impaired
	Teeth	Edentulous	Edentulous	Full dentition	Impaired	Edentulous	Full dentition	Full dentition	Full dentition	Full dentition	Full dentition
	Mastication	Soft nutrition	Soft nutrition	Normal	Soft diet	Soft diet	Normal	Normal	Normal	Normal	Normal
	Swallowing	Impaired	Impaired	Normal	Normal	Impaired	Normal	Normal	Normal	Normal	Normal
	Breathing	No nasal airway	Tracheostomy	No nasal airway	No nasal airway	No nasal airway	Slightly obstructed	No nasal airway	Normal	No nasal airway	Slightly obstructed
	Speech	Unclear	Unclear	Normal	Unclear	Impaired	Normal	Impaired	Normal	Normal	Normal
Periorbital	Eyelid function	Ectropium, lagophthalmos, enophthalmos, blind	Ectropium, lagophthalmos, enophthalmos	Ectropium, lagophthalmos, enophthalmos	No right eyelid (blind eye), right periorbital region normal	Normal	Normal	Impaired (ectropium, scarred eyelids)	Impaired (ectropium, scarred eyelids)	Normal	Impaired (ectropium, scarred eyelids)
	Visus	Blind	right: normal; left: impaired	Blind	right: normal; left: impaired	Normal	Normal	right: normal; left: impaired	Normal	Normal	Normal
Sensation	Forehead and scalp	Normal	Absent	Absent	Absent	Absent	Normal	Normal	Normal	Normal	Impaired
	Periorbital	Impaired	Impaired	Impaired	Absent	Impaired	Normal	Normal	Impaired	Impaired	Impaired
	Perioral	Absent	Absent	Impaired	Impaired	Absent	Impaired	Impaired	Impaired	Impaired	Impaired
	Cheeck and ears	Impaired	Impaired	Impaired	Absent	Impaired	Impaired	Impaired	Impaired	Impaired	Impaired
	Chin	Absent	Absent	Impaired	Absent	Absent	Normal	Normal	Impaired	Impaired	Impaired
Mimic muscles	Forehead wrinkling	Normal	Absent	Absent	Impaired	Normal	Normal	Normal	Normal	Normal	Normal
	Anger	Absent	Absent	Absent	Impaired	Absent	Normal	Absent	Normal	Normal	Impaired
	Smile	Impaired	Impaired	Impaired	Impaired	Absent	Impaired	Absent	Normal	Impaired	Impaired
	Mouth pucker	Impaired	Impaired	Impaired	Impaired	Absent	Normal	Absent	Normal	Impaired	Impaired
Sunnybrook	Left*	50	24	25	75	NA	NA	40	96	NA	50
	Right*	58	43	25	4	NA	NA	32	86	NA	46
	Severity (mean score)**	**1,20**	**1,55**	**1,24**	**1,25**	**1,33**	**0,27**	**1,06**	**0,35**	**0,6**	**0,76**

	Not relevant	1	Impaired	NA: Data not available
0	Normal or near normal	2	Severely affected or non-functional	* Maximum Sunnybrook score 100

** Mean value for all categories

impairment in three patients and unilaterally in one patient. Moderate scores were awarded in two patients bilaterally and one patient unilaterally. Only one patient scored near to normal scores. (Table 2).

Aesthetic evaluation

Twenty plastic surgeons individually assessed the patients' aesthetic appearance. The mean aesthetic score was 6.4 (range 3.8 to 8.5; 1 being normal and 9 most severely affected) (Table 3).

Quality of life and social impairment

HRQoL data were available from 7 patients (all native Finnish speaking). Regarding the EORTC QLQ-HN35 (range 35 to 130 points), a lower score indicated a better quality of life. The scores varied between 47 to 82. The patients' mean 15D score was 0.780 (range 0.533 - 0.914). This is 0.164 lower than the mean 15D score in the age-and gender-matched general population. This suggests that the mean HRQoL of the patients was much worse (severely impaired) compared with the comparable general population. This applied to all individual patients, except one that had only a slight deterioration. The patients were on average markedly worse off on all 15D dimensions except two (sleeping and excretion) (Table 3). The mean SDS (0 to 30) was 17 (range 7 to 27). All patients demonstrated some social impairment, whereas there was only minor impairment in social activities in three patients (score 7/30). Three patients had moderate social impairment, which restricted their social behaviour (scores 17-20/30); such as not being able to eat publicly. Four patients had severe restrictions in their social activity due to their disfigurement (23-27/30); such as one patient who was not able to leave home, except occasionally, due to the facial disfigurement. (Table 3).

Table 3. Scores for aesthetic, social and quality of life impairment

	Patient	1	2	3	4	5	6	7	8	9	10
Aesthetic disfigurement score*		7	7	9	8	5	4	8	4	6	7
Social impairment score**		20	23	17	20	23	27	23	7	7	7
QOL	EORTC HN-35	55	56	82	74	50	N/A	N/A	39	N/A	47
	15D***	0,656	0,854	0,533	0,791	0,872	N/A	N/A	0,843	N/A	0,914
	15D Control group median value****	0,949	0,925	0,93	0,944	0,918	N/A	N/A	0,95	N/A	0,949
	15D Difference in scores	-0,293	-0,071	-0,397	-0,153	-0,046	N/A	N/A	-0,107	N/A	-0,035
	QOL impairment score	2	2	2	2	1			2		1

0	Normal or near normal
1	Impaired
2	Severely affected

* Scoring: 1: normal, 9: worst possible
** Sheehan Disability Score: 0: normal, 30: worst possible
*** Values between 0-1; 1 representing full quality of life
**** Age- and sex matched comparison group 15D value in Finnish population for each patient
Values given as median for aesthetic disfigurement score
Value estimated from patient charts for social impairment

Comorbidities and potential contraindications

Mental health issues were documented in four patients, problems with alcohol consumption in two patients, and liver cirrhosis in one patient. Seven of the 10 patients had additional injuries related to their facial injury. All five facial burn patients had suffered burns also to their torsos and extremities. The NF1 patient also had significant incapacitating tumours in his torso and extremities. Five patients had suffered hand injuries, two of whom had severe injuries and were also considered as candidates for hand transplantation (Table 4).

Table 4. Immunological status and potential contraindications

Patient	1	2	3	4	5	6	7	8	9	10
Blood type	O+	O+	A-	B+	A+	A+	A+	O+	O+	A+
HLA-ab	Cl 1: B13, Cw 7	Class I +, Class II -	Class I -, Class II -	Class I -, Class II -	Class I +, Class II -	N/A	Class I -, Class II -	Class I -, Class II -	N/A	Class I -, Class II -
PRA	Cl 1: 13% Cl 2: 0%	Cl 1; 12% Cl 2: 0%	Cl 1: 1%, Cl 2: 0%	Cl 1: 0%, Cl 2: 0%	Cl 1: 23% Cl 2: 0%	N/A	Cl 1: 0%, Cl 2: 0%	Cl 1: 0%, Cl 2: 0%	N/A	Cl 1: 0%, Cl 2: 0%
Contraindications			Psych. issues		Psych. issues	Psych. issues	Psych. Issues		Alcohol	
					Alcohol				Liver cirrhosis	

0	Minimal preimmunization or no contraindications
1	Mild preimmunization or relative contraindications
2	Severe preimmunization or absolute contraindications

Immunological status

HLA-ab and PRA data were available for eight patients. The calculated PRA varied between 0 to 23% (Class I antibodies). None of the patients demonstrated any Class II antibodies. Interestingly, none of the three patients with major burns were sensitized at a clinically relevant level (PRA 0 to 1%) and this was in spite of multiple blood transfusions (Table 4.)

Summary in all categories

In order to summarize the overall impact of the facial injury, all parameters including the affected anatomical regions, functional, aesthetic and social impairment, and effect on quality of life were graded from 0 to 2 (0: mild deficiency, 1: moderate deficiency, 2: severe deficiency). A mean score of all these parameters was calculated for each patient (0-0.67: mild deficiency, 0.68-1.33: moderate

deficiency, 1.34-2: severe deficiency). Six patients had a mean score graded severe deficiency (including 2 actual face transplant patients from Helsinki), 3 patients had a moderate deficiency and one patient a mild deficiency (Table 5).

Table 5. Summary of different categories

Patient	1	2	3	4	5	6	7	8	9	10
Affected anatomical regions	1,4	1,6	1,00	1,40	1,50	0,60	1,00	0,50	0,70	0,90
Functional defect	1,20	1,55	1,24	1,25	1,33	0,27	1,06	0,35	0,60	0,76
Aesthetic defect	2	2	2	2	1	1	2	1	1	2
Social defect	1	2	1	1	2	2	2	0	0	0
QOL	2	2	2	2	1	N/A	N/A	2	N/A	1
Summary*	1,52	1,83	1,45	1,53	1,37	0,97	1,52	0,77	0,58	0,93
Contraindications for FT			Yes		Yes	Yes	Yes		Yes	

0 - 0,67	Mild deficiency
0,68 - 1,33	Moderate deficiency
1,34 - 2	Severe deficiency

* Mean value

N/A: Data not available

QOL: quality of life score

None of the patients were highly immunized. Five patients had significant contraindications for FT. Of the six severely affected patients, three had contraindications for FT (mental issues and substance abuse). Thus, there remained three patients following this analysis who were deemed to overall have a severe facial deficiency and no contraindications for FT (patients 1, 2 and 4). We have performed a FT in two of these 3 patients (patients 1 and 2).

Discussion

At present there is no consensus on which parameters are required when evaluating and selecting candidates for FT. Furthermore, there exists no consensus on how to define success or failure in FT. The complex and subtle interplay between facial anatomy, function and aesthetics helps explain the difficulty thus far in defining the parameters necessary for evaluation in patient selection for FT.

Our study provides the first attempt in the literature to perform a comprehensive analysis of the different aspects of facial disfigurement and their combined effect on patients in the context of FT. Herein we created a systematic method for evaluating 10 patients with severe facial disfigurement. Five categories were analyzed in all patients: the anatomical zones of facial injury, functional deficiencies, the aesthetic appearance, and HRQoL as well as social impairment. The overall impact of facial disfigurement was then graded in order to estimate whether or not an individual patient would be a suitable candidate for FT.

Previously it has been stated that FT is indicated in adults with a severe facial defect and functional deficits that cannot be adequately addressed with conventional reconstruction techniques (8). At present this includes: a person with loss of periorbital tissues, total loss of perioral tissues or an extensive loss of facial structures. This definition is broad and does not define which functions are considered essential in this respect nor does it take into account the psychosocial effects of the deficit in a specific person. In view of the fact that FT is such a major procedure associated with high risks and that the immunosuppressive treatment may have severe side effects, there is a need to develop a universal instrument to aid patient selection. In addition, in order to define whether a FT

has succeeded and has been beneficial for the patient, we need to be able to demonstrate improvements in well-defined parameters that have been evaluated prior to FT.

Affected anatomical zones

The most obvious parameter to analyze was the affected facial anatomical zone(s). We defined 10 different anatomical zones for assessment. In our material, there were four patients with injury to the maxilla and/or mandible and these patients would thus be potential candidates for composite FT. Three of the latter four patients had injuries in all 10 zones except for one patient who had injuries in 9 zones. The remaining six patients who only had a soft tissue injury would be potential candidates for soft tissue FT. Four of these six patients had injuries in 7 of 8 soft tissue zones and two patients had 5 or 6 injured zones. In summary, these patients often have panfacial injuries or large areas of their face injured. In addition to the injury from the original trauma there are often additional iatrogenic facial injuries that may occur during attempts of conventional reconstruction. There has been some debate whether patients should be subject to a full or partial FT. The Boston group has advocated preserving all of the patient's functional tissue and only removing and restoring what is non-functional (19). From the perspective of the aesthetic outcome, a partial FT is often more discernible and might not restore a near to normal appearance and consequently facilitate the stigma of FT. Moreover, if the aesthetic outcome is considered to be one parameter of success it would then be advisable to perform a full FT in a patient with a large portion of their face injured (20). The flip side is that the latter would increase the stakes in view of possible early or late graft failure.

Seven of our patients had additional injuries affecting other parts of their body. These patients might benefit from additional vascular composite allotransplantations (VCA) in addition to FT. A

burn patient for instance might benefit from soft tissue transplantation to restore other burned areas of their body. Five patients had coexistent hand injuries and one of these patients would also have been a candidate for hand transplantation. The possibility of an additional VCA under the same immunosuppression could be considered an additional factor that supports the decision to proceed with FT. However, so far, all simultaneous face and upper extremity transplantations have suffered serious complications (21) and thus the current opinion advises against performing these simultaneous transplants.

Functional deficit

In this study we analyzed facial functions with several parameters, including labial continence, periorbital function, mimic muscle movements, and sensation. All our patients had a reduced Sunnybrook scale score. The severity of impaired facial mimic function varied between the patients and there is certainly a need for a scale to reflect the severity of impairment. The Sunnybrook scale has been used previously by the Boston group in FT patients and is at present the most suitable instrument to use in the absence of any scales evaluating bilateral facial function deficiency (22). There are several reports on the functional mimic muscle recovery after FT and it has been shown that facial function suitable for social interaction can be restored at least partially (22-25). We propose a 3-grade scale that should include an analysis of individual muscle function as well as the ability to express different emotions.

In this study, facial sensation was impaired in all patients and in 5 patients the entire face had impaired sensation and in 3 patients sensation was impaired in most facial regions. A full or close to full recovery of sensation after FT has been documented by several groups (26). Therefore, sensation should be included in the evaluation.

Mouth opening was affected in 7 patients whereas oral competence in all 10 patients. All four patients with bone injuries had impairments in their other oral functions such as mastication and swallowing. Seven patients had impaired breathing and 5 patients had impaired speech. Similarly, 7 patients had impaired eyelid function. Severe injuries to the central face are overexpressed in this patient population since these have the most impact on facial function. There are reports in the literature regarding improvements in oral competence, eating, breathing and speaking after FT (23-26). Therefore, oral functional impairment should be included in the evaluation and it should include several different functions with a grade to score the severity of the impairment.

Aesthetic deficit and social impairment

One of the goals of FT as in all of reconstructive surgery is to restore normal appearance. Even though FT should not be performed for solely aesthetic reasons there is still an important need for these patients to look normal and to integrate socially without attracting undue attention to their facial deformity. We used the single-item, nine-point Likert scale that measures the degree of disfigurement previously described by Katz et al (14). The mean aesthetic score in our group of patients was 6.4. Interestingly both of our FT patients scored 7, hence neither being awarded the worst aesthetic score possible of 9. Six patients in this study were evaluated to look 'very abnormal' (range 7-9) and 4 patients 'moderately abnormal' (range 4-6). Facial disfigurement lead to the reduction in the number of social contacts in all 10 patients in this study. The face is hence an important mediator in social communication and although FT does not focus only on regaining normal aesthetics, a normal human-like appearance is a key factor in social integration and appearance enhancement has proven to improve quality of life [14]. The other reasons for social impairment were reduced capability to express emotions and impaired speech. Labial

incompetence resulted in unwillingness to eat publicly. In addition to the aesthetic score, one of the major goals for FT is to improve the social well-being of these patients. In fact, by including severe social disability as a patient inclusion criterion, FT can be considered even lifesaving in some patients (27).

Quality of life

All VCA teams that have reported their FT results have included QoL instruments in their evaluation; however, there have been several different instruments used (1). There exists no validated HRQoL-measurement scale for facial trauma patients. The FaCE Scale and Face-Q are not yet validated in the Finnish language (28,29). We used a head and neck cancer oriented measurement (16), since we consider this to most resemble the study patient group as well as the generic HRQoL instrument 15D which has been widely used and validated in the Finnish population and can be used to estimate the overall changes in HRQoL (15). The 15D has good psychometric properties and provides also 15D data from a large, representative sample of the general population. The self-administered 15D questionnaire measures mobility, vision, hearing, breathing, sleeping, eating, speech (communication), excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity, each on a 5-level scale.

We found severe impairment in the generic HRQoL in 9 out of the 10 patients. Interestingly, the one patient with only a mildly reduced HRQoL score did however score poorly in his functional and esthetic evaluations. Indeed, one may question is it justified to perform FT in a patient with a near to normal HRQoL? Functional evaluations of sensation recovery or airway volume are physician-oriented measurements and therefore report only one side of the potential success of the

treatment. We advocate that the comprehensive evaluation of a FT candidate should include a generic HRQoL instrument as well as a FT-specific facial disfigurement QoL assessment instrument.

As FT is such a major undertaking for any patient, aspects other than just the facial disfigurement need to be taken into account during the decision-making process. Patients with severe comorbidities should in general be excluded. In our study group, there was one patient with liver cirrhosis which is considered to be an absolute contraindication for FT. A thorough psychological and psychiatric evaluation is essential to rule out any psychiatric disorders that may jeopardize the postoperative recovery as well as negatively influence the patient's compliance with immunosuppressive medication. The immunological status of the patient also needs to be evaluated. Preformed HLA-antibodies present a risk for subsequent antibody-mediated rejection and needs to be assessed in view of donor specific antibodies present at the time of FT (30). Interestingly, in our data, all three burn patients had received multiple blood products as well as cadaveric skin substitutes during their acute burn treatment period, but yet had no clinically relevant HLA-antibodies present. The highest PRA scores were recorded in the ballistic injury patients who had received blood products before 2001 prior to when all red cell products in Finland were changed to leucodepleted products.

Regarding the selection of our two FT recipients, although they were not originally selected using our proposed systematic instrument (as this has only evolved with the benefit of experience and hindsight), it is interesting to comment on how they would have scored. Both patients had all facial zones affected including both the maxilla and mandible. Both had a severely affected nasal area and intraoral area. The second patient additionally had severely affected periorbital areas and lips. They also had impaired facial function, a severe aesthetic disfigurement, suffered from social impairment

and had a severely reduced HRQoL. Their overall score considering all parameters indicated a severe deficiency.

Conclusion

The aim of this study was to evaluate 10 patients with severe facial disfigurement and to create a scoring system to analyze their suitability for FT. Owing to the numerous variables and that the evaluation is partly subjective, it may be impossible to create a rigid numerical scoring system. It is also debatable how to weight different parameters. Is social impairment as important as functional deficiency? However, there is an important need to have a commonly accepted and comparable method in which to evaluate potential FT candidates. The number of FT patients worldwide is growing steadily but is still very small and data is only gradually accumulating. A valid preoperative evaluation chart would also help when evaluating whether or not the executed FT has been a success. Hence for FT candidates, we propose a systematic and comprehensive tool, which takes into account the affected facial regions, wide ranging functional analyses and an aesthetic, HRQoL and social impairment evaluation.

Authors Contributions

Conception or design of the work (AL, PL); data collection (MS, ELK, AL, TYK, HS, JL, PL); Data analysis and interpretation (MS, ELK, AL, PL); Drafting the article (MS; ELK, AL, PL); Critical revision of the article and final approval of the version to be published (MS, ELK, AL, TYK, HS, JL, PL).

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Figure Legends

Figure 1: Affected anatomical facial regions

Table 1: Demographic data

Table 2: Functional Impairment evaluation

Table 3: Scores for aesthetic, social and quality of life impairment

Table 4: Immunological status and potential contraindications

Table 5: Summary of different categories