# Appendix 1. Additional questions

The bottleneck analysis formed the basis for the questions for the guideline. The questions were formed according to the PICOT Framework and are presented in each guideline chapter. To provide a clear and readable chapter, questions in the guideline were formulated in a broad and clinically relevant way. More specified questions to facilitate the literature search are specified in this chapter.

The guideline is divided into a non-surgical and surgical part. Questions for the non-surgical chapters (Chapter 4 (4.1 to 4.8)) are formulated in a similar way. Likewise, questions for the surgical chapters (Chapter 5 (5.1 to 5.4)) are also formulated in a similar way.

* Chapter 4.x.1
  + What is the type, prevalence and severity of X problems in craniofacial microsomia?
    - What is the type of problems?
    - What is the prevalence of problems?
    - What is the severity of problems?
* Chapter 4.x.2
  + What is the policy for screening of X problems (e.g. OSA) in patients with craniofacial microsomia?
  + What is the policy for monitoring of X problems (e.g. OSA) in patients with craniofacial microsomia?
    - What are the consequences if patients with breathing problems remain untreated?
    - What is the impact of these consequences on patients?
    - Will these consequences be prevented if patients get screened for breathing problems?
    - What does screening involves?
    - What is the impact of screening on patients?
    - Which tests are needed for screening?
    - Who is responsible for screening?
    - How often should patients be screened?
    - What does monitoring involves?
    - What is the impact of monitoring on patients?
    - Which tests are needed for monitoring?
    - Who is responsible for monitoring?
    - How often should patients be monitored?
* Chapter 4.x.3
  + What are the indications and policy for treatment of X problems (e.g. OSA) in patients with craniofacial microsomia?
    - What are the different types of treatment?
    - What are preconditions or requirements for initiating treatment?
    - What are preconditions or requirements for NOT initiating treatment?
    - What are symptoms that might influence your choice of treatment?
    - What are advantages and disadvantages of a treatment?
    - What are complications of a treatment?
* Chapter 5.x.1
  + What is the indication for surgical treatment of X in patients with craniofacial microsomia?
    - What are the different types of treatment?
    - What are preconditions or requirements for initiating treatment?
    - What are preconditions or requirements for NOT initiating treatment?
    - What are the clinical problems patients with CFM encounter?
    - What are the consequences of not treating this deformity?
    - When is treatment indicated?
* Chapter 5.x.2
  + What is the most optimal treatment modality and its timing related to ..
    - What are the available treatment options?
    - To what extent do the various treatment modalities treat the deformity?
    - What is the treatment-related burden for patients of the various treatment options? (i.e. hospital stay, operation time, complications risk, bleeding etc.)
    - What are the short and long term results of the various treatment modalities?
    - What are advantages and disadvantages of a treatment?
    - What are complications of a treatment?

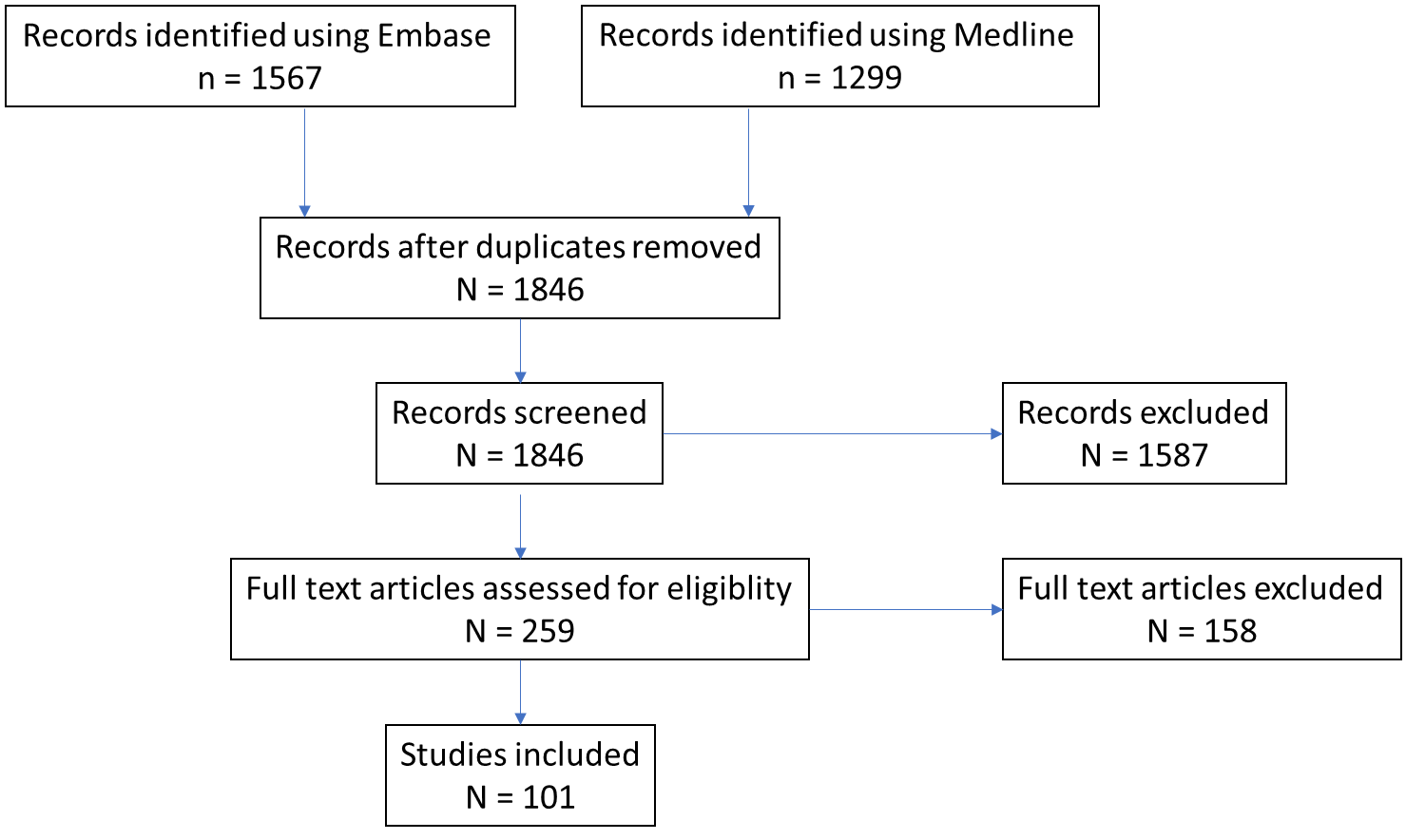
# Appendix 2. Literature searches

A total of four literature searches have been performed to include all relevant literature related to craniofacial microsomia. One main literature search and three separate literature searches for three separate chapters were performed.

All searches were performed in both Embase and Medline. In this appendix we only present the search performed in Medline.

**1. Main literature search**

*Search process*

**

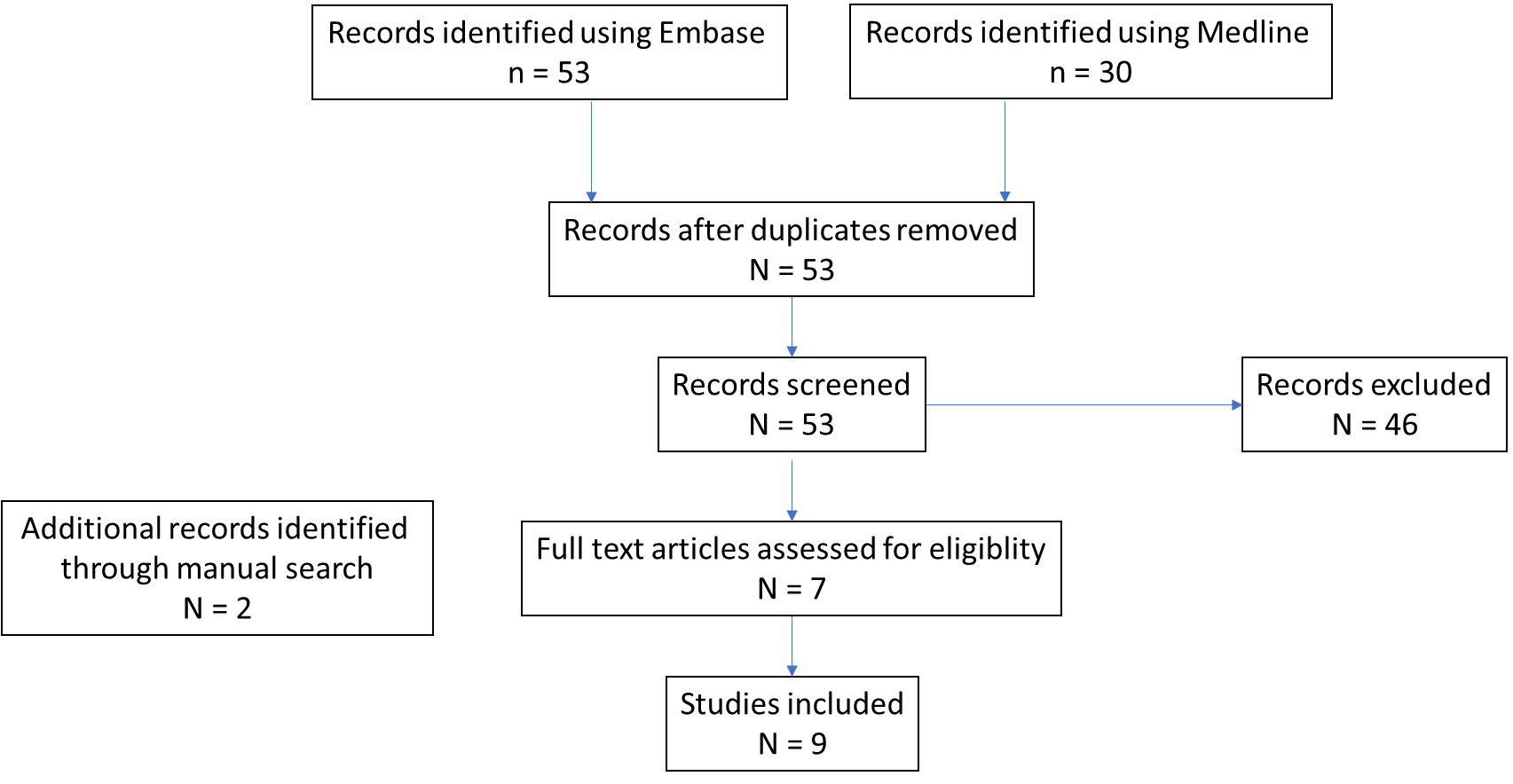
*Search*

Date: 23 November 2018

(exp \*"Mandibulofacial Dysostosis"/ OR (((facial OR face OR hemifacial OR orbitocranial OR facies OR cranial OR mandibulofacial OR otomandibular OR craniofacial OR faciocranial OR hemimandibular ) ADJ3 (microsom\* OR asymmetr\* OR dysosto\* OR dysplasia OR anomal\* OR deformit\* OR hypoplasia OR syndrom\* OR malformation\*)) OR goldenhar OR oculoauriculovertebral\* OR facioauriculovertebral\* OR (auriculo ADJ vertebral\*)).ti.) AND (((1# OR 2# OR (3# NOT 3D) OR 4# OR 5# OR 6# OR 7# OR 8# OR 9# OR (1## NOT 1st) OR (2## NOT 2nd) OR (3## NOT 3rd) OR (4## NOT 4th) OR (5## NOT 5th) OR (6## NOT 6th)OR (7## NOT 7th)OR (8## NOT 8th) OR (9## NOT 9th) OR 10## OR 11## OR 12## OR 13## OR 14## OR 15## OR 16## OR 17## OR 18## OR 190# OR 191# OR 192# OR 193# OR 194# OR 195# OR 196# OR 197# OR 198# OR 202# OR 203# OR 204# OR 205# OR 206# OR 207# OR 208# OR 209# OR 21## OR 22## OR 23## OR 24## OR 25## OR 26## OR 27## OR 28## OR 29## OR (3### NOT 3P##) OR 4### OR 5### OR 6### OR 7### OR 8### OR 9###) ADJ3 (patient\* OR subject\* OR person OR persons OR men OR women OR male\* OR female\* OR participant\* OR people OR children OR adolescent\* OR boys OR girls OR teens OR teenagers OR infants OR newborns)) OR ((ten OR eleven OR twelve OR thirteen OR fourteen OR fifteen OR sixteen OR seventeen OR eighteen OR nineteen OR twenty\* OR thirty\* OR forty\* OR fifty\* OR sixty\* OR seventy\* OR eighty\* OR ninety\* OR hundred\* OR thousand\*) ADJ6 (patient\* OR subject\* OR person OR persons OR men OR women OR participant\* OR people)) OR ((n OR included OR cohort-of OR sample-of) ADJ (1# OR 2# OR (3# NOT 3D) OR 4# OR 5# OR 6# OR 7# OR 8# OR 9# OR (1## NOT 1st) OR (2## NOT 2nd) OR (3## NOT 3rd) OR (4## NOT 4th) OR (5## NOT 5th) OR (6## NOT 6th)OR (7## NOT 7th)OR (8## NOT 8th) OR (9## NOT 9th) OR 10## OR 11## OR 12## OR 13## OR 14## OR 15## OR 16## OR 17## OR 18## OR 190# OR 191# OR 192# OR 193# OR 194# OR 195# OR 196# OR 197# OR 198# OR 202# OR 203# OR 204# OR 205# OR 206# OR 207# OR 208# OR 209# OR 21## OR 22## OR 23## OR 24## OR 25## OR 26## OR 27## OR 28## OR 29## OR (3### NOT 3P##) OR 4### OR 5### OR 6### OR 7### OR 8### OR 9###))).ab,ti.

**2. Search mandible/micrognathia surgery**

*Search process*

**

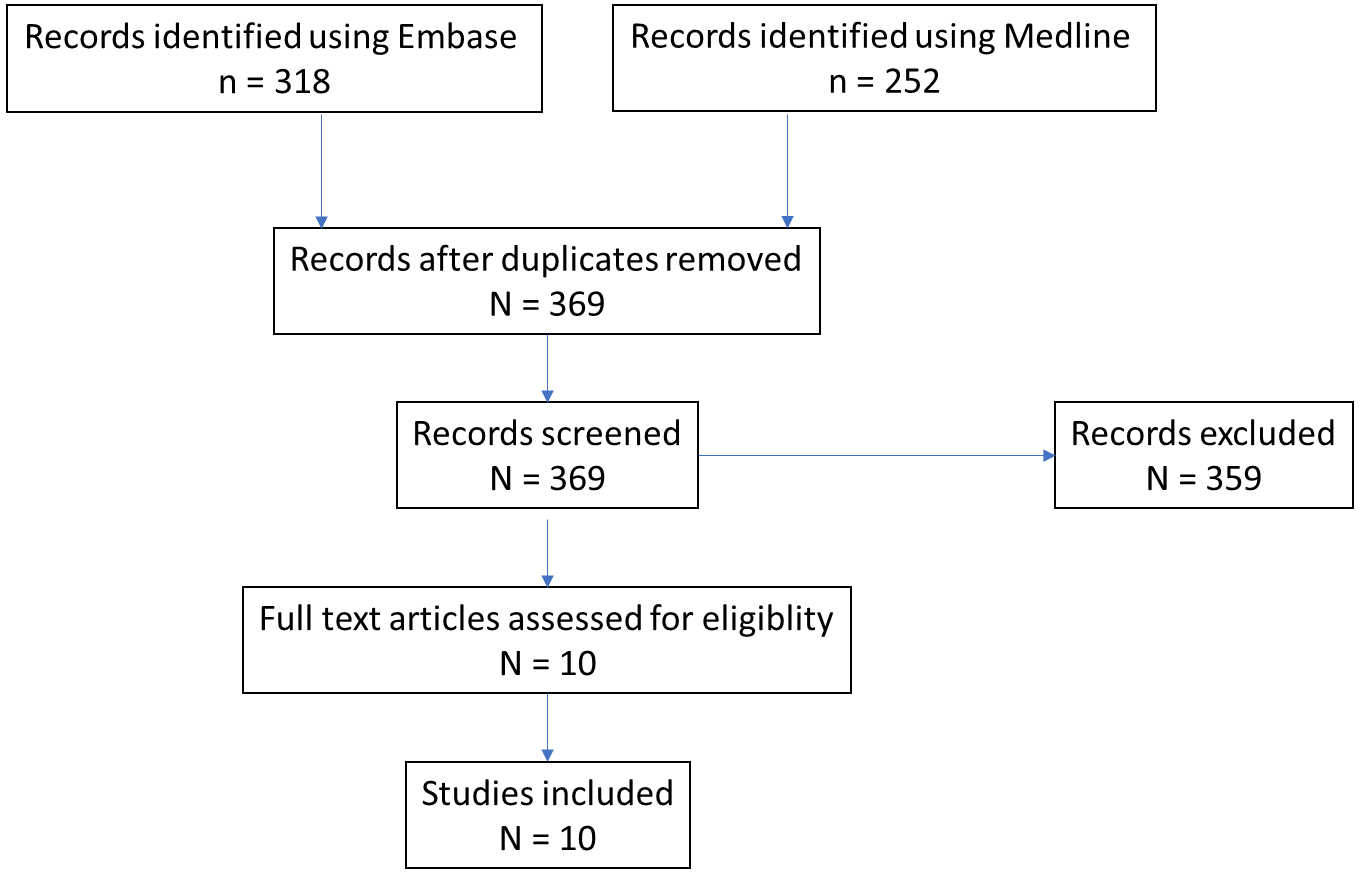
*Search*

Date: 9 July 2019

(Micrognathism/ OR Retrognathia/ OR Pierre Robin Syndrome/ OR (micrognath\* OR hypognath\* OR retrognath\* OR pierre-robin OR Robin-Sequence OR ((Mandib\* OR Maxill\*) ADJ3 Hypoplas\*) OR small-jaw\*).ab,ti.) AND (Surgical Procedures, Operative/ OR Fibula/ OR mandibular distraction osteogenesis/ OR surgery.fx. OR (surger\* OR surgical\* OR operative OR distraction\* OR osteotom\* OR prosthe\* OR reconstruct\* OR lefort OR le-fort OR flap OR fibula OR rib OR (mandib\* ADJ3 advancement\*)).ab,ti.) AND (systematic review.pt. OR Meta-Analysis.pt. OR ((systematic\* ADJ3 review\*) OR meta-analy\* OR metaanaly\*).ab,ti.)

**3. Search ear reconstruction**

*Search process*

**

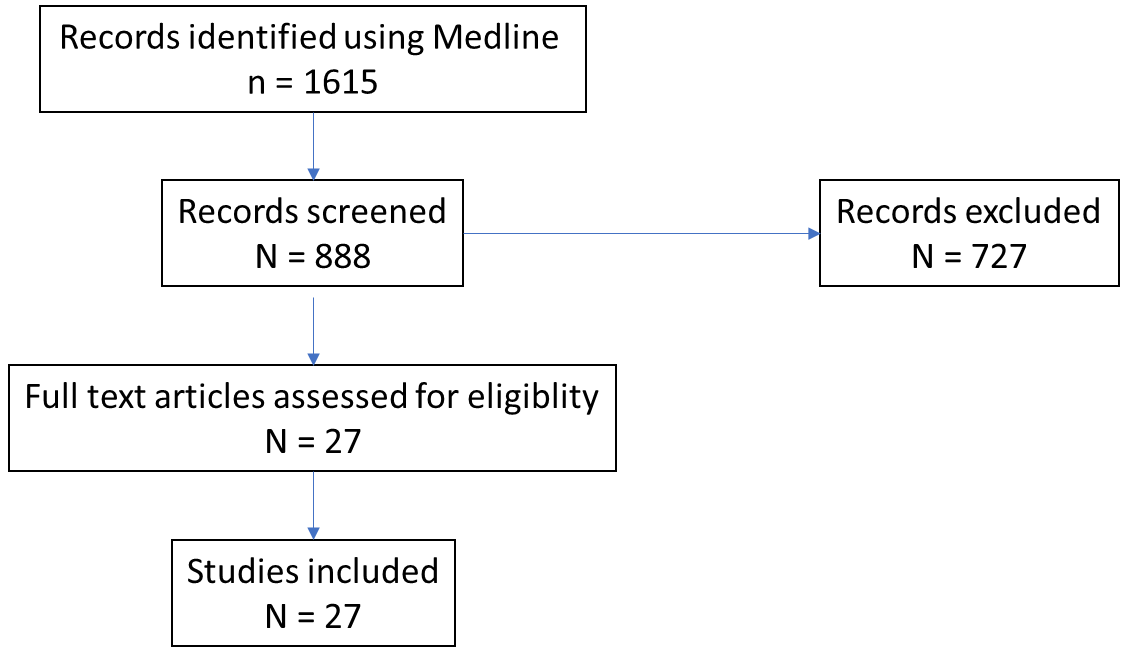
*Search*

Date: 9 July 2019

(Congenital Microtia/ OR (microtia OR ((auric\* OR external-ear) ADJ3 (hypoplas\* OR reconstruct\* OR malform\* OR congenital\* OR defect\*)) OR ear-reconstruct\* OR small-ear\*).ab,ti.) AND (Surgical Procedures, Operative/ OR surgery.fx. OR (surger\* OR surgical\* OR operative OR prosthe\* OR reconstruct\* OR rib OR implant\* OR alloplast\* OR medpor).ab,ti.) AND (systematic review.pt. OR Meta-Analysis.pt. OR Cohort Studies/ OR Retrospective Studies/ OR ((systematic\* ADJ3 review\*) OR meta-analy\* OR metaanaly\* OR cohort\* OR retrospect\*).ab,ti.)

**4. Search Facial Nerve**

*Search process*

**

*Search*

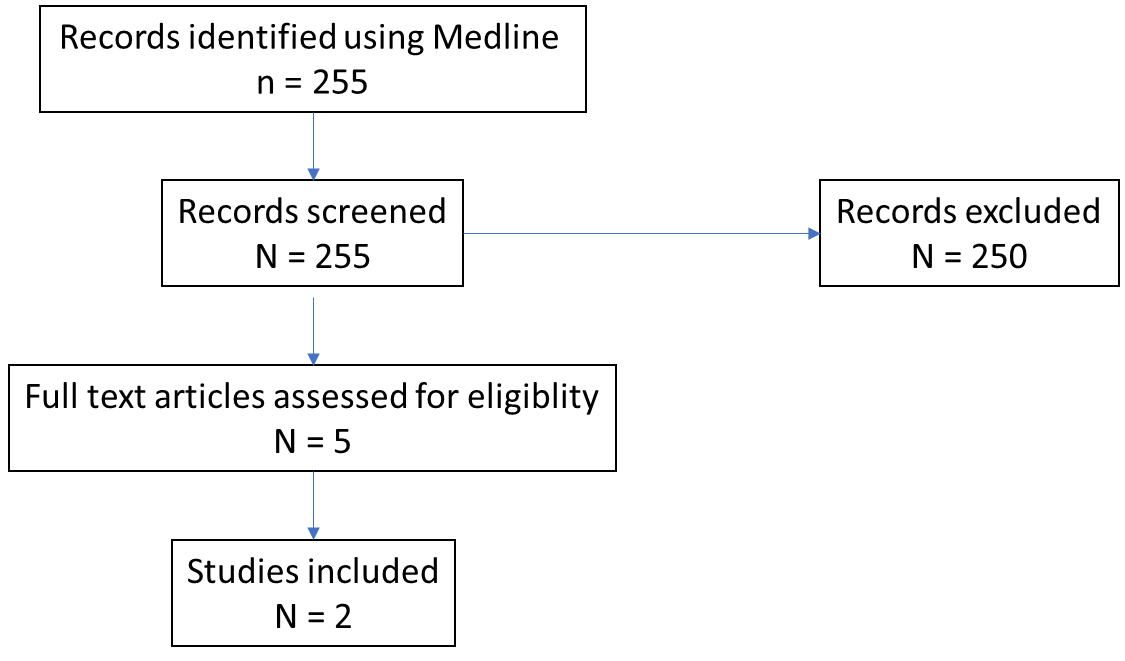
Date: 21 June 2019

Search criteria were based on the criteria from the Dutch Guideline Facial Palsy

("Facial-Nerve-Diseases"[MESH] OR "Bell-Palsy"[MESH] OR "Facial-Hemiatrophy”[MESH] OR "Facial-Nerve-Injuries"[MESH] OR "Facial-Neuralgia"[MESH] OR "Melkersson-Rosenthal-Syndrome"[MESH] OR "Mobius-Syndrome"[MESH] "Facial-Paralysis"[MESH] OR “facial palsy” OR “facial paralysis” OR ((facial OR idiopathic OR congenital) NEAR/3 (paraly\*OR palsy))) AND ("Ophthalmic-Solutions"[MESH] OR "Corneal-Diseases"[MESH] OR "Eyelid-Diseases"[MESH] OR "Eyelids"[Mesh] OR "Surgery-Plastic"[MESH] OR "Surgical-Flaps"[MESH] OR "Microsurgery"[MESH] OR "Anastomosis-Surgical"[MESH] OR "Nerve-Regeneration"[MESH] OR "Neurosurgical-Procedures"[MESH] OR "Nerve-Transfer"[MESH] OR explode "Reconstructive-Surgical-Procedures"[MESH] OR "Neurosurgical-Procedures"[MESH] OR "Nerve-Transfer"[MESH] OR "Botulinum Toxins"[Mesh] OR “reconstruction” OR (nerve NEAR/3 graft\*) OR (muscle NEAR/3 transp\*) OR (facial NEAR/3 sling) OR (plastic NEAR/3 recontruct\*) OR ((repair) NEAR/3 (cosmetic OR function\*)))

**5. Search Eye – epibulbar dermoid**

*Search process*



*Search*

Date: 2 May 2019

"epibulbar dermoid"[tiab] OR "epibulbair dermoid"[tiab] OR "orbital dermoid\*"[tiab] OR "corneal dermoid\*"[tiab] OR "limbal dermoid\*"[tiab]

# Appendix 3. Bottlenecks from patient’s perspective

1. **Introduction**

Patient involvement in drawing up guidelines has increased in the last decade. Where a guideline used to be a document for professionals, today a guideline is developed with and for the patient. To improve the distribution to patients, a patient summary is often written. Participation of patients ensures a better match between the wishes of patients and practice. In addition, it improves the quality of the guideline and facilitates implementation (1).

1. **Methods**

All doctors included in the ERN-CRANIO, subgroup ‘craniofacial microsomia’, were asked to

approach all their CFM patients. An online survey was set up with open and closed questions. All patients and parents were asked what difficulties they (had) experienced in the healthcare process and in their life in general. The questionnaire was built up according to the proposed guideline chapters and the structure of the healthcare process, namely diagnosis and referral, organisation of care, communication and information, breathing problems, feeding problems or speech problems, surgical treatments, care for microtia, orthodontic treatment, vertebral anomalies, psychosocial aspects of care, and follow-up. Additionally, all patients were asked to name the top three difficulties they experienced in the care process. Results were analysed by the research fellow and nurse specialist.

1. **Results**

*Patient population*

A total of 32 patients with CFM or parents were included: 14 from Italy, 13 from Germany, 4 from the Netherlands, and 1 from Sweden. This includes 9 patients and 23 parents of patients. The age of the patients varied from 2-31 years with a mean age of 16 years. Six parents and two patients did not complete the questionnaire.

*Referral and diagnostics*

A total of 53% ( n = 17/32) of patients or parents of patients with CFM encountered problems in the period of referral or during the diagnostic process. Examples of problems mentioned are unknown or random diagnosis, doctors who refuse to refer to a specialist, incorrect statements, different opinions between different specialist, and inexperienced doctors.

*Organisation of care*

A total of 48% (n=14/29) of patients or parents of patients with CFM experienced difficulties in organisational aspects of care. Examples of mentioned problems are different organisations do not work together, knowledge is not shared across specialists, health insurance not adjusted to rare diseases, unclear timing of treatments, and large travel distance.

*Communication and information*

A total of 37% (n=10/27) of patients or parents of patients with CFM experienced problems regarding communication and information. Interviewees mentioned that there was hardly any communication and that they received contradictory statements about treatment, therapies, future prospects, necessary screenings, and incomplete information.

*Functional problems*

A total of 28% (n = 7/25) of patients or parents of patients with CFM encountered breathing problems, feeding problems or speech problems. Two parents of patients mentioned problems with breathing, feeding and speech. One parent and three patients mentioned only feeding problems. One parent only mentioned breathing problems (snoring and apnoea).

*Surgical treatments*

A total of 36% (n=9/25) of patients or parents of patients with CFM encountered problems with aspects of care for surgical treatments. Examples of difficulties mentioned are inexperienced surgeons and, different medical opinions concerning timing and need for an operation.

*Care for microtia*

A total of 40% (n=10/25) of patients or parents of patients with CFM encountered problems with aspects of care for microtia. Difficulties mentioned mainly related to hearing aid: finding suitable hearing aid, problems with payment for proper hearing aid. Other problems mentioned were different points of view of experts regarding whether to treat or not, and finding an experienced surgeon.

*Orthodontic treatment*

A total of 27% (n=7/25) of patients or parents of patients with CFM encountered problems with aspects of orthodontic treatment. Examples of problems mentioned are inexperienced doctors, difficulties finding a proper orthodontist.

*Vertebral anomalies*

A total of 20% (n=5/25) of patients or parents of patients with CFM encountered problems with aspects of vertebral anomalies. Problems that were mentioned difficulties finding a specialist nearby and the fact that speech problems will affect the patient for the rest of their life.

*Psychosocial care*

A total of 21% (n=5/24) of patients or parents of patients with CFM encountered problems with psychosocial care. Most often the lake of psychosocial care was mentioned, as well as the fact that parents and patients have to deal with it themselves.

*Follow-up*

A total of 21% (n=5/24) of patients or parents of patients with CFM encountered problems with follow-up. Examples of problems mentioned are absence of follow-up, no coordination of follow-up, and there not being someone with an overview.

In the end, patients and parents of patients were asked about the top three problems. Problems mentioned in the top three are communication with teachers, communication with experts, health insurance, diagnosis, psychosocial problems, networks, information on treatments and timing, correct diagnosis, (knowledge of) specialised institutions, and hearing aids.

1. **Discussion**

Most patients and parents of patients mentioned problems during the referral and diagnosis (53%) and regarding organization of care (48%). Functional problems, surgical problems and psychosocial problems were less prominent.

*Limitations*

Patients or parents of patients from only four of the eleven invited countries filled in the questionnaire. Unfortunately, no patients from Eastern European countries filled in the questionnaire. Since the ERN-CRANIO is a European network, results might not be representative for the total patient population originally included. A total of eigth patients or parents of patients did not complete the questionnaire. This is 25% of the complete population. The questionnaire was only written in the English language; this might be a barrier for some patients or parents of patients.

1. **Reference**

1. https://www.patientenfederatie.nl/producten/kwaliteitsstandaarden/patientbetrokkenheid-bij-richtlijnen.

# Appendix 4. Definitions

*O.M.E.N.S classification*: A classification which describes the degree of hypoplasia of the Orbit (O), Mandible (M), Ears (E), Facial Nerve (N), and Soft Tissue (S).

*Pruzansky classification*: A classification of the mandibular deformity, based on radiograph. In this classification model the level of underdevelopment of the mandible is grade as I, IIA, IIB, and III.

*Obstructive sleep disordered breathing (SDB)*: A syndrome of upper airway dysfunction during sleep. It is characterised by snoring and/or increased respiratory effort due to increased airway resistance and pharyngeal collapsibility

*Obstructive apnoea*: apnoea for at least the duration of at least two breaths during baseline breathing and associated with the presence of respiratory effort throughout the entire period of absent airflow.

*Central apnoea:*Apnoea with absent inspiratory effort throughout the entire duration of the event that lasts 20 seconds or longer, or at least the duration of two breaths during baseline breathing and is associated with an arousal, ≥ 3% oxygen desaturation.

*Hypopnea*: The peak signal excursions drop by ≥ 30% of pre-events baseline, during at least two breaths, with a ≥ 3% desaturation from pre-event baseline or the event is associated with an arousal.

*Apnoea Hypopnea Index (AHI)*: index to describe the severity of OSA.

*Continuous positive airway pressure (CPAP)*: oxygen therapy with positive airway pressure.

*Non-invasive positive-pressure ventilation (NPPV)*: oxygen therapy through a noninvasive interface such as a mask or nasal plugs.

*Conductive hearing loss*: hearing loss due to a problem in transferring sound waves from the outer ear to the middle ear.

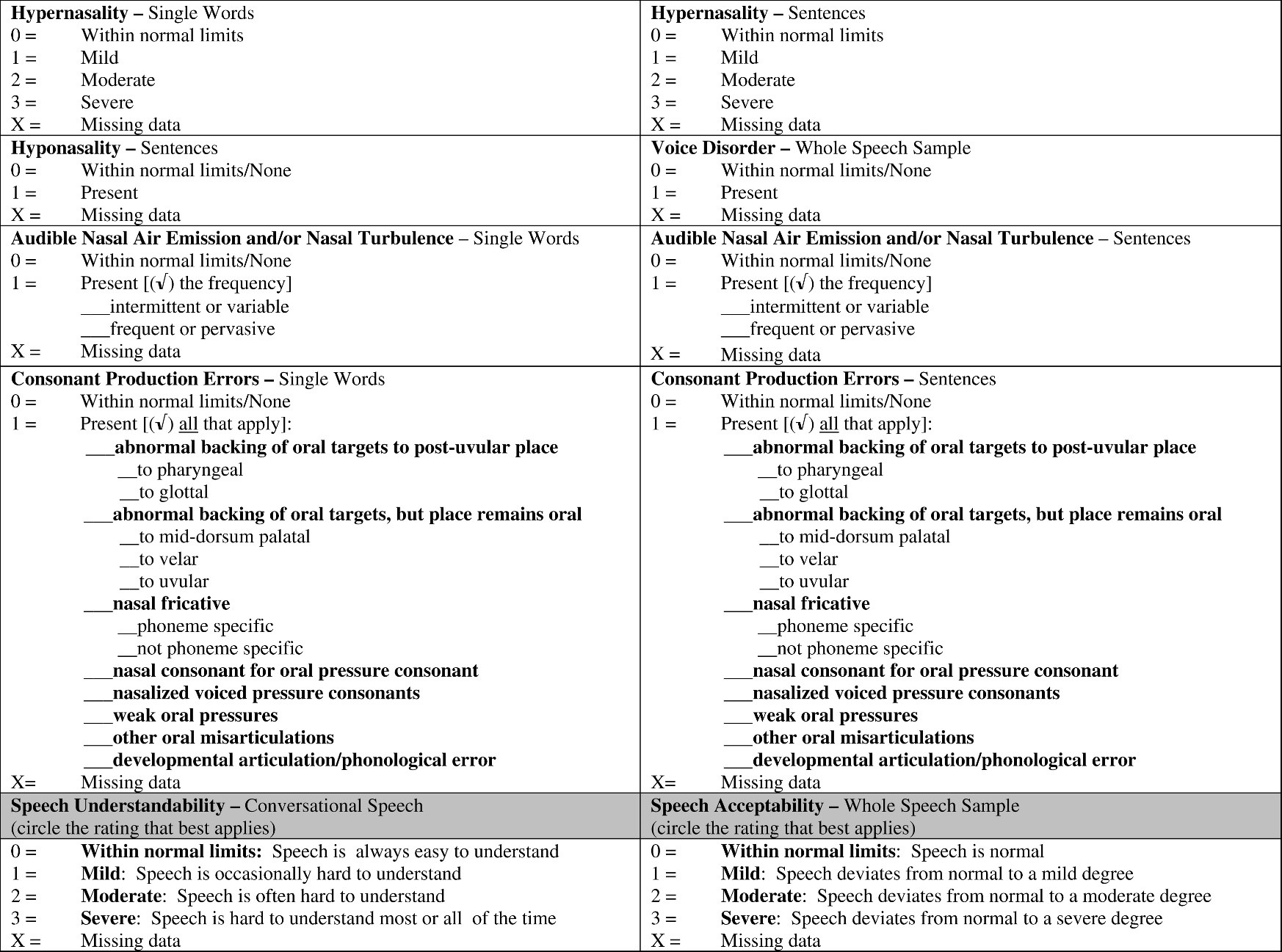
*Sensorineural hearing loss*: hearing loss due to a problem in the transformation from sound waves to electric signals to the brain.

*Colobomata:* Clinical feature of CFM. An eye anomaly caused by incomplete closure of embryonic fissures which may lead to ocular defects of the eyelids, lens, and/or choroid and retin.

*Epibulbar dermoids*:Clinical feature of CFM. Benign, ectopic, congenital neoplasms that vary in composition (dermoid or lipodermoid) or location (corneal or limbal).

# Appendix 5. Reporting speech outcomes

Table 1. From Henningsson G, Kuehn DP, Sell D, Sweeney T, Trost-Cardamone JE, Whitehill TL, et al. Universal parameters for reporting speech outcomes in individuals with cleft palate. Cleft Palate Craniofac J. 2008;45(1):1-17.



# Appendix 6. Evidence table

**Chapter 3 – Diagnosis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Caron et al. 2017 - Craniofacial and extracraniofacial anomalies in CFM | Retro-spective study | C | The aim of this study is to analyse the largest population of patients with CFM with regard to severity, laterality and gender ratio as well as possible correlations among the different components of the PAT-CFM, including cleft lip and palate, and extracraniofacial anomalies. Furthermore, we investigated whether certain combinations of anomalies occur more frequently than others by using PCA, which might provide more insight into the embryologic processes that cause CFM. | Inclusion:  Patients were included only if medical photography and/or radiography of the face and medical history were available.  Exclusion:  Patients with isolated microtia, i.e., without mandibular hypoplasia on radiologic images, and patients diagnosed with other craniofacial syndromes that include craniofacial hypoplasia (e.g., Treacher Collins syndrome) were excluded. | Included number of patients: 755  86 patients had bilateral CFM (11,4%), 669 (88,6%) unilateral. In patients with unilateral CFM, 371 were right and 298 left (ratio of 1,2:1). 408 (54%) males were included, 347 females (46%). | The term goldenhar syndrome should be discarded.  It was not possible to identify specific groups of patients with PCA, as all clusters overlapped with at least one other cluster, suggesting that CFM is a continuum of anomalies that coexist in all combinations and degrees of severity.  Even patients with a minor clinical presentation should be screened for extracraniofacial anomalies, including cardiac, renal, spinal and vertebral deformities. |
| Tuin et al. 2015- Clarifying the Relationships among the Different  Features of the OMENS+ Classification in  CFM | Retro-spective study | C | To evaluate associations among the individual components of the OMENS+ classification. | Inclusion:  Patients with unilateral or bilateral CFM seen in The Children's Hospital of Philadelphia from 1990 to 2012.  Exclusion:  Patients with incomplete chart documentation of their deformities based on the OMENS+ classification were excluded. | Included number of patients: 105  61 male, 44 female (ratio 1.4-1). 81 patients (77%) had unilateral CFM, 24 (23%) bilateral. | Not described |
| Tuin et al. 2015- Distinguishing Goldenhar syndrome from CFM | Retro-spective study | C | To evaluate the use of the term Goldenhar syndrome and to determine the differences between patients with Goldenhar and CFM.  Moreover, this study attempts to determine whether patients with all additional features of Goldenhar syndrome are phenotypically different than patients diagnosed with CFM, outside of the presence of epibulbar dermoids and/or vertebral anomalies. | Inclusion:  Patients with unilateral or bilateral CFM seen in The Children's Hospital of Philadelphia from 1990 to 2012.  Exclusion:  Patients with incomplete chart documentation of the diagnosis or associated anomalies were excluded. | Included number of patients: 138  72 (52%) male, 66 (48%) female.  Vertebral anomalies in 34%, epibulbar dermoids in 17%. Combination of these in 7.2% | This analysis reveals that there were more patients diagnosed as having Goldenhar syndrome than the number of patients with epibulbar dermoids and vertebral anomalies. Furthermore, not every patient presenting one of these features was subjectively diagnosed with Goldenhar. Moreover, patients subjectively considered to have a Goldenhar diagnosis had a more severely affected mandible, soft tissue deformity, were more likely to have bilateral involvement and macrostomia. |
| Heike et al. 2016 - Characterizing facial features in CFM | Case-control study | C | To develop a standardized approach to assess and describe the facial characteristics of the study cohort, using multiple sources of information gathered over the course of this longitudinal study and to create case subgroups with shared phenotypic features. | Inclusion:  Eligible if they were < 48 months of age and had received a diagnosis of hemifacial microsomia, facial asymmetry, unilateral or bilateral microtia, OAVS, Goldenhar syndrome by a pediatrician, geneticist, or surgeon affiliated with a craniofacial team; and who did not have a diagnosis of a known syndrome or chromosomal anomaly.  Exclusion: none | Included number of patients:  142 patients with CFM (61% male) and 316 controls. | Not described |

**Chapter 4.1 Breathing difficulties**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Caron et al. 2017 | Retro-spective cohort study | B | 1. Analyse the prevalence of OSA in patients with CFM;  2. Determine the relationship between the severity of CFM and the risk of OSA;  3. Analyse the chosen treatment modalities and their outcomes | Inclusion:  Patients with CFM and clinical and/or radiographic images  Exclusion:  None | Included number of patients:  755 | OSA is more prevalent in patients with CFM than in the healthy population, especially in patients with unilateral CFM and Pruzansky IIB or III, or with bilateral CFM. These patients should be screened for OSA with PSG. Furthermore, clinicians should be aware of the higher risk for OSA in patients with Pruzansky I or IIA.  Several treatment modalities are available for the treatment of OSA in patients with CFM. However, the treatment of OSA in patients with CFM should be individualized and should be based on clinical symptoms, the severity of the deformity, and on comorbidities. |
| Caron et al. 2015 | Systematic review | C | 1. What is the prevalence of OSA in patients with CFM?;  2. What are treatment modalities for OSA reported in CFM?;  3. What is known about follow-up after treatment for OSA in CFM? | Inclusion:  All articles on the prevalence and treatment of OSA in patients with CFM  Exclusion:  None | 4 papers included on prevalence of OSA in CFM,  10 papers included describing treatment of OSA in CFM,  2 papers included describing prevalence and treatment of OSA in CFM.  Article by Luna-Paredes et al. was excluded since it only included 9 patients.  10 articles on treatment excluded since all other papers included less than 10 patients with CFM. | With the lack of papers on non-surgical treatment, no criteria can be defined to identify those patients who require surgical treatment. The heterogeneous outcome measurements and the lack of information on follow-up make it impossible to come to a consensus regarding the ideal treatment of OSA in patients with CFM. There is no proof in the literature to support the surgical treatment of OSA as being superior to non-surgical treatment in the long-term. |
| Szpalski et al. 2015 | Retro-spective study | C | To investigate the incidence of OSA in patients with unilateral CFM and to determine significant associations | Inclusion:  Patients with uCFM and complete data. Diagnosis based on clinical signs and radiography  Exclusion:  None | Included number of patients:  62 patients, 40 male, 22 female.  Polysomnography was only performed in patients with signs or symptoms of OSA. | We propose vigilance in screening for OSA in patients with unilateral disease to avert neurologic, and Gcardiovascular sequelae of sleep-disordered breathing. |
| Cohen et al. 1999 | Retro-spective study | C | Not described | Inclusion:  Hemifacial microsomia  Exclusion:  None | Included number of patients: 38 | Prevalence: 24%. 9 patients had a definid history of OSA or required tracheostomy or OSAS treatment (no PSG information). 7 patients had a mecial history suspect for intermittend OSA or had a perioperative apneic event.  No outcome of PSG reported.  Patients with bilateral CFM, bilateral hearng loss, extracraniofacial anomalies, or a more severe orbital and mandibular deformity appear to be at greater risk for OSA. |
| D'Antonio et al. 1998 | Cross-sectional | C | To describe the occurrence and magnitude of pharyngeal and laryngeal anomalies in a population of patients with OAVS. | Inclusion:  (1) the diagnosis of OAVS was stated specifically in the team report, (2) the team geneticist reported OAVS as the diagnosis whether or not it was specifically stated in the craniofacial team report, and/or (3) the patient was diagnosed by the team geneticist with one of the labels considered synonymous with OAVS.  Exclusion:  None | Included number of patients: 41 patients  23 patients were available for a series of clinical evaluations  27 male, 14 female  35 right, 13 left, 3 bilateral | Prevalence: 12%. 22% (9 patients) reported symptoms of airway obstruction.  No outcome of PSG reported |
| Sculerati et al. 1998 | Retro-spective study | C | Not described | Inclusion:  CFM, Goldenhar and microtia  Exclusion:  None | Included number of patients:  41 patients. 14 Goldenhar, 12 CFM, 15 bilateral microtia | Prevalence: 22%. 9 patients required tracheostomy.  No outcome of PSG reported |
| Sher et al. 1986 | Retro-spective study | C | Not described | Inclusion:  Facio-auriculo-vertebral sequence  Exclusion:  None | Included number of patients: 84 | Prevalence: 7%. 6 patients had OSA.  No outcome of PSG reported |
| Cloonan et al. 2009 | Case-control study | B | Not described | Inclusion:  HFM including Goldenhar and isolated microtia  Exclusion:  Patients with mendelian inheritance, chromosomal anomalies or prenatal isotretinoin exposure, adoptees | Included number of patients:  124 patients with CFM, 349 controls. Of the 124 patients supplemental sleep items were filled in by 84 patients and 248 controls | Prevalence: 8%. Of the 15 CFM patients that had a PSG, 10 had OSAS (=8%). 20% of the CFM patients had a PSG compared to 2% of the controls. In the controls 4 patients had OSA of the 4 that had a PSG.  No outcome of PSG reported.  Patients with moderate/severe HFM (based on assessment by craniofacial specialist) had a higher incidence of sleep disordered breathing compared to microtia/mild HFM. |

**Chapter 4.2 Feeding difficulties**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Caron et al. 2015 | Systematic review | C | The aim of this review is to give an overview of the literature regarding CFM and the prevalence and treatment of feeding difficulties based on the following key questions: (1) What is the prevalence of feeding difficulties in patients with CFM and what types of feeding difficulties are reported? (2) How are feeding difficulties treated in patients with CFM? | Inclusion: Articles on the prevalence and treatment of patients with CFM and feeding difficulties.  Exclusion:  Expert opinions | 8 articles were included. 5 articles had <10 patients. 1 article <1980.  Two articles included for the guideline. Stromland 2007, Cohen 1995  See manuscripts Cohen & Stromland | See manuscripts Cohen & Stromland |
| Cohen 1995 | Cross-sectional study | C | To examine the neurodevelopmental profile of children with Goldenhar syndrome and to determine if physical manifestations are indicative of poor developmental outcomes | Inclusion:  All newly diagnosed patients with OAVS over a 5 year period. Diagnosed by one of the four clinical geneticists (board certified)  Exclusion:  None | Included number of patients:  24 patients.  Each patient was referred for neurodevelopmental evaluation.  Number of patients with cleft lip/palate not reported.  16 male, 8 female  Age birth to 57 months. | The great heterogeneity of the complex of OAV spectrum disorders necessitates the involvement of many different specialties in the process of diagnosing and in the management of these patients.  Dysphagia could mostly be explained by oral motor impairment and orofacial dysmorphology but in some cases problems with feeding and eating were mainly due to other symptoms affecting general condition of the patient like heart defect, difficulties with breathing, and gastrointestinal problems. |
| Strömland 2007 | Retro-spective study | C | To survey the systemic and functional defects in a group of Swedish patients with characteristics of OAV spectrum with a multidisciplinary team. | Inclusion:  The patients were referred for Goldenhar syndrome, OAV or hemifacial microsomia. For inclusion in the study the patient had to have malformations in at least two of four areas i.e. oro-cranio-facial, ocular, auricular, and vertebral.  Exclusion:  The presence of additional syndromes | Included number of patients:  18  Number of patients with cleft lip/palate: 5.  11 male, 7 female.  Age 8 months to 17 year. | The great heterogeneity of the complex of OAV spectrum disorders necessitates the involvement of many different specialties in the process of diagnosing and in the management of these patients.  Dysphagia could mostly be explained by oral motor impairment and orofacial dysmorphology but in some cases problems with feeding and eating were mainly due to other symptoms affecting general condition of the patient like heart defect, difficulties with breathing, and gastrointestinal problems. |
| Brotto et al. 2018 | Retro-spective study | C | To define the rate of parotid and submandibular gland abnormalities and to investigate their association with OAVS neuroimaging phenotype, i.e., with the presence of concomitant cranial nerve, internal carotid artery, inner ear, brain, eye, or spine abnormalities. | Inclusion:  All patients with OAVS that had a MRI scans of the head  Exclusion:  MRI scans that did not include the salvivary gland regions | Included number of patients:  25 OAVS patients,  11 control patients | OAVS seems to encompass commonly an abnormal development of the salivary gland apparatus ipsilateral to hemifacial microsomia.  According to the present study, more than 80%OAVS patients disclosed hypoplasia if not aplasia of the parotid gland, and about 25% had concomitant submandibular gland abnormalities, highlighting that abnormal development of the salivary gland should be considered a typical feature of OAVS. |
| Van de Lande et al. 2018 | Retro-spective study | C | To document the incidence of swallow difficulties in patients with CFM and gain more insight into swallow difficulties in patients with CFM by studying the outcomes of videofluoroscopic swallow studies at three major craniofacial units. | Inclusion:  Patients with CFM seen in three major craniofacial centre's  Exclusion:  Incomplete reports of the VFS-studies and VFS-studies performed following mandibular reconstruction were excluded. | Included number of patients:  755 patients in total,  42 patients with VFS.  24 male, 18 female;  31 unilateral, 11 bilateral;  13 patients with cleft lip/palate. In 7 patients repair was done before VFS-study, in 3 patient the cleft was unrepaired and in 3 patients the status was unknown;  8 patients with tracheostomy during VFS-study, 4 patients with history of tracheostomy | For clinicians, treatment of feeding difficulties and swallow difficulties should preferably be started early in life. Therefore, it is recommended to have all patients with CFM screened for SD by a speech and language therapist and to perform a VFS-study in patients with a type III Pruzansky–Kaban classification or with a high risk for SD after screening by a speech and language therapist. |
| Caron et al. 2017 | Retro-spective study | C | To analyse the prevalence of feeding difficulties in patients with CFM. The purpose of the study was to (1) determine the associations between the severity of CFM and the risk for feeding difficulties, and (2) to describe the treatment modalities used and their respective clinical outcomes. | Inclusion:  patients with clinical and/or radiographic images, i.e. panoramic X-rays and/or CT head scans, were included for further analyses.  Exclusion:  Patients with isolated microtia | Included number of patients:  755 patients in total.  408 male, 347 female;  669 unilateral, 86 bilateral;  180 patients had extracraniofacial anomalies;  133 patients were diagnosed with OSA | In this multicenter study the prevalence of FD in patients with CFM was 26.4%.    Risk factors for FD were bilateral CFM, cleft lip/palate, OSA, and Pruzansky-Kaban III mandibular deformity. Also, several patients had extracraniofacial anomalies, which increased the risk for FD.  All patients with CFM should be screened for FD before the age of 1 year by a speech and language therapist. After the age of 1 year, special attention to FD in patients with CFM is still needed, and patients should be monitored by a feeding specialist on a regular basis. |

**Chapter 4.3 Speech and language difficulties**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Chen et al. 2009 | Retro-spective study | B | To determine the number of patients who had a documented tongue anomaly and any relation to the development of abnormal speech. | Inclusion:  Patients with a diagnosis of craniofacial microsomia from 1986 to 2006  For the prospective phase of our study, all patients who arrived in the clinic during a consecutive 12-month span (July of 2006 to June of 2007) with craniofacial microsomia were examined meticulously for tongue anomalies.  Exclusion:  Incomplete OMENS score in prospective part of the study | Included number of patients: 167 patients were retrospectively analysed  65 patients were prospectively seen. Ten were excluded due to incomplete OMENS classification. 55 patients included.  Prospective part: 29 patients had unilateral CFM, 26 bilateral CFM | Given the mild nature of the majority of these cases, tongue anomalies are probably often overlooked in the affected infant. The high prevalence (43.6 percent in our prospective study) mandates careful intraoral examination in all patients with craniofacial microsomia. |
| Cohen et al. 1995 | Cross-sectional study | C | To examine the neurodevelopmental profile of children with Goldenhar syndrome and to determine if physical manifestations are indicative of poor developmental outcomes | Inclusion:  All newly diagnosed patients with OAVS over a 5 year period. Diagnosed by one of the four clinical geneticists (board certified)  Exclusion:  None | Included number of patients: 24 patients  Each patient was referred for neurodevelopmental evaluation.  16 male, 8 female  Age birth to 57 months.  5 patients bilateral CFM, 19 unilateral | The study suggests that children with CFM are at a higher risk for neurodevelopmental delay than the normal population. Every child with CFM should have a multidisciplinairy examination, including a neurodevelopmental assessment and full audiometric testing. |
| D'Antonio et al. 1998 | Cross-sectional study | C | To describe the occurrence and magnitude of pharyngeal and laryngeal anomalies in a population of patients with OAVS. | Inclusion:  (1) the diagnosis of OAVS was stated specifically in the team report, (2) the team geneticist reported OAVS as the diagnosis whether or not it was specifically stated in the craniofacial team report, and/or (3) the patient was diagnosed by the team geneticist with one of the labels considered synonymous with OAVS.  Exclusion:  None | Included number of patients: 41 patients  23 patients were available for a series of clinical evaluations  Of the 23 patients, 19 had speech evaluations four were excluded due to young age).  27 male, 14 female  35 right, 13 left, 3 bilateral | The structural abnormalities found in the pharyngeal and laryngeal airway of these patients may predispose patients with CFM to obstructive sleep apnea and difficulties with intubation.  Results suggest that early evaluation of the airway should be considered in patients with OAVS, especially if stridor or other evidence of airway, laryngeal, or other vocal tract dysfunction is present. |
| Funayama et al. 2007 | Cross-sectional study | C | To ascertain the frequency of UHP/VPI in HFM patients and statistically determine the phenotypes correlated with it. Moreover, we examined cleft palate with HFM and observed the velopharyngeal pattern and function compared to cleft palate without HFM. The ultimate purpose of this study is to develop clinical means to detect speech problems in HFM patients sooner and initiate the appropriate treatment. | Inclusion:  Unilateral HFM or microtia seen at Hokkaido University Graduate School of Medicine, Japan  Exclusion:  None | Included number of patients:  52.  48 patients with unilateral CFM or microtia without cleft palate  4 patients with CFM and repaired unilateral cleft palate (after primary palate push-back), of which 2 had a cleft soft palate and 2 unilateral cleft lip and palate | We suggest that patients with affected first or second branchial arches undergo careful periodic speech evaluation as an essential part of their overall management. |
| Strömland 2007 | Retro-spective study | C | To survey the systemic and functional defects in a group of Swedish patients with characteristics of OAV spectrum with a multidisciplinary team. | Inclusion:  The patients were referred for Goldenhar syndrome, OAV or hemifacial microsomia. For inclusion in the study the patient had to have malformations in at least two of four areas i.e. oro-cranio-facial, ocular, auricular, and vertebral.  Exclusion:  The presence of additional syndromes | Included number of patients:  18  Number of patients with cleft lip/palate: 5.  11 male, 7 female.  Age 8 months to 17 year (53%). 5 patients had no speech, one had severe and two slight speech difficulties | Testing of hearing is important early in childhood and should be repeated if not conclusive. CT scan or MRT should be performed to evaluate the middle and inner ear. Early habilitation is important.  Methods: A team of dentists and a speech language pathologist made the orofacial examination. The Mun-H-Center Observation Chart was used for recording orofacial morphology, odontology, and oral motor function, and speech. photographs and video recordings were used to document facial expression, tongue motility and speech. |

**Chapter 4.4 Hearing difficulties**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Bassila et al. 1989 | Retrospective study / case-series | C | To cite the prevalence of clinical features of 50 CFM patients, with special reference to facial paresis, hearing loss and facial anomalies | Inclusion:  The most recent 50 patients, all patients had a complete pediatric, dysmophologic and genetic work-up  Exclusion:  No chromosomal abnormalities or history of teratogenesis | Number of included patients: 50  27 male, 23 female. 38 unilateral and 12 bilateral patients  33 patients had microtia, 21 patients preauricular skin tags or pits. Total of 92% had auricular anomalies  11 patients had facial nerve paralysis or paresis. 9 of these patients had microtia and the other 2 had skin tags  All patients underwent full audiometric testing including brainstem responses with bone conduction when indicated  Cephalometric/panaramic x-rays and CT-scan were reviewed | No relevant conclusion described |
| Bisdas et al. 2005 | Case-serie | C | To investigate the inner ear malformations in aptients with Goldenhar syndrome | Inclusion:  Clinical criteria of Goldenhar syndrome (unknown which criteria) | Included number of patients: 14  7 female, 7 male, avarge age 6.5 years | The oculoauricolovertebral spectrum (Goldenhar syndrome) is a syndrome with heterogeneous manifestations in the ear. |
| Carvalho et al. 1999 | Retro-spective study / case-serie | C | To determine the frequency of auditory and facial nerve dysfunction and its relationship to more severe forms of bilateral HFM | Inclusion:  Patients with HFM and complete medical records were included  Exclusion  age >18 years, presence of chromosomal abnormalities, and a known history of teratogenesis. | Included number of patients: 99  46 male, 53 female  30 bilateral patients, 30 left and 39 right  71 patients had a mandibular deformity, 91 auricular anomalies | Auricular abnormalities, conductive hearing loss, sensorineural hearing loss and facial nerve dysfunction are common in HFM. There should be a high index of suspicion for sensorineural hearing loss and all children diagnosed as having HFM should undergo complete audiologic evaluation. |
| Cohen et al. 2017 | Cross-sectional study | C | The aim of this study was to define the type and frequency of maxillofacial and systemic malformations in a cohort of HFM patients and to discuss the appropriateness of the commonly used OMENS-plus classification. | Inclusion:  the presence of either at least three craniofacial deformities identified by the OMENS classification or at least two craniofacial manifestations associated with other systemic abnormalities and/or preauricular tags, macrostomia and other eye defects.  Exclusion:  lack of sufficient clinical, radiographic, or follow up data. | Included number of patients: 89  54 male, 41 female  Mean age 11.5 years, range 2 months to 46 years | No relevant conclusion described |
| Cousley et al. 1993 | Retro-spective study | C | To compare two classificaiton systems: SAT and OMENS | Not described | Included number of patients: 50  47 unilateral, 3 bilateral  29 male, 21 female | No relevant conclusion described |
| Davide et al. 2017 | Cross-sectional study | C | To investigated the type, frequency and phenotype correlations of intracranial anomalies among OAVS patients. | Not described | Included number of patients: 35 patients, 32 underwent a MRI.  21 male, 14 female. Mean age 4.8 years; age range 0.3–30  19 patients with Goldenhar criteria (ocular or cervical vertebral abnormalities) | The impressive spectrum of intracranial malformations in OAVS compels for an enlarged neuroimaging evaluation that goes far beyond the structures derived from the first and second pharyngeal arches, especially because some of these changes might have a significant clinical and surgical impact. |
| Engiz et al. 2007 | Case-series | C | To describe the phenotypic featurs and laboratory findings of 31 OAVD or Goldenhar patients | Not described | Included number of patients: 31  15 male, 16 female. Age 0-16 years | Chromosomal and cranial imaging should be performed in every patients with Goldenhar syndrome. Each patient should be evaluated by multidisciplinary approach. |
| Goetze et al. 2017 | Cross-sectional study | C | The aim of this study is to verify the hearing features presented by patients with OAVS and provide additional information that may contribute to improvement of speech therapy. | Inclusion:  We considered patients with OAVS those with clinical alterations in at least two of the following areas: (i) oro-craniofacial; (ii) ocular; (iii) auricular; and (iv) vertebral.  Exclusion:  None | Included number of patients: 10  5 males, 5 females. Age 1 - 27 years, median 4.5 years | There is obvious need for further studies to investigate speech pathology associated with OAVS. This will delineate more clearly what abnormalities are associated with this syndrome and may indicate what type of radiological and laboratory investigation are the most appropriate. |
| Heike et al. 2016 | Retro-spective cohort study | B | To develop a standardized approach to assess and describe the facial characteristics of a cohort of children with facial features within the CFM spectrum and children without known craniofacial anomalies. | Inclusion:  Cases: children were ascertained in Phase 1 from craniofacial specialty clinics, eligible if they were < 48 months of age and had received a diagnosis of hemifacial microsomia, facial asymmetry, unilateral or bilateral microtia, OAVS, Goldenhar syndrome by a pediatrician, geneticist, or surgeon affiliated with a craniofacial team.  Controls inclusion: within 2 months of the matching cases’ ages at the time of recruitment  Exclusion:  A diagnosis of a known syndrome or chromosomal anomaly | Included number of patients:  142 cases and 290 controls.  61% of the cases was male  average age was 13.5 years (standard deviation, 1.3 years; range, 11.1–17.1 years) | No relevant conclusion described |
| Hennersdorf et al. 2014 | Retrospective cohort study / case series | C | Assessment of the presence of inner ear malformations is an important component in the otologic care of patients with GS. In this article, we conducted a retrospective review of temporal bone changes in patients with GS imaged and treated in our institution | Inclusion:  The diagnosis was established according to clinical criteria.  Exclusion:  None | Included number of patients: 21.  13 males, 8 females. Age 2 months - 13 years  3 patients bilateral malformations | In our study, we demonstrate that approximately one-third of patients have additional inner ear abnormalities, which may lead to sensorineural hearing loss.  Inner ear changes do not always correlate with the severity of external and middle ear abnormalities. Therefore, high-resolution CT or MRI of the temporal bones should be performed. |
| Jacobsson et al. 1997 | Retrospective cohort study | B | to compare an endogenous, fully-developed syndrome (mandibulofacial dysostosis) with the hemisyndrome (hemifacial microsomia) and an exogenous syndrome (the thalidomide syndrome restricted to the first andsecond branchial arches) to elucidate possible similarities and differences and to understand better the reasons for the malformations. | Inclusion:  Those patients that could be classified as having fully developed mandibulofacial dysostosis (26) and hemifacial microsomia (6) were studied specifically.  Exclusion:  None | Included number of patients:  26 patients with HFM, 4 of these have Goldenhar syndrome.  16 right HFM, 10 left HFM | No relevant conclusion described |
| Llano-Rivas et al. 1999 | Retro-spective cohort study | B | To study the clinical and genetic behavior of microtia in the childhood populations seen at th e National Institute of Pediatrics in Mexico | Inclusion:  unilateral or bilateral microtia. The diagnosis of hemifacial skeletal microsomia was reached when using frontal plane radiograph studies, the frontal midline was rotated toward the healthy side, and the skeletal midline toward the affected side. Hemifacial skeletal microsomia was classified according to the three degrees of severity cited in the literature, by comparing the two jawbone arches in the lateral plane.  Although only patients with microtia were included with no other data of a known syndrome, 58 patients were identified that had mild OAVS characteristics. Therefore, two groups were made. One with isolated microtia and one with OAVS characteristics.  Exclusion:  microtia that was part of a syndrome | Included number of patients: 145  145 patients with microtia, of which 58 patients had CFM. Age 3 months - 18 years. Male:female ratio 1.5:1  46 of the 58 patients had HFM of the soft tissues.  24 of the 58 patients had hemifacial skeletal microsomia Grade I, 8 patients had grade II.  3 of the 58 patients had macrotomia, 9 cervical vertebral anomalies, 4 thoracic vertebral anomalies, 2 renal anomalies | The clinical findings did not show significant differences between isolated microtia and HFM patients.    The findings related to this study support the proposal that unilateral or bilateral microtia and the OAVS are the same entity, and that the former is a minimal expression of the latter. |
| Mitchell et al. 2017 | Retro-spective cohort study | B | To evaluate the association between craniofacial phenotype and hearing loss in children with CFM | Inclusion:  patients with craniofacial microsomia. This required at least one of the following: microtia; anotia; facial asymmetry with preauricular tags, facial tags, epibular dermoid or macrostomia; preauricular tags with epibulbar dermoid or macrostomia; facial tag with epibulbar dermoid; or macrostomia with epibular dermoid.  Exclusion:  Parent non-English- or non-Spanish speaking or known syndrome with microtia and underdevelopment of the jaw and/or abnormal chromosome studies. | Included number of patients: 79  mean age 9 years (range 1-23 years). 61% was male  bilateral CFM in 39 patients, unilateral CFM in 40 patients  94% of the patients had microtia. 76% mandibular hypoplasia, 60% soft tissue deficiency, 53% orbital hypoplasia or displacement, 32% facial nerve palsy | Hearing loss is strongly associated with malformations of the ipsilateral ear in craniofacial microsomia and is most commonly conductive. Hearing loss can occur contralaterally to the side with malformations in children with apparent hemifacial involvement. |
| Rahbar et al. 2001 | Retro-spective cohort study | B | To evaluate the clinical, audiologic and temporal bone CT findings in patients with HFM and to use the OMENS grading system to assess possible correlations between the severity of dysmorphic features with the type of abnormalies in the temporal bone and with degree of hearing deficit | Inclusion:  Patients with the diagnosis of HFM, complete medical records who had undergone temporal bone CT scan and audiologic workup  Exclusion:  None | Included number of patients: 40.  17 male, 23 femal. Age 2 - 37 years (mean 12 years)  7 bilateral CFM, 17 left, 16 right | In patients with abnormal hearing, temporal bone CT scan must be obtained to further assess the degree of stenosis and atresia of external auricular canal, status of the ossicular chain and middle ear and inner ear abnormalities.  The timing of the temporal CT scan must be individualized based on the age of the patient, severity or worsening of the hearing status, and no otologic surgery.  The authors strongly recommend a complete audiologic evaluation of every child with a diagnosis of HFM, regardless of the type or the severity of the clinical manifestations. |
| Rosa et al. 2011 | Case series | C | To investigate the ear abnormalities of a sample of patients with OAVS | Inclusion:  Alterations in at least two of the following bodily regions: oro-cranial-facial, ocular, auricular, and vertebral.  Patients that underwent masoid CT and with normal karyotype.  Exclusion: | Included number of patients: 12.  9 male, 3 female. Age 1 day - 17 years (10 patients were <10 years of age). | Ear anomalies are frequent and varied in OAVS patients; often there is no correlation among external, middle, and inner ear findings.  Therefore, it is important to assess these structures using radiologic methods (such as computed tomography of the mastoid) whenmanaging patients with OAVS. |
| Sleifer et al. 2014 | Cross-sectional study | C | To analyze the audiological findings of patients with oculo-auriculo-vertebral spectrum through liminal pure-tone audiometry and speech audiometry test | Inclusion:  oculo-auriculo-vertebral spectrum and clinical findings on at least two of the following areas: orocraniofacial,  ocular, auricular, and vertebral  All patients underwent tonal and vocal hearing evaluations  Exclusion:  None | Included number of patients: 10.  7 male, 3 female. Age 3 - 27 years (mean 6.6 years, median 9 years) | The results show a higher frequency of conductive hearing loss among individuals with the oculo-auriculo-vertebral spectrum phenotype, especially moderate loss affecting the right side.  Conductive hearing loss is often observed in individuals with OAVS. It is usually of moderate degree and more often affectsthe right side. This is arguably related to the auricular abnormalities found and is common in patients with OAVS, which affects the conductive component of the auditory system. |
| Stromland et al. 2007 | Retro-spective study | C | To survey the systemic and functional defects in a group of Swedish patients with characteristics of OAV spectrum with a multidisciplinary team. | Inclusion:  The patients were referred for Goldenhar syndrome, OAV or hemifacial microsomia. For inclusion in the study the patient had to have malformations in at least two of four areas i.e. oro-cranio-facial, ocular, auricular, and vertebral.  Exclusion:  The presence of additional syndromes | Number of included patients: 18.  Number of patients with cleft lip/palate: 5.  11 male, 7 female.  Age 8 months to 17 year. | The great heterogeneity of the complex of OAV spectrum disorders necessitates the involvement of many different specialties in the process of diagnosing and in the management of these patients.  The results of this study stress the importance of a thorough otolaryngological investigation in cases where craniofacial malformations are present. Testing of hearing is important early in childhood and should be repeated if not conclusive. CT scan or MRT should be performed to evaluate the middle and inner ear. |
| Wan et al. 2003 | Retro-spective cohort study | B | To identify further relationships between clinical findings, temporal bone anatomy, and audiological findings in patients with CFM | Inclusion:  Inclusion in the study required (1) diagnosis of hemifacial microsomia or microtia, (2) complete medical records adequate for determining Orbit, Mandible, Ear, Nerve, Soft Tissue (OMENS) classifications, (3) available temporal CT scan, and (4) available audiogram results.  Exclusion:  Patients with chromosomal abnormalities, teratogenic history, and patients related to others included in the study were excluded. | Included number of patients: 70.  42 (60%) male, 28 (40%) female. 17 (24%) bilateral CFM, 53 unilateral.  19 patients (27%) wore hearing aids. | Temporal bone CT findings were related significantly to clinical measurements of ear hypoplasia, mandibular hypoplasia, and overall severity of dysmorphology as measured by OMENS score.  Interestingly, the degree of dysmorphology and the severity of temporal CT findings were not predictive of hearing loss in this cohort of patients. Consequently, audiology should not be deferred on the basis of relatively mild clinical findings. |

**Chapter 4.5 Eye anomalies**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Caron et al. 2017 | Retro-spective cohort study | B | to analyse a large population of patients with regard to demographics, typical phenotypes including craniofacial and extracraniofacial anomalies, and the correlations between the different variables of this condition. | Inclusion:  patients diagnosed with CFM presented at one of the units from January 1980 until January 2016.  Patients were included only if medical photography and/or radiography of the face and medical history were available.  Exclusion:  Patients with isolated microtia, i.e., without mandibular hypoplasia on radiologic images, and patients diagnosed with other craniofacial syndromes that include craniofacial hypoplasia (e.g., Treacher Collins syndrome) were excluded. | Included number of patients: 755.  bilateral CFM in 86 patients (11,4%) and unilateral CFM in 669 patients (88,6%) | Statistical analyses showed that the structures derived from the first pharyngeal arch correlated more with one another than with the structures derived from the second pharyngeal arch, and vice versa.  Extracraniofacial anomalies were positively, although not strongly, correlated with CFM. Further research is needed to determine a possible correlation is the pathogenesis.  Although phenotypically no specific groups of patients could be identified, patients with bilateral CFM were more severely affected than patients with unilateral CFM. Therefore, these bilaterally affected patients should be approached more comprehensively.  Even patients with a minor clinical presentation should be screened for extracraniofacial anomalies, including cardiac, renal, spinal and vertebral deformities. |
| Cohen et al. 2017 | Cross-sectional study | C | The aim of this study was to define the type and frequency of maxillofacial and systemic malformations in a cohort of HFM patients and to discuss the appropriateness of the commonly used OMENS-plus classification. | Inclusion:  the presence of either at least three craniofacial deformities identified by the OMENS classification or at least two craniofacial manifestations associated with other systemic abnormalities and/or preauricular tags, macrostomia and other eye defects.  Exclusion:  lack of sufficient clinical, radiographic, or follow up data. | Included number of patients: 89  54 male, 41 female  Mean age 11.5 years, range 2 months to 46 years  36 bilateral CFM, 53 unilateral CFM | All patients suspected of expanded HFM should undergo a complete systematic clinical and instrumental investigation based on a precise timetable that should consider the age of the patient and the scheduling of surgical procedures in order to limit invasive exams.  No correlation was observed between the severity of the systemic abnormalities and the severity of the maxillofacial deformities, suggesting that the OMENS-plus score is clinically insufficient for prognostic aspects, morbidity, and quality of life. |
| Ewart-Toland et al. 2000 | Not described | C | To study the possible relationship between craniofacial anomalies and maternal diabetes. | Inclusion:  Patient population born to insulin dependent or oral hypoglycemic treatment-dependent diabetic mothers, whose diabetes was diagnosed prior to pregnancy.  All patients had shared features including hemifacial microsomia, microtia, and hearing loss  Exclusion:  individuals born to mothers with isolated gestational diabetes  Incomplete medical records  Cases with a known chromosomal abnormality, autosomal dominant hemifacial microsomia, or a recognizable syndrome including Townes-Brocks syndrome, branchio-oto-renal syndrome, Treacher Collins syndrome, or Nager syndrome. | Included number of patients: 21 patients  14 patients with hemifacial microsomia | The list of teratogenic effects of maternal diabetes should include hemifacial microsomia and other anomalies associated with the OAV complex. Infants of diabetic mothers should be evaluated for craniofacial anomalies including hearing loss and individuals with OAV/Goldenhar complex assessed for maternal diabetes exposure. |
| Stromland et al. 2007 | Retro-spective cohort study | C | To survey the systemic and functional defects in a group of Swedish patients with characteristics of OAV spectrum with a multidisciplinary team. | Inclusion:  The patients were referred for Goldenhar syndrome, OAV or hemifacial microsomia. For inclusion in the study the patient had to have malformations in at least two of four areas i.e. oro-cranio-facial, ocular, auricular, and vertebral.  Exclusion:  The presence of additional syndromes | Included number of patients: 18.  11 male, 7 female.  Age 8 months to 17 year.  3 patients had bilateral microsomia, 13 unilateral microsomia, and two patients no microsomia | The great heterogeneity of the complex of OAV spectrum disorders necessitates the involvement of many different specialties in the process of diagnosing and in the management of these patients. Especially important seems to be aware of functional defects such as autism spectrum disorders. |
| Mansour et al. 1985 | Retrospective study | C | To study the ocular findings in a large series of patients with CFM | Inclusion:  unknown  Exclusion:  unknown | Included number of patients: 57 patients  Most of the patients were examined by pediatric ophthalmology servica and the others were examinded by their ophthalmologists. | Ocular findings were more common in  the patients with epibulbar choristomas. Of  the various features of the Goldenhar-Gorlin  syndrome (skin tags, microtia, hemifacial microsomia,  and vertebral anomalies), only skin  tags correlated positively with the laterality of  epibulbar choristomas. Preauricular and facial  tags represent choristomas, explaining their  association with epibulbar choristomas and  the laterality they share. |
| Hertle et al. 1992 | Retro-spective study | C | To report the ocular and adnexal findings of patients with CFM seen between 1979 and 1989 at the ophthalmology department | Inclusion:  All patients with the diagnosis of hemifacial or bifacial microsomia alone who were seen in the Craniofacial Clinic between 1979 and 1989.  Exclusion:  Patients who had enough stigmata to classify them as having Goldenhar syndrome, TreacherCollins syndrome, and Miller or Nager syndromes are excluded from the analysis. | Included number of patients: 49.  5 bilateral CFM, 44 unilateral  Ages at last examination ranged from 2 months to 20 years (mean, 5.3 years). | Sixteen percent of patients had unilateral amblyopia diagnosed during one of their visits to the craniofacial clinic. This amblyopia was multifactorial with contributions from refractive errors, strabismus, nystagmus, and blepharoptosis.  Anisometropia (8%) and refractive errors (27%) were present in a large number of patients compared with the normal population.  22% of the patients in this report with less severe facial and ocular abnormalities had strabismus. Of these 11 patients, 6 had noncomitant strabismus (3 Duane, 2 sixth nerve palsies, and 1 bilateral superior oblique palsies). These forms of strabismus probably reflect the maldevelopment of contiguous orbital and facial structures.  Forty-one percent of patients had associated lid or adnexal malformations, most commonly dacryostenosis and blepharoptosis. |
| Pirouzian | Narrative review | C | To review the data in the published literature (PubMed from 1937 to 2011) concerning the medical and surgical management of pediatric limbal dermoids. | Not described | Not described | Current standard medical treatment for grade I pediatric limbal dermoids (ie, with superficial corneal involvment) is initially conservative. In stages II (ie, affecting the full thickness of the cornea with/without endothelial involvement) and III (ie, involvement of entire cornea and anterior chamber), a combination of excision, lamellar keratoplasty, and amniotic membrane and limbal stem cell tranplantation are advocated. |
| Matsuo | Case series | C | So far, no study has ever addressed this question on clinical decision- making in ocular surface dermoids or dermolipomas (grade I). In this study, 13 consecutive patients with ocular surface dermoids or dermolipomas at one institution were reviewed to describe their clinical features from the viewpoint of clinical decision, either surgical resection or observation. | Inclusion:  patients with limbal dermoids or conjunctival fornix dermolipomas  Exclusion:  None | Included number of patients:  13 patients.  8 with surgical resection and 5 with observation. No patient with either observation or surgical resection had irritating symptoms or redness of the eye, or the habit of eye-rubbing in the follow-up period. | The visual acuity check-up is recommended in all children with ocular surface dermoids or dermolipomas, irrespective of wearing full-correction glasses which are prescribed by cycloplegic refraction once a year.  The patients with dome-shaped limbal dermoids chose surgical resection while the patients with flat-shaped dermoids chose observation. Surgical timing for ocular surface dermoid or dermolipoma resection by an ophthalmologist was influenced by the consultation with a plastic surgeon who was planning preauricular appendage resection. Large dome-shaped limbal dermoids were associated with large degree of astigmatism while flat limbal dermoids in observation and conjunctival fornix dermolipomas were not associated with astigmatism. |

**Chapter 4.6 Dentofacial deformities**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Ahiko et al. 2015 | Retro-spective study | C | To compare the dental development of affected versus unaffected sides in a group of Japanese patients with CFM. | Inclusion: unilateral CFM  Exclusion:  None | Included number of patients: 24  12 male, 12 female  15 right side HFM, 9 left | We found that the A/U ratios of the mandibular body and ramus correlated with SNB, ANB, convexity, and mandibular plane measurements. These findings suggest that the correlation between lateral and frontal measurement parameters is pathognomonic for this condition.  Our investigation also revealed that the mandibular molars on the affected side exhibited delayed calcification. |
| Farias et a. 1998 | Retro-spective study | C | To determine whether tooth size and morphology are affected in HFM. | Inclusion:  Plaster casts of the upper and lower jaws obtained from 40 subjects between 8 and 21 years of age with varying degree of HFM were studied  Severity of CFM was based on: radiographic classitcation [8], which divides HFM into five types with increasing severity of expression as follows: type I: absence of condylar cartilage and disc; type II: no condylar head or neck on condylar process; type III: ankylosis or syndesmosis of joint; type IV: presence of coronoid process only; and type V: coronoid and condylar processes missing.  The mesiodistal width of each permanent tooth and its corresponding antimere was measured with a vernier gauge calibrated to 0.1 mm.  Exclusion:  None | Included number of patients: 40.    8 - 21 years  Severity: 18 type I, 2 type II, 2 type III, 14 type IV, 4 type V | This study shows that patients with HFM have a tendency to develop smaller permanent mandibular teeth on the affected than on the contralateral side, and that the difference in tooth size increases as the severity of HFM increases. It seems, therefore, that the degree of tooth size involvement is closely related to the magnitude of jaw abnormality.  the permanent mandibular canine and permanent mandibular first molars are significantly smaller on the aected side than on the contralateral side;  the incidence of cusp asymmetry of the permanent mandibular first molar is significantly higher on the affected than on the contralateral side  the aberrations in tooth size and morphology are more extensive in individuals with the severe types of HFM than in those with milder expression of the condition. |
| Jacobsson et al. 1997 | Retro-spective study | C | to compare an endogenous, fully-developed syndrome (mandibulofacial dysostosis) with the hemisyndrome (hemifacial microsomia) and an exogenous syndrome (the thalidomide syndrome restricted to the first and second branchial arches) to elucidate possible similarities and differences and to understand better the reasons for the malformations. | Inclusion:  Those patients that could be classified as having fully developed mandibulofacial dysostosis (26) and hemifacial microsomia (6) were studied specifically.  Any possible exogenous influence on the malformation was ruled out and patients with a proven exogenous syndrome induced by thalidomide affected the ears and surrounding facial structures were also studied.  To be classified as hemifacial microsomia the malformation should be unilateral and contain ear malformation, malar bone hypoplasia, and maxillary and mandibular micrognathia.  Exclusion:  None | Included number of patients: 26 patients with HFM, 4 of these have Goldenhar syndrome.  16 right HFM, 10 left HFM | The findings of congenitally missing teeth are in accordance with our earlier studies on experimentally induced malformations of the first and second branchial arches in rats, in which the molars were missing but not the incisors |
| Seow et al. 1998 | Case-control study | C | The purpose of this study was to investigate tooth dimensions in a group of subjects with hemifacial microsomia compared with a group of matched normal controls. | Inclusion:  Maxillary and mandibular stone casts of 50 hemifacial microsomia patients who were registered in the Craniofacial Center were included.  These dental casts had been constructed as part of routine diagnostic and treatment procedures.  A group of control casts was randomly selected of control subjects as part of routine orthodontic diagnosis  The control subjects were matched with hemifacial microsomia subjects for dental age. In addition, the dental casts were checked to ensure that the subjects were similar in terms of the numbers and types of teeth present.  Exclusion:  Patients with bilateral CFM  Patients with cleft palate  Teeth which showed enamel defects, or had restorations or orthodontic bands, were not measured. In addition, teeth which were not fully erupted, or malpositioned to the extent that accurate measurements could not be taken, were eliminated. | Included number of patients: 50. 25 male, 25 female. 27 right, 23 left.  Pruz I in 15 patients (30%), Pruz II in 18 patients (36%), Pruz III in 13 patients (26%), 4 patients (8%) not classified.  Twenty (40%) patients had casts of the primary dentition, and each of another 15 (30%) had casts of the mixed (transitional) and permanent dentitions.  50 control casks (patients). 20 sets of casts of the primary dentition, 15 of the mixed dentition, and 15 of the permanent dentition. | Our results showed that in the hemifacial microsomia subjects, the two most posterior teeth in the affected side in the mandible, i.e., the primary second molar and the permanent first molar teeth, were significantly reduced in their mesiodistal diameter compared with the unaffected side.  Of equal importance is the finding that the teeth on the apparently unaffected sides measured significantly smaller in the mesiodistal dimensions compared with controls, indicating that the putatively "normal" sides were also affected, although to a lesser extent.  With regard to this finding, a gradient of severity was found, with the most significant changes noted in the last two molars of the mandible and maxilla, and no observable changes in the anterior region of the dental arches.  The dental changes are limited to only the mesiodistal dimension and not the faciolingual. |
| Maruko et al. 2001 | Retro-spective study | C | (1) to describe the patterns of missing teeth in patients with hemifacial microsomia (HFM) and (2) to compare the prevalence of missing teeth in subjects with HFM with a group of unaffected subjects. | Inclusion:  available records of children with HFM  Panoramic radiographs were examined to determine the presence or absence of teeth.  Methodology: Teeth were noted as present if any portion of the follicle, tooth bud, or tooth was visible on the panoramic radiograph. Calcification within the follicle was not a criterion for tooth presence  Exclusion:  Subjects were excluded if there were only postsurgical or postorthodontic panoramic radiographs.  Third molars were excluded from the analysis because of their high incidence of congenital absence in the general population | Included number of patients: 122.  65 male, 60 female. Age 4-32 years, mean 10.9 years.  Pruzansky type I, 41.6% (n = 52); type IIA, 32.8% (n = 41); type IIB, 14.4% (n = 18); and type III, 11.2% (n = 14).  76 patients were 4 years of age or older and had a presurgical panoramic radiograph available, thus meeting the criteria for entry into the radiographic analysis for hypodontia.  To compare the prevalence of missing teeth in subjects with HFM with a group of unaffected subjects, 45 controls and 52 HFM patients (age 8 or older and had a panoramic radiograph) were included. | This study demonstrated an increase in hypodontia with increasing severity of HFM. Additionally, this study demonstrated an increased prevalence of hypodontia in patients with HFM as compared with a group of unaffected subjects. |
| Ongkosuwito et al. 2010 | Retro-spective study | C | To compare dental development between affected and non-affected mandibular sides in patients with HFM and to compare these data with those collected from Dutch control children. | Inclusion:  Only patients with unilateral expression and at least one orthopantomogram (OPT) were included.  Exclusion:  When 2 or more mandibular teeth were agenic on the same side, the OPTs were excluded because no dental maturity score can be determined reliably in these cases. | Included number of patients: 84.  37 male, 47 female  The median age at which the OPTs were taken was 10.0 yrs, with a range from 3.7 to 31 yrs. | In these patients with HFM, we found no significant difference between dental development of the affected and nonaffected sides. We also did not find progressive development over time (any differences in velocity) between the affected and non-affected sides. Neither did we find a difference in any other velocity pointing to the absence of a progressive developmental effect over time. This means that asymmetric progression of dental development probably does not occur. However, when both sides were considered together, the data differed significantly from those for the Dutch norm. In Pruzansky/Kaban types IIb and III, dental development was significantly later than the norm. However, the development over time was at the 50th percentile faster than the norm, suggesting the presence of a dental development ‘catch-up phenomenon’.  both Pruzansky/Kaban types IIb and III are associated with early delayed development as compared with Pruzansky/Kaban type I, type IIa, and the Dutch norm. |
| Silvestri et al. 1996 | Retro-spective study | C | This study evaluated the incidence of agenesis and dental inclusions of patients with hemifacial microsomia. | Inclusion:  Not specifically described  Exclusion:  Patients under age 8 were not assest for third molar buds. If no sign of third molar buds were not considered to have agenesis of these teeth. | Included number of patients: 63.  27 male, 36 female. Age 7-43, average 18.7 years.  Unilateral HFM in 61 patients, bilateral in two patients | Our results indicate that patients with hemifacial microsomia are more likely than unaffected patients to present agenesis or dental inclusions. |
| Silvestri et al. 1996 | Case series | C | This study evaluates the skeletal response to functional orthodontic therapy in growing children with hemifacial microsomia (HM). A method of classification for mandibular growth subsequent to treatment is also suggested. | Inclusion:  Sixteen growing children with unilateral HM were treated. Each patient was graded according to the skeletal, auricular, tissue (SAT) classification.  Exclusion:  Patients graded S4,-S5, were excluded because the severity of the malformation made them unsuitable for functional orthodontic treatment. | Not described | Use of the asymmetrical functional activator (AFA) in growing patients with unilateral hemifacial microsomia makes it possible to induce, either totally or partially, balanced maxillomandibular growth. In less severe cases with an S1,-S2/T1 classification, the AFA is capable of producing functional recovery of the neuromuscular system and of creating stimuli for growth of the mandibular ramus and body to counteract the malformation. Subsequent orthodontic treatment with a fixed appliance has the sole purpose of perfecting the occlusion. |

**Chapter 4.7 Vertebral anomalies**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Cohen et al. 2017 | Cross-sectional study | C | The aim of this study was to define the type and frequency of maxillofacial and systemic malformations in a cohort of HFM patients and to discuss the appropriateness of the commonly used OMENS-plus classification. | Inclusion:  the presence of either at least three craniofacial deformities identified by the OMENS classification or at least two craniofacial manifestations associated with other systemic abnormalities and/or preauricular tags, macrostomia and other eye defects.  Exclusion:  lack of sufficient clinical, radiographic, or follow up data. | Included number of patients:  54 male, 41 female. Mean age 11.5 years, range 2 months to 46 years.  47% (n=40) patients had vertebral anomalies  Type of vertebral anomalies: butterfly vertebrae (n=8), hemivertebrae (n=20), vertebral fusion (n=9), vertebral schisis (n=8), spina bifida (n=3), scoliosis (n=18), rib anomalies (n=10), other vertebral anomalies (n=10). | all patients suspected of expanded-CFM should undergo a complete systematic clinical and instrumental investigation based on a precise timetable that should consider the age of the patient and the scheduling of surgical procedures in order to limit invasive exams.  No correlation was observed between the severity of the systemic abnormalities and the severity of the maxillofacial deformities, suggesting that the OMENS-plus score is clinically insufficient for prognostic aspects, morbidity, and quality of life. A more complete classification is needed. |
| Davide et al. 2017 | Retro-spective study | C | To study the type, frequency and phenotype correlations of intracranial vascular, bone, and brain abnormalities among OAVS patients. | Inclusion:  hemifacial microsomia and microtia  Method: All OAVS patients had petrous bone or head CT. Thirty-two OAVS patients underwent MRI.  Exclusion:  None | Included number of patients:  35 | The impressive spectrum of intracranial malformations in OAVS compels for an Benlarged^ neuroimaging evaluation that goes far beyond the structures derived from the first and second pharyngeal arches, especially because some of these changes might have a significant clinical and surgical impact. |
| Renkema et al. 2017 | Systematic review | C | To study the available literature on vertebral anomalies and their respective prevalence rates in patients with CFM. | Inclusion:  A systematic search of the literature was performed to identify papers focusing on CFM and its synonyms combined with synonyms for spinal and central nervous system anomalies.  Studies concerning CFM in relation to vertebral anomalies were further reviewed. Those in which prevalence and/or the types of vertebral anomalies in CFM were mentioned were included. The articles had to report original studies.  Exclusion:  Case reports were excluded  studies describing solely patients with isolated microtia were not included | Included number of patients:  31 articles were identified for inclusion in the review. Twenty-six articles described the prevalence of vertebral anomalies and 22 articles described the types of vertebral anomalies in their investigated population  2 studies included <10 patients (Al Kaissi et al. & Healey et al.) | From this literature study, it may be concluded that vertebral anomalies are present in a substantial proportion of CFM patients. Mostly, these anomalies are present in the cervical spine, but thoracic and rib anomalies often occur. Hemivertebrae, block vertebrae, scoliosis/ kyphoscoliosis, and spina bifida are frequently seen.  Since these vertebral anomalies can present without symptoms but can have harmful effects, careful and extensive physical and neurological examination of CFM patients is important to diagnose these anomalies at an early stage. |
| Renkema et al. 2018 | Retro-spective study | C | The aim of this study was to report the prevalence, types, and symptoms of vertebral anomalies in a large group of patients. Furthermore, a secondary objective of this endeavour was to identify which CFM patients are at risk of having vertebral anomalies and whether these anomalies are associated with other extracraniofacial anomalies in CFM. | Inclusion:  Since CFM is a clinical diagnosis, patients with clinical and/or ra- diographic images, i.e. panoramic X-rays and/or computed tomography (CT) scans of the head, were included in this study  Exclusion:  Although microtia is part of CFM, isolated microtia was not seen as CFM; therefore these patients were excluded. Patients for whom the diagnosis of CFM was uncertain were excluded as well. | Included number of patients: 991.  More male patients (n = 527) than female patients (n = 464) were included. Most patients had unilateral CFM (n = 827); 117 had bilateral CFM, and the affected side was unknown for 47 patients. | Patients with bilateral CFM, a higher Pruzansky–Kaban score, and/or a higher orbit, nerve, and/or soft tissue score on the OMENS scale had a significantly higher risk of having vertebral anomalies; the odds ratios were 2.21, 1.39, 1.13, 1.27, and 1.23, respectively.  Patients with vertebral anomalies had a higher risk of other extracraniofacial anomalies, including anomalies of the CNS, circulatory, gastrointestinal, and urogenital tracts. |
| Pegler et al. 2016 | Retro-spective study | C | To describe the most prominent clinical features of a cohort of patients with oculo-auriculo-vertebral (OAV) dysplasia in Brazil. | Inclusion:  Involvement of at least two of the following sites: 1) mouth, skull and face, 2) eyes, 3) ears and 4) vertebrae. And a normal G-banding karyotype.  Exclusion:  Individuals with chromosomal abnormalities or incomplete medical records were excluded from the study. | Included number of patients: 49.  19 (46.3%) were male and 22 (53.7%) female | The participation of a multidisciplinary team is crucial so that patients can be addressed globally for proper support. |
| Connell et al. 2018 | Retrospective review | C | To evaluate the radiographic results and complications of growth-friendly (GF) surgery in the treatment of early-onset scoliosis (EOS) associated with Goldenhar syndrome. | Inclusion:  diagnosed with Goldenhar syndrome and scoliosis with onset less than 10 years of age. All patients had a minimum of one lengthening surgery and at least two-year follow-up from their initial implantation surgery.  Primary outcomes measured included scoliosis (major curve), maximum kyphosis, spine height (coronal T1eS1 height), hemithoracic height, and hemithoracic width.  Exclusion:  None | Included number of patients:  17 patients with Goldenhar syndrome.  Ten patients were treated with growth-friendly surgery, three patients were treated with fusion, three patients were observed, and one patient was treated with a brace. | Our results indicate that for this patient population, growth-friendly surgery tends to improve scoliosis, total spine height, and hemithoracic height and that 80% of the patients experienced severity grade I or II complications.  At minimum two-year follow up, growth-friendly surgical intervention for the treatment of EOS associated with Goldenhar syndrome trended toward improvements in scoliosis and spine height, but had a significant improvement in convex hemithoracic height; however, the majority of patients experienced severity grade I or II complications. |

**Chapter 4.8 Psychosocial problems**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Neurodevelopmental delay | | | | | | |
| Cohen et al. 1995 | Cross-sectional study | C | Ro examine the neurodevelopmental profile of children with OAV and to determine if certain physical manifestations are indicative of a poor neurodevelopmental outcome. | Inclusion:  All newly diagnosed patients over a 5 year period were referred to the Center fo rInfant and Toddler Development at Children's National Medical Center for a neurodevelopmental evaluation.  Exclusion:  None | Included number of patients:  16 male, 8 female. 5 bilateral CFM, 19 unilateral  Age: birth to 57 months  71% had extracraniofacial anomalies. | Of the patients evaluated, 21% were mentally retarded, 33% were significantly delayed in gross motor skills, 20% in fine motor skills, 32% in receptive language skills, and 37% in expressive language skills.  Although the study group is small and the patients have a more severe phenotype than those routinely seen in craniofacial outpatient services, it suggests that children with OAV are at a higher risk for neurodevelopmental delay than the normal population. |
| Cohen et al. 2017 | Cross-sectional study | C | The aim of this study was to define the type and frequency of maxillofacial and systemic malformations in a cohort of HFM patients and to discuss the appropriateness of the commonly used OMENS-plus classification. | Inclusion:  the presence of either at least three craniofacial deformities identified by the OMENS classification or at least two craniofacial manifestations associated with other systemic abnormalities and/or preauricular tags, macrostomia and other eye defects.  Exclusion:  lack of sufficient clinical, radiographic, or follow up data. | Included number of patients:  89 patients,  54 male, 41 female,  Mean age 11.5 years, range 2 months to 46 years | No relevant conclusion described |
| Collett et al. 2011 | Case-control study | C | To determine whether preadolescent children with hemifacial microsomia (HFM) have higher risk of neurodevelopmental delays than unaffected control individuals | Inclusion:  Study participants were originally enrolled in infancy as part of a study of pregnancy risk factors for HFM.  Exclusion:  Known chromosomal anomalies, mendelian inherited disorders, in utero isotretinoin exposure, having been adopted, and age older than 36 months.  Controls were excluded if they had any major malformation. | Included number of patients:  136 children with CFM and 568 health controls | In conclusion, these findings suggest that children with HFM have an elevated risk of delays in receptive language, visuomotor skill, and academic function. Clinically, these early-stage findings suggest that routine neurodevelopmental screening is warranted in this population. Early detection and management of speech, hearing, and vision impairments may help to offset some of the elevated risk in children with HFM.  Children with HFM exhibit poorer verbal, nonverbal, and academic skills than unaffected controls. For example, children with HFM were 3 times as likely to score in the at-risk range of performance on the PPVT-III, implying that they are more likely than their peers to require specialized instruction to ameliorate receptive language delays. |
| Johansson et al. 2007 | Cross-sectional study | C | The aims of the present study were: (1) to use current standardized autism diagnostic instruments to analyze the relation between OAV and Autism spectrum disorder (ASD) in a group of patients with OAV; (2) identify CNS- and chromosomal abnormalities and pre- and perinatal risk factors, that might contribute to the pathogenesis of ASD in OAV; and (3) to determine the period of development during which these might have operated. | Inclusion:  Inclusion criteria were malformations in two of the four areas: orocraniofacial, ocular, auricular, and vertebral  Exclusion:  None | Included number of patients:  20 patients,  11 patients had MRI/CT scans of the brain which were reviewed by a neuroradiologist. EEG recordings were available for 7 patients, choromosomal analysis for 14 patients, and DNA analysis for 4 patients.  12 males, 8 females; age range 8mo–17y, mean age 8y 1mo at neuropsychiatric examination | The proportion of more than a third (45%) with learning disabilities in our OAV group is higher than in most previous reports. Forty-two per cent of our patients fell into the category of autism spectrum disorder, and 11% met full criteria for autism.  It cannot be definitely concluded from our data that brain malformations underlie the development of autistic symptoms in patients with OAV.  The finding of ASD in more than a third of our patients indicates that ASD is common in OAV. Awareness of the occurrence of autism spectrum problems in OAV is important in the habilitation care of these children. The brain and systemic anomalies in the patients with OAV and ASD in this series suggest that, at least in some cases, autism is associated with maldevelopment of the early embryonic brain. |
| Speltz et al. 2017 | Case-control study | C | (1) In comparison with unaffected peers, do adolescents with CFM have continuing problems in two key domains of neurodevelopment, global IQ and academic achievement? (2) Is the cognitive/academic status of adolescents with CFM related to their craniofacial phenotype; i.e., different combinations of anomalies such as microtia with or without other craniofacial malformations? | Inclusion:  Diagnosis of hemifacial microsomia, facial asymmetry, unilateral microtia, OAVS, or Goldenhar syndrome from a craniofacial physician.  Approximately three controls were recruited for each case and were eligible if they had no known birth defects, had not been adopted, and were within 2 months of the cases’ age at the time of recruitment.  Exclusion:  Diagnosis of another known syndrome or chromosomal anomaly.  Cases without microtia and/or at least 2 CFM-associated malformations were excluded from the current analyses in order to include only cases with the most accepted features of CFM1 and to maximize sample homogeneity. | Included number of patients:  142 cases and 316 controls,  13 years of age on average (range = 11 to 17 years) | After adjusting for demographic variables associated with neurodevelopment, we found that cases scored lower on average than unaffected controls on standardized measures of IQ and academic achievement. However, these effects were relatively modest and case-control group differences were smaller than those observed in the elementary school assessment. The proportion of youth with learning problems—an important metric for identifying children in need of special education—was higher among cases than controls (38% vs. 25%, respectively), but this effect was also relatively small.  At this early stage of research on CFM and neurodevelopment, our findings should be viewed primarily as hypothesis-generating, rather than as firm conclusions. |
| Speltz et al. 2018 | Case-control study | C | To determine whether infant cases with craniofacial microsomia (CFM) evidence poorer neurodevelopmental status than demographically similar infants without craniofacial diagnoses (“controls”), and to examine cases’ neurodevelopmental outcomes by facial phenotype and hearing status. | Inclusion:  cases had to have (1) at least 1 of the CFM inclusion criteria developed by the Facial Asymmetry Collaborative for Interdisciplinary Analysis and Learning network; (2) an age between 12 and 24 months (corrected for prematurity, when applicable, for children born between 34 and 36 weeks of gestational age); and (3) a legal guardian who was able to provide informed written consent and be willing to participate for the duration of the study  Exclusion:  Exclusion criteria for cases included (1) diagnosis of a known syndrome (eg, Townes- Brocks, Treacher Collins, branchio-oto-renal, or Nager syndromes); (2) presence of an abnormal karyotype or major medical or neurologic conditions (eg, cancer, cerebral palsy); (3) premature birth (less than 34 weeks of gestation); (4) any circumstance that would preclude the family’s ability to participate fully in the research; (5) a sibling already participating in the CLOCK study, or (6) a consenting parent who did not speak English or Spanish. | Included number of patients:  108 cases and 84 controls,  aged 12-24 months,  Cases were more likely than controls to be male, to be Hispanic or Latino, and to undergo their assessment in Spanish or a combination of Spanish and English. | Although learning problems have been observed in older children with CFM, we found no evidence of developmental or language delay among infants. Variation in outcomes across prior studies may reflect differences in ascertainment methods and CFM diagnostic criteria.  We found no evidence for neurodevelopmental differences between infants with and without CFM in the first to second year of life.  In this baseline assessment, we found no evidence for neurodevelopmental differences among infants with CFM between the ages of 1 and 2 years. This suggests that the academic problems observed in some older children with CFM might not be accurately assessed or present at this age, or might be influenced by the increasing toll of CFM-related risk factors on postinfancy development (eg, hearing and speech impairments). As many older children with CFM show average or above average achievement, it is important to understand which variables in early childhood best distinguish delayed from nondelayed cases. |
| Stromland et al. 2007 | Retrospective study | C | To survey the systemic and functional defects in a group of Swedish patients with characteristics of OAV spectrum with a multidisciplinary team. | Inclusion:  The patients were referred for Goldenhar syndrome, OAV or hemifacial microsomia. For inclusion in the study the patient had to have malformations in at least two of four areas i.e. oro-cranio-facial, ocular, auricular, and vertebral.  Exclusion:  The presence of additional syndromes | Included number of patients:  18 patients,  Number of patients with cleft lip/palate: 5.  17 patients could be evaluated regarding autism spectrum disorder,  Age 8 months to 17 year. | Our data suggest that autism spectrum disorder is more common inOAV than in the general population. Two patients met the criteria for chilhood autism/autism disorder/autistic-like condition and one of them met full criteria for autism.  It is of great importance that educational approaches and behavioral interventions for children with autism are tried for children with OAV and autistic behavior. |
| Psychosocial | | | | | | |
| Dufton et al. 2011 | Case-control study | C | To determine whether children with hemifacial microsomia (HFM) have higher risk for psychosocial problems than children without HFM. | Inclusion:  Study participants were originally enrolled in infancy as part of a study of pregnancy risk factors for HFM.6  Exclusion:  Known chromosomal anomalies, mendelian inherited disorders, in utero isotretinoin exposure, having been adopted, and age older than 36 months.  Controls were excluded if they had any major malformation. | Included number of patients:  136 children with CFM and 568 health controls,  All chilren are aged 5-10 years | Although teachers rated children with HFM as having more behavior problems and social difficulties, parents of cases and controls provided nearly equivalent ratings of their children’s behaviors in these areas. The only exception for parents was a higher average score for cases on the social problems scale of the CBCL. However, group differences on this scale may have been inflated by the inclusion of one item (‘‘speech problems’’), an area of known difficulty for children with HFM (Collett et al., 2010). |
| Johns et al. 2018 | Cross-sectional study | C | First, to elicit feedback from caregivers of children with CFM, as well as adult patients with CFM. Secondly, to describe the experiences of individuals with CFM and their caregivers across their home, school, community, and medical settings. And thirdly, to report on resources participants found helpful, their advice to others affected by CFM, and their suggestions for improving healthcare. | Inclusion:  diagnosis within CFM spectrum, including HFM, oculo-auriculo-vertebral spectrum, microtia, and/or Goldenhar syndrome; CFM-associated features: facial asymmetry, preauricular or facial skin tags, anotia or microtia, aural atresia, lateral oral clefts, and epibulbar dermoid; and fluency in English. | Included number of patients:  42 caregivers and 9 adults with CFM,  Most caregivers were mothers (90%) with male children (71%) who had a mean age of 7 years (SD=4; range 0–17).  Most adults with CFM were female (78%) and the mean age was 45 years (SD=6; range 24–76).  Individuals with CFM generally received the diagnosis at birth (74%) and the most common diagnosis was microtia (84%), with or without HFM, CFM, and/or Goldenhar syndrome. Common facial features of CFM were microtia (86%), aural atresia (78%), and facial asymmetry (75%). | This study adds to our understanding of the perspective of individuals with CFM and their caregivers’ stressors across settings. The range of adaptive coping strategies and supports described and their corresponding suggestions for providers can inform standards for care. |
| Khetani et al. 2013 | Case-control study | C | To compare health-related quality of life (HRQOL) among children with and without hemifacial microsomia (HFM) as assessed by parents and the children themselves during the elementary school years.  (1) How do parents’ of children with and without HFM compare in their perceptions of the child’s HRQOL? and (2) How do children with and without HFM compare in their perceived HRQOL? | Inclusion:  Exclusion:  twin gestations because quality of life may be impacted by twin status | Included number of patients:  136 patients with CFM,  568 controls  CFM: 9 females, mean age = 6 years, 11.9 months, SD = 1.004.  Controls: 285 females, mean age = 6 years, 10.2 months, SD = 0.998 | The present study expanded upon previous studies by including reports of health-related quality of life (HRQOL) by parents and their children, recruiting a large group of cases with hemifacial microsomia (HFM) and a demographically matched control group, and adjusting for selected demographic factors.  We observed significant case-control differences in parental report of their child’s HRQOL during the early and middle childhood period (5–12 years), but we did not find meaningful group differences in children’s report. |
| Luquetti et al. 2018 | Cross-sectional study | C | To explore the diagnostic, treatment-related, and early psychosocial experiences of individuals with CFM and their caregivers using a mixed method approach. | Inclusion:  Individuals with CFM older than 18 years of age and adult caregivers of children with CFM were invited to participate via advocacy and family association websites.  Exclusion:  None | Included number of patients:  42 caregivers and nine adults with CFM.  Most caregivers were mothers (90%) with male children (71%) who had a mean age of 7 years (SD 4, range 0–17). Most adults with CFM were female (78%) and the mean age was 45 years (SD 16, range 24–76).  The most common diagnosis was microtia (84%), with or without HFM, CFM, and/or Goldenhar syndrome. The most common facial features of CFM were: microtia (86%), aural atresia (78%), and facial asymmetry (75%) | The detailed information provided by parents and adults illustrates the intricacy and challenges of their CFM healthcare and psychosocial experiences from the moment of diagnosis through adulthood. The need for ongoing psychological assessment and intervention for patients and families was highlighted in their responses.  Families expressed strong interest in understanding CFM etiology, diagnostic criteria, and treatment guidelines. Stronger collaboration between scientific communities, families, and patient organizations can help explain expectations related to all ages of CFM medical care management and treatment. |
| Ongkosuwito et al. 2016 | Cross-sectional study | C | The first was to examine which child characteristics (i.e., characteristic appearance, feeding problems, articulation problems, hearing problems, learning difficulties, and psychosocial problems) are related to higher levels of parental stress.  Our second objective was to analyze whether the parental cognitive coping styles of rumination, acceptance, and positive reappraisal were associated with parental stress. | Inclusion:  Couples or single patients of patients with CFM  Exclusion:  None | Included number of patients:  31 parents of patients,  59 couples or single parents raising a child with HFM (ages 3–19 years) were addressed. A total of 31 questionnaires were completed and included in this study. | Learning difficulties of the child with HFM and parental acceptance affect stress in parents with a child with HFM the most and are important in the search for a targeted tailoring of intervention for parents with high levels of parental stress. |
| Padwa et al. 1991 | Cross-sectional study | C | To evaluate psychosocial adjustment in different groups of children with craniofacial deformities in order to examine the relationships between symmetry, funcitonal impairments, and social adaptation | Inclusion:  Children with craniofacial deformities that visit the craniofacial clinic  Exclusion:  None | Included number of patients:  11 patients with CFM. 30 patients in total | The results suggested that children with symmetric or non-HFM asymmetric craniofacial deformities were more depressed, had more behavioral problems, and had more difficulties socializing than children with asymmetrical disorders or HFM.  All children seemed to exhibit poor self-concept on projective psychologic measure. Children tended to deny problems when directly questioned about their social lives and feeling.  The results of this study suggested that earlier operative intervention may be psychosocially beneficial to children with symmetric craniofacial deformities. |
| Volpicelli et al. 2017 | Cross-sectional study | C | We prospectively recruited a cross-section of children with craniofacial anomalies in active treatment and compared the differences in psychosocial outlook among the different age groups using the validated, National Institutes of Health Pediatric Patient-Reported Outcomes Measures Information System.  Introduction: Age is a frequent consideration for surgical timing in pediatric craniofacial surgery for optimal psychosocial development. However, systematic evaluations of the effects of age in children under active treatment have not been thoroughly evaluated.  The hypothesis of this study is that differences in anger, anxiety, depression, and quality of peer relationships may exist in craniofacial patients in an age-dependent manner. | Inclusion:  Pediatric patients with craniofacial anomalies (8 to 17 years of age) were consented and prospectively enrolled  Exclusion:  None | Included number of patients:  99 patients with craniofacial anomalies,  22 patients with CFM (21.6%),  44 patients with cleft lip and palate (43.1%), 7 patients with cleft palate (6.9%), and 29 patients (28.4%) with other craniofacial anomalies (including cerebrocostomandibular syndrome, cherubism, otocephaly, ectodermal dysplasia, Kabuki syndrome, Mobius syndrome, Nager syndrome, neurofibromatosis, Treacher Collins syndrome, and craniosynostoses).  Ages of 8 to 17 years,  youngest group: age 8-10 years,  middle/older group: age 11-13 years,  oldest group: 14-17 years | Younger children aged 8 to 10 years with craniofacial anomalies report psychosocial dysfunction in multiple measures of mental and social health when compared to craniofacial children of older age groups despite active treatment. Augmentation of prevention and intervention methods may be necessary from families and schools for this high-risk subset of children with craniofacial anomalies. |
| Wallace et al. 2018 | Case-control study | C | (1) determine whether adolescents with CFM would exhibit or report worse psychosocial adjustment than adolescents without CFM and (2) among cases, assess the association between psychosocial status and phenotype. | Inclusion:  Diagnosis of hemifacial microsomia, Goldenhar syndrome, or unilateral anotia/microtia, as diagnosed by a craniofacial geneticist or surgeon.  Exclusion:  Children with chromosomal anomalies or Mendelian-inherited disorders, in utero isotretinoin exposure, as well as children who were adopted or older than 36 months were excluded. | Included number of patients:  142 adolescents with CFM (cases) and 316 peers without CFM (controls).  Mean age: 13.4 years (SD = 1.4, range= 10 to 17 years) | There was little evidence for variation in case-control differences across different facial phenotypes or as a function of hearing status.  Our results suggest that in spite of multiple risk factors, adolescents with CFM exhibit behavior problems no more frequently than their peers without CFM.  Across all respondents, adolescents with CFM consistently had fewer reported externalizing problems than did controls, but worse scores on most indicators of social functioning. The magnitude of the observed differences in externalizing scores and social functioning was small, generally corresponding to standardized ESs of 0.25 or less, and a number of estimates were imprecise with confidence intervals that included the null. |

**Chapter 5.1 Surgical treatment**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Nagy et al. 2009 | Systematic review | C | To summarize the results of follow-up studies and to determine the long-term stability of mandibular dimensions after early osteodistraction (performed before skeletal maturity; aged 16 years or younger at the time of distraction) in patients with hemifacial microsomia. | Inclusion:  We included prospective and retrospective case series of infants and adolescents, not older than 16 years of age, who had undergone singlestage, early unilateral osteodistraction of the mandible for correction of hemifacial microsomia or its equivalents, and follow-up for a duration longer than the active distraction phase.  Exclusion:  Reports on bilateral craniofacial dysmorphology (no asymmetry) and case reports (low level of evidence10) were excluded. | Included number of patients:  The mean follow-up was 4 ± 3.5 years (range, 0.5 to 12 years).19 Most studies had follow-up periods ranging from 3 to 5 years or less.  The mean number of patients with genuine hemifacial microsomia in the individual studies was 8.8 ± 7.6, varying between 1 and 28. The sum of all genuine hemifacial microsomia patients in the studies was 115.  The age of patients ranged from 1.5 to 16 years; the mean age at the time of distraction was 7.8 ± 2.6 years. | Each study based the effectiveness of osteodistraction on the long-term stability of mandibular dimensions. Even accepting the shortcomings of the study designs and evaluation methods, none of the studies showed convincing stability. Although more than 50 percent of the studies concluded stable results at the end of the follow-up period, (2,12,14,18 –20,22) these could only prove shortterm stability (12) or used a nonobjective evaluation method (18,20).  Type IIb and III deformities were admitted to show relapse2 or “occlusal disaster” with need for reoperation (19). Even clinically stable results showed measurable relapse (22). Objective evaluation showed unpredictable stability of facial symmetry in the long-term, especially of the affected ramus height (13,15–17,21,23). |
| Pluijmers et al. 2014 | Systematic review | C | The purpose of this systematic review is to provide an overview of the surgical correction of the mandible in unilateral CFM in the growing patient, and its long-term outcome and stability. | Inclusion:  Articles reporting prospective and retrospective studies of children and adolescents not older than 16 years of age (N 4) who had undergone surgical correction of a craniofacial microsomia spectrum condition by grafts, osteotomies, DO, or a combination of these interventions, were included. The period of follow-up was selected to be 1 year.  All literature until 18 October 2012 was included.  Exclusion:  Reports on heterogeneous patient groups and/or study groups with fewer than four patients were excluded due to possible bias and an expected low level of evidence | Included number of patients:  30 studies were included, 17 had to be combined due to the same studied patient sample.  All-in all, a total of 19 studies were used for the analysis.  The age of the patients ranged from 2 to 15.3 years, with a mean age of 8.9 years (n = 247).  The mean follow-up time was 4.3 years (n = 230). Two hundred and twenty-six patients had a follow-up time of at least 1 year post-surgery. However, eight studies had a follow-up time of more than 5 years. | In conclusion, this systematic review of the surgical correction of the patient with UCM shows that the outcome is not so much treatment-dependent, but more patient-dependent, i.e. deformity gradation- dependent. The type I to IIa Pruzansky–Kaban patients demonstrated the best results with regard to minimal relapse and/or minimal increase in asymmetry. However, one must bear in mind that the levels of evidence of the articles in this systematic review are OCEBM level 4. Single-stage correction of the asymmetry should be postponed until the permanent dentition stage, or even until skeletal maturity. It can be concluded that in the treatment of the severely hypoplastic mandible, the patient will benefit from a multi-stage treatment protocol if indicated for functional or psychological problems. |
| Ascenco et al. 2014 | Retrospective study | C | The aim of this study was to evaluate patients with unilateral craniofacial microsomia who were treated with mandible distraction and with follow-up of more than 5 years. | Inclusion:  None  Exclusion:  None | Included number of patients:  33 patients.  All unilateral CFM, All unilateral MDO.  Mean age of treatment was 7.3 years (range 2.3 -19.3 years).  Mean follow up of 9 years (5-15 years) | In this team’s series, 90% of patients had recurrence and were referred for orthognathic surgery despite the initially good results after bone distraction. This highlights the importance of comprehensive education for the patient and family as to the probably temporary and not definitive outcome of mandibular distraction.  Independent of previous mandibular distraction, orthognathic surgery will be indicated for a majority of patients. Given this, one must then consider the value of the ability to normalize the appearance of a deformed child’s face for several years, which may yield positive results in their normative development as well as in their lifetime outcomes for mental health, positive socialization, productivity, and even lifetime earnings. |
| Kaban et al. 1986 | Case series | C | To assess the long-term outcomes of MDO in patients with HFM during growth | Inclusion:  Sufficient data had to be available.  Exclusion:  None | Included number of patients:  17 patients.  Of the 20 patients who had early correction of hemifacial microsomia, 17 had sufficient data and follow-up to be included in this study. | This follow-up study has shown that early correction of the mandibular hypoplasia in hemifacial microsomia can improve maxillary growth and decrease the endstage deformity. |
| Kaban et al. 1988 | Case series | C | To assess the long-term outcomes of MDO in patients with HFM during growth | Inclusion:  Sufficient data had to be available.  Exclusion:  None | Included number of patients:  17 patients.  Of the 20 patients who had early correction of hemifacial microsomia, 17 had sufficient data and follow-up to be included in this study. | We conclude that the benefits of early mandibular correction in HFM are sufficiently clear that a prospective, randomized study cannot be undertaken. |
| Ko et al. 2017 | Retrospective cohort study | B | This study was conducted to analyze the long-term facial growth of patients with craniofacial microsomia (CFM) after early mandible distraction osteogenesis | Inclusion:  1) unilateral CFM with grade II mandible deformities; 2) complete traceable radiographic records for previous treatment in the DO group; 3) the completion of facial growth and maturation of physical growth; and 4) CBCT record at the time of the completion of facial growth and before definitive facial correction in both groups.  Exclusion:  None | Included number of patients:  20 patients.  Patients with early mandible DO (n = 9), and the NDO group, comprising those without early mandible DO (n = 11).  The mandible DO was performed at ages ranging from 5 to 9.4 years.  Mean follow-up of 13.08 (SD 3.25) years. | After 13 years of follow-up in patients with early mandible DO, the maxilla demonstrated forward and downward growth; the amount of growth was fairly consistent compared with longitudinal growth changes of maxilla in the norm14. However, the growth of the ramus length and the whole mandible was lower on the affected side than on the nonaffected side. Thus, the ramus length ratio was reduced from 90.84% to 69.46%. The chin exhibited considerable downward growth and limited forward growth. The mandibular growth pattern was similar to that in untreated patients with unilateral CFM. |
| Meazzini et al. 2012 | Case-control study | C | Comparison of the long-term follow-up until the completion of growth of two homogeneous samples of children affected by hemifacial microsomia (HFM), one treated by mandibular distraction osteogenesis (DO) in the deciduous or early mixed dentition, the other not subjected to any treatment until adulthood. | Inclusion:  Only patients with a condyle and ramus (vertically severe type I, with a vertical disproportion of at least 75%, and type II) (Pruzansky, 1969) where included in this study, given that absence of the condylar unit might be a confounder in evaluating mandibular growth.  Only patients with an age at distraction of between 5 and 7 years (late deciduous or early mixed dentition) of age where included in the study (average age 5.9 ± 0.8 years), with a follow up longer than 10 years (average follow-up 11.2 ± 2.4 years).  Exclusion:  None | Included number of patients:  24 patients.  14 patients (vertically severe type I, with a vertical disproportion of at least 75%, and type II) underwent DO.  The control sample consisted of 8 HFM patients (severe Type I or Type II) who had not, for different reasons, undergone early surgery, although their severity was comparable to the treated sample | At the completion of growth after DO performed during infancy, the ratio between affected and non affected rami is similar to what it would have been without distraction.  The comparison of treated and untreated patients followed until the completion of craniofacial growth shown in this study, clearly demonstrates that the genetic input guiding the neuromuscular imbalance tends to reject any new “musculo-skeletal geometry” imposed during active growth. Therefore, although DO is still the preferred treatment in bilateral mandibular hypoplasia where respiratory distress is associated (Bouchard et al., 2009), in unilateral cases its indications are not as strong. |
| Caron et al. 2017 | Retrospective cohort study | B | 1. Analyse the prevalence of OSA in patients with CFM 2. Determine the relationship between the severity of CFM and the risk of OSA 3. Analyse the chosen treatment modalities and their outcomes | Inclusion:  Patients with CFM and clinical and/or radiographic images  Exclusion:  None | Included number of patients:  755 patients.  One hundred and two of the 133 patients diagnosed with OSA were treated for OSA. | These results imply that MDO might not be a successful treatment option for OSA in patients with unilateral mandibular hypoplasia. Further research is needed to support this hypothesis |
| Lam et al. 2014 | Retrospective cohort study | B | To assess the rate and predictors of surgical success and complications among (1) patients who underwent MDO prior to other airway procedures (MDO first), and (2) patients who required an initial tracheotomy and were subsequently treated with MDO (tracheotomy first).  Surgical success was defined as (1) avoidance of tracheotomy among patients who were treated first with MDO and (2) successful decannulation among patients who initially underwent tracheotomy prior to MDO. | Inclusion:  any patients who underwent initial MDO during the study period.  Exclusion:  Patients who were lost to follow-up afterMDOor had incompletemedical recordswere excluded. | Included number of patients:  123 patients.  69 male, 54 female.  56% of the patients were diagnosed as having an associated syndrome.  11 (9%) patients with CFM. Seven had tracheotomy first and 4 MDO first.  Median age at time of distraction was 21 months (range, 6 days–24 years). Sixty-two patients (50.4%) underwent an initial tracheotomy prior to MDO while 61 (49.6%) underwent MDO first. Median follow-up time was approximately 5 years (range, 30 days–16.2 years). The median distraction amount was 22 mm (range, 7-52 mm).  One hundred seven patients (87.0%) underwent a single distraction, while the remainder of the cohort required repeated distractions. | we can reasonably conclude that among patients who required a tracheotomy as an initial procedure, patients with CFM–Goldenhar syndrome seem to have a far worse chance of success with subsequent MDO than patients with isolated PierreRobin sequence. This association does not seem to hold among patients who underwentMDOfirst in the absence of a tracheotomy.  It is clear from our analysis that patients who were syndromic or had additional airway disease abnormalitieswere more likely to have an initial tracheotomy to address multilevel disease. Mandibular distraction osteogenesis should be considered only as an initial procedure in a setting in which there is no other indication for tracheotomy, such as multilevel airway obstruction, ventilator dependence, or persistent dysphagia. |
| Pluijmers et al. 2019 | Retrospective chart study | C | The purpose of this retrospective study was to evaluate the type of surgical corrections of the craniofacial anomaly in patients with craniofacial microsomia. Additional objectives were to evaluate the timing of the procedures and the total number of surgical corrections performed. Lastly, the number of surgical procedures in correlation to the severity, including a unilateral versus bilateral phenotype, was evaluated. | Inclusion:  Patients with CFM  Exclusion:  Patients in whom adequate diagnosis based on the orbital, mandibular, ear, neural, and soft-tissue–plus classification or phenotypic assessment tool for craniofacial microsomia was not able to be determined were excluded. | Included number of patients:  565 patients.  The male-to-female ratio was 1.2:1. A total of 496 patients (87.8 percent) had a unilateral presentation of craniofacial microsomia. The distribution between right and left craniofacial microsomia was 1.2:1 (n = 496) as well.  Most patients with unilateral craniofacial microsomia had a Pruzansky-Kaban type I (26.8 percent) or IIa (26.6 percent) mandible followed by the Pruzansky-Kaban type IIb (23.2 percent) and type III (15.9 percent) mandibles.  443 (78.4 percent) of all patients with craniofacial microsomia received some form of surgery during their life | With regard to mandibular surgery, age at the first surgical procedure is shown to have an influence on the number of surgical procedures needed throughout life. Patients, both unilateral and bilateral, who underwent three or more surgical corrections of the mandible were treated significantly earlier at a mean age of 9.73 years (n = 35), compared with those who underwent “only” one or two surgical procedures of the mandible, who were on average treated at 12.81 years (n = 116; t149 = 2.11; p = 0.036). Also, the linear regression model indicated that for every year decrease in age, the number of operations performed went up, independent of the Pruzansky-Kaban type mandible. In other words, those who are treated earlier in life for correction of asymmetry of the mandible will undergo more surgical procedures to correct the asymmetry, possibly suggesting that the operations might be responsible for impaired growth, which then increases the need for more operations. This reinforces the policy of correcting mandibular asymmetry at an older age unless there are significant functional problems (e.g., obstructive sleep apnea). |
| Rachmiel et al. 2000 | Case series and literature review | C | To compare extraoral and intraoral distraction osteogenesis in the treatment of HFM | Inclusion:  None  Exclusion: None | Included number of patients:  22 patients.  12 extraoral DO (10 unidirectional and 2 multidirectional devices). Age range 6-15 years.  10 intraoral DO (ages 6-13 years).  Stages of treatment: 1. surgery; 2. 3-day latency period; 3. distraction period of 1 mm per day for 18-25 days; 4. 6-week retention period; 5. device removal. Follow-up 1 year. | The extraoral device is uncomfortable and socially unacceptable to young patients. The main disadvantage is the residual two cutaneous scars at the area of pin insertion transbuccally.  The intraoral device is more socially convenient and does not cause extraoral scarring when a side dirll is used for screw drilling. Nevertheless, even when using the transbuccal approach for dirlling, a small, unnoticeable scar remains in the gonial area. |
| Rachmiel et al. 2014 | Case-series | C | We will compare external and internal distraction devices for mandibular lengthening in terms of effectiveness, results, patient comfort, and complications. | Inclusion:  None  Exclusion: None | Included number of patients:  37 patients in total,  14 patients with CFM.  All treated with bilateral MDO at age 6 months - 14 years.  20 with external DO, and 17 with interal DO.  Twenty-one patients suffered from respiratory distress and were tracheotomy candidates, and 16 patients were tracheotomy dependent. | Overall stability with internal devices is greater than with the external devices. The relapse rate was 23.52% with external versus 13.33% with internal devices. This can be explained by the fact that during distraction there is some bending of the pins with less precise rate of lengthening, resulting in compromised ossification during the retention period.  Internal devices are more comfortable to the child with a precise and predictable vector of lengthening and lower risk of relapse. They leave less visible scars and should be considered first. Their main disadvantage is the second operation for device removal under general anesthesia. |
| Santamaría et al. 2008 | Case-series | C | The authors present their experience with the use of the fibula osteocutaneous free flap for mandibular reconstruction in severe hemifacial microsomia patients. | Inclusion:  None  Exclusion: None | Aged 3 to 10 years (mean, 7.2 years) six were girls and four were boys.  Previous operations included eight failed bone grafts in five patients, six iliac crests and two costochondral. Two patients had previously undergone closure of clefts of the lip and palate.  9/10 patients with grade III mandible, 1/10 with IIB.  Mean follow-up was 45.4 months (range, 12 to 94 months). | The free flap is a safe, effective procedure for mandibular reconstruction in children with Pruzansky grade III and severe grade IIB mandibles. We propose this procedure as the first choice for mandibular reconstruction in patients where distraction osteogenesis is not feasible. |
| Suh et al. 2013 | Retrospective study | C | The purpose of this study was to evaluate the results of long-term follow-up in patients with relatively severe unilateral craniofacial microsomia after mandibular distraction. | Inclusion:  Patient with relatively severe unilateral CFM that underwent MDO  Exclusion: None | Included number of patients:  26 patients.  16 male, 10 female. 19 right, 7 left.  13 type IIa, 11 type IIb, 2 type III.  The average age at surgery was 6.08 years (range, 3.6 to 11.9 years).  The overall mean distraction amount was 23 mm vertically (range, 12 to 33 mm) and 21 mm horizontally (range, 8 to 27 mm).  The average cephalometric follow-up period was 130.7 months (range, 95 to 228 months). | Early distraction of the mandible in craniofacial microsomia not only reduces the severity of the deformity but also promotes psychosocial functionality in patients. However, in cases of severe craniofacial microsomia, there were more relapses and less growth of the distracted mandible, which eventually called for an additional operation, such as repeated distraction or orthognathic surgery.  Therefore, efforts to find a solution that improves the results are seriously needed. We have considered a longer consolidation period and more supportive orthodontic management as possible solutions to relapse. This study is not a comparative study, so future studies are required to evaluate the differences of growth between patients treated with distraction osteogenesis and patients with untreated unilateral craniofacial microsomia. |
| Wang et al. 2018 | Retrospective study | C | This study focused mainly on the safety and unexpected incidents of mandibular distraction osteogenesis in treating patients with hemifacial microsomia. | Inclusion:  Patients with unilateral Pruzansky type II and type III mandibular hypoplasia undergoing mandibular distraction osteogenesis at the maxillofacial surgery center of the hospital from February of 2010 to March of 2015  Exclusion: None | Included number of patients:  71 patients.  Unilateral CFM. Pruzansky IIA (n=18), IIB (n=52) and III (n=1).  Patients aged 5 to 14 years at the time of distraction were included in the study, and they were followed up for over 1 year, with an average follow-up length of 33.2 ± 15.7 months. | Mandibular distraction osteogenesis is a widely used procedure for treating patients with hemifacial microsomia. It is extremely important to be fully aware of a variety of incidents occurring during and after the surgical procedure to minimize the frequency of occurrence of such incidents. |
| Weichman et al. 2017 | Retrospective study | C | There is controversy regarding the treatment of young patients with unilateral craniofacial microsomia and moderate dysmorphism. The relative indication for mandibular distraction in such patients poses several questions: Is it deleterious in the context of craniofacial growth and appearance? This study was designed to address these questions.  In the absence of obstructive sleep apnea, feeding difficulty, or severe craniofacial dysmorphism, the indications for elective distraction are not as clear. This investigation looks at long-term outcomes of patients with mild to moderate unilateral craniofacial microsomia who underwent early distraction to determine the factors and predictors contributing to satisfactory long-term results. | Inclusion:  Patients included for analysis had unilateral craniofacial microsomia, a Pruzansky-Kaban type I or type IIa mandible (the study definition of mild to moderate deformity), age of distraction younger than 10 years (the study definition of early distraction), attainment of skeletal maturity at the time of analysis, and longitudinal long-term follow-up with both photographs and cephalograms.  Exclusion:  Patients were excluded from analysis if they had bilateral involvement, Pruzansky-Kaban type IIb or type III mandibles, lack of skeletal maturity at the time of investigation, or lack of longitudinal long-term follow-up. | Included number of patients:  19 patients.  All had unilateral CFM, Pruzanksy I or IIA.  The average age at the time of follow-up was similar in both cohorts at 16.5 ± 4.2 years in the satisfactory cohort and 16.9 ± 3.1 years in the unsatisfactory cohort.  Patients in both cohorts (satisfactory and unsatisfactory) displayed similar incidences of Pruzansky-Kaban type I and Iia mandibles. | In a study of patients having unilateral craniofacial microsomia with mild to moderate dysmorphism, more than half of treated patients were judged to have satisfactory outcomes if operated on at a younger age and overcorrection was documented before discontinuation of activation. In addition, this distraction did not have deleterious effects on the quality of bone stock required for further operations. |
| Zhang et al. 2018 | Retrospective study | C | The authors compared the need for orthognathic surgery in skeletally mature craniofacial microsomia subjects who either did (study group) or did not (control group) undergo early mandibular distraction osteogenesis. | Inclusion:  Subjects with a Kaban-Pruzansky grade I to III mandible who were at least 14 years of age at the time of latest follow-up with the multidisciplinary craniofacial surgery team at our institution were included.  Exclusion:  None | Included number of patients: 38 patients,  17 patients early distraction,  21 patients non distraction.  The cohorts had a similar mean age (mandibular distraction osteogenesis, 18.95 ± 2.82 years; non–mandibular distraction osteogenesis, 17.95 ± 2.14 years; p = 0.246). | The results of this study seem to suggest that there is no significant difference in rates of orthognathic surgery at skeletal maturity between craniofacial microsomia patients who did and patients who did not undergo early mandibular distraction osteogenesis.  Thirty-five percent of mandibular distraction osteogenesis subjects underwent repeated distraction, suggesting that long-term management of craniofacial microsomia patients may require further correction of mandibular asymmetry beyond the initial intervention. |
| Bertin et al. 2017 | Retrospective study | C | The aim of this study was to evaluate architectural and aesthetic long-term outcomes for primary mandibular surgery in patients with HFM. | Inclusion:  Patient with HFM that presented between 1981 and 2015.  When feasible, the primary mandibular surgery was performed when the patient was between 9 and 12 years of age, after the permanent mandibular canine teeth had begun their eruption, so that an associated genioplasty could be performed.  Exclusion:  Patients who had not undergone operation; primary mandibular surgery carried out in another centre; and patients who had been operated on without primary mandibular surgery. | Included number of patients:  39 patients.  43.6% had a Pruzansky IIA, 30.8% Pruzansky IIB, and 25.6% Pruzansky III.  Depending on the nature of the mandibular deformity, patients were treated using a costochondral graft (CCG) or a vertical ramus osteotomy (VRO). | Costochondral graft and vertical ramus osteotomy continue to be suitable and safe procedures for the primary mandibular reconstruction in children with type II and type III hemifacial microsomia. We report good aesthetic and cephalometric outcomes at the end of growth after a single-stage correction.  A secondary orthognathic procedure was needed with 23% of the patients after completion of growth, due to a trend for the chin deviation and maxillary occlusal canting to relapse, probably as a result of soft tissue hypoplasia. |
| Padwa et al. 1998 | Retrospective study | C | To document vertical midfacial growth after costochondral graft mandibular ramus construction in children with type IIB and type III HFM | Inclusion:  None  Exclusion: None | Included number of patients:  33 patients.  All type IIB or III mandibles that had unilateral mandibular elongation and rotation by constochondral graft construction between 1980 and 1990. | Costochondral graft construction of the ramus and condyle in type IIB to III growing HFM patients converts the deformity in these children to a more symmetrical and functional type IIA deformity. Success depends on maintenance of the open bite and regulation of tooth eruption to produce vertical midfacial and dentoalveolar growth. In patients who do not achieve adequate ramus/condyle growth, a secondary lengthening procedure may be required. The ideal time for construction is the mid-mixed dentition when there is active tooth eruption and alveolar growth. |
| Tahiri et al. 2015 | Retrospective chart study | C | The purpose of this article is to present our experience with costochondral rib grafting for mandibular reconstruction in children with Pruzansky/Kaban type 2B and type 3 mandibular hypoplasia. | Inclusion:  All patients with craniofacial microsomia who underwent costochondral rib grafting for mandibular reconstruction  Exclusion: None | Included number of patients:  22 patients.  12 male, 10 female.  The average age was 7 years 2 months at the time of rib grafting, ranging from 2 years 2 months to 15 years 10 months.  Twelve hemimandibles were classified as type 2B and 21 hemimandibles were classified as type 3. | We present our experience with costochondral rib grafting for type 2B and type 3 mandibular hypoplasia in the setting of craniofacial microsomia, and specifically hemifacial microsomia and Goldenhar syndrome. Using our technique described above and adhering to a relatively early range-of-motion protocol postoperatively, we were able to obtain reliably good results. |
| Fattah et al. 2014 | Retrospective study | C | Our purpose was to retrospectively determine the cephalometric outcome of orthognathic surgery in this challenging patient group, specifically examining the stability of the surgical movement more than 1 year after surgery. | Inclusion:  All cases of HFM treated with orthognathic surgery by the senior author (J.P.) between 1993 and 2006.  Both unilateral and bilateral cases were included.  Patients were included if complete posterior-anterior (PA) cephalometric and orthodontic records at 3 time points were available (T1: Presurgical, T2: immediate postsurgical, and T3: at least 1 year after surgery).  Exclusion: Patients were excluded if they had other craniofacial abnormalities (eg, craniosynostosis or cleft lip/palate) or underwent distraction osteogenesis of the mandible. | Included number of patients:  10 patients with CFM.  The mean age at surgery was 17.8 years (range, 12.8Y20.9 y) and the mean length of follow-up was 3.1 years (range, 1.1Y4.75 y).  6 patients were right-sided; 2, left-sided; and 2, with bilateral cases. | Our approach to the management of the occlusion in this patient population is based on the premises that the deformity does not worsen with age and that surgical results are most stable when performed on skeletally mature patients.8,9 Previous methods of correction have included a 2-stage approach comprising vertical ramus osteotomies at the mixed dentition stage and, subsequently, at maturity10 because of relapse. We do not believe that early surgery ‘‘unlocks the growth’’6,11 and therefore limit the number of surgeries by delaying definitive reconstruction until skeletal maturity whenever possible. As a result, we avoid early distraction because of the lack of data advocating its efficacy as an isolated treatment modality12 and limit our use of costochondral grafts to those patients who lack a ‘‘functional’’ articulation with the skull base, that is, the absence of the ascending ramus and temporomandibular joint with compromised mouth opening. |
| Liu et al. 2017 | Case series | C | We propose an approach that combines bimaxillary distraction osteogenesis with staged orthognathic surgery and evaluate its long-term clinical outcomes in the treatment of adult HFM patients.  The aim of bimaxillary distraction osteogenesis was to achieve a horizontal occlusion plane rather than absolute facial symmetry, because the hypoplasia was usually inconsistent at other regions such as gonial angles; thus, secondary orthognathic operations were always necessary. | Inclusion:  Patients that underwent bimaxillary distraction osteogenesis.  Patients with severe occlusion disorder had received orthodontic therapy preoperatively.  Exclusion:  None | Included number of patients:  12 patients.  Only patients with a type I and IIA mandible. Five had a type 1 mandible and seven a type Iia.  Ages ranged from 18 to 29 years old, and the follow-up was more than 36 months | In conclusion, our study indicated that the surgical effect of single bimaxillary DO for HFM patients is limited. Certainly, bimaxillary DO is a great approach to level the occlusal plane and elongate hypoplastic jaws as well as surrounding soft tissues to address integral asymmetry. But chin deviation and other local asymmetry could not be fully managed via bimaxillary DO only; thus, stage II orthognathic procedures would be necessary. And the results show that combined bimaxillary DO associated with orthognathic surgery operations improved facial symmetry in all HFM patients in long-term follow-up. Thus, this approach should be recommended as a treatment alternative for adult patients with face countenance asymmetrical deformities. |
| Yamaguchi et al. 2017 | Retrospective study | C | The purpose of this study is to examine the validity of an integrated treatment protocol for correction of this facial deformity.  We have developed a two-stage treatment protocol for adult patients with HFM including bone surgery and soft tissue management. The first step is to correct the osseous asymmetry using two-jaw OGS combined with facial contouring procedures. The remaining facial deficiency is augmented using a microautologous fat transplantation technique in the second stage [11]. | Inclusion:  The 2-staged treatment protocol was applied to all patients with HFM who had finished their growth spurt and had functioning temporomandibular articulation. A chart review included all adult HFM patients who underwent OGS and facial contouring procedures.  Exclusion:  We excluded the following patients: 1) Pruzansky-Kaban classification type III, 2) follow-up less than 6 months after the last surgery, 3) incomplete or missing data, and 4) patient rejection to be included in the study. | Included number of patients:  14 patients.  The mean age at OGS surgery was 21.7 years (SD 3.8). The mean follow-up duration after OGS and fat injection was 25.8 months (SD 11.8) and 16.8 months (SD 10.3) respectively.  Four patients were categorized as type I, while the remaining 10 patients were type II (7 patients type IIA, 3 patients type IIB). | Our integrated approach using orthognathic surgery, facial contouring surgery and subsequent fat injection is satisfactory and obtain significant improvement of the facial deformity considering the complexity of HFM.  In terms of soft-tissue, the correction of the occlusal plane and bone configuration does not promise to achieve sufficient facial symmetry. Especially for patients with prominent soft tissue discrepancy, OGS can accentuate the deficiency around the jawline on the affected side due to shifting of the maxilla and mandible and stretching out of the soft tissue regardless of bony augmentation (Fig 1). Our integrated approach reduces this discrepancy, and the subsequent soft tissue augmentation becomes more convenient. |
| Polley et al. 2018 | Systematic review | C | We present a consecutive series of skeletally mature patients with Pruzansky Grade III hemifacial microsomia treated successfully utilizing alloplastic reconstruction of the missing/deformed temporomandibular region | Inclusion:  Ten consecutive patients with Pruzansky Grade III hemifacial microsomia were reconstructed between October 2014 and July 2017.  All patients underwent alloplastic reconstruction of the affected glenoid fossa and its articular surface, mandibular condyle, condylar neck, and ascending mandibular ramus. All patients also underwent surgery on the unaffected mandibular ramus (except the bilateral case), with or without autogenous bone grafting, and simultaneous LeFort I maxillary surgery (with or without segmentalization)  Exclusion:  None | Included number of patients:  10 patients,  All Pruzansky grade III.  Surgery at skeletal maturity. Follow-up was 6 - 50 months (8/10 patients >1 y follow-up).  Eleven alloplastic implants were utilized in these 10 patients (one bilateral joint replacement). | Alloplastic TMJ and mandibular reconstruction in severe grades of hemifacial microsomia has demonstrated consistent, excellent results in this series of skeletally mature patients. We have no experience with and do not recommend its use in the growing craniofacial skeleton.  We feel it is the best solution for the salvage of patients who have failed autogenous reconstructions, of which there are many. The question of whether early autogenous reconstructions should be abandoned for a definitive alloplastic reconstruction at skeletal maturity is yet to be determined. |
| Pluijmers et al. 2018 | Retrospective study | C | The purpose of this study was to evaluate a possible correlation between the maxillary cant and the mandibular hypoplasia, and to review the types of maxillary correction in our cohort of CFM patients. | Inclusion:  Unilateral affected patients with available (ConeBeam) CT-scan of the mandible and the medical history were included.  Exclusion:  CT-scans of patients who had had treatment of the upper jaw prior to the CT-scan were excluded. | Included number of patients:  81 patients.  All unilateral CFM,  A total of 8 patients had a Pruzanksy-Kaban type I mandible, 11 had a type IIa, 29 were diagnosed with a type IIb and 32 patients had a type III mandible.  Overall, most patients had a mild (42%) to moderate (28.4%) cant. | There is a positive correlation between the severity of mandibular hypoplasia and canting of the maxilla.  Comparable with the systematic review, maxillary surgery was performed during the skeletal maturity with a mean age at time of surgery of 18,2 years old. Based on PartOne and Part two correction of themaxillo-mandibular asymmetry, it is suggested to wait until permanent dentition, if there are no definite indications for early surgery such as functional (e.g. Obstructive Sleep Apnoea) and/or psychological impairments.  In contrast to the systematic review of the literature, the most often performed type of maxillary surgery in the studied groupwas a bimaxillary osteotomy. It must be noted that nearly half of these patients had mandibular surgery earlier in life. |
| Van de Lande et al. 2018 | Systematic review | C | The aim of this systematic review is to provide an overview of the surgical options for maxillary correction in patients with unilateral CFM. | Inclusion:  Studies reporting patients with unilateral CFM (n > 4) who had maxillary correction (with/without simultaneous mandibular correction) with a minimal follow-up of 6 months.  Exclusion:  Studies reporting a heterogeneous study population and/or studies reporting exclusively bilateral cases were excluded due to possible bias; studies with fewer than 4 patients and studies with a followup time of less than 6 months were excluded for expected low level of evidence. | Included number of patients:  7 studies were included.  Included studies were prospective (n = 2) and retrospective case series (n = 5). All studies met the OCEBM criteria for level IV evidence.  A total of 57 patients with unilateral CFM had maxillary correction.  In all cases the mandibular asymmetry was treated simultaneously at a mean age of 20.2 years (range: 12.0-26.0 years).  The mean follow-up time was 24.8 months (range: 6.0-75.0 months). | This systematic review shows that surgical correction of the maxilla was performed simultaneously with correction of the mandible in all reported patients at a mean age of 20.2 years in a total of 57 patients with unilateral CFM.  Types I and IIa would benefit from LeFort + MDO; Type IIb from LeFort + MDO or BiMax; and Type III from BiMax (of which 50% of the cases had preceding mandibular surgery, including the use of a patient-fitted prosthesis.  However, due to lack of data, no hard conclusions can be drawn on the ideal surgical treatment to correct the asymmetry and the timing in patients with CFM. Moreover, additional (aesthetical) procedures were frequently suggested to achieve the desired end-result. |
| Breik et al. 2016 - Does the rate of distraction or type of distractor affect the outcome | Systematic review | C | A variety of surgical protocols are available in the literature for performing mandibular distraction. This study aims to determine the ideal rate of distraction and compare outcomes between internal and external distractors in children and infants with upper airway obstruction due to micrognathia. | Inclusion:  All the studies included children who had clinical evidence of micrognathia and underwent bilateral MDO.  Children with syndromic and nonsyndromic micrognathia were included, but some particular conditions were excluded.  Exclusion:  Children with bilateral temporomandibular joint (TMJ) ankylosis, unilateral hemifacial microsomia, and other conditions that may have contributed to the airway obstruction for reasons other than the micrognathia alone were excluded. In addition, children with known lower airway abnormalities before treatment were excluded. | Included number of patients:  66 articles overall included.  43 articles on surgical outcomes.  A subgroup analysis was performed to evaluate the effect of distraction rate per day on the risk of failure and complications. Overall, the patients included in this analysis were divided into 3 main groups based on distraction rate: 1 mm/d, 1.1 to 1.9 mm/d, and 2 mm/d or greater. | When comparing mean ages at different rates of distraction in the included studies, we found that the mean age of patients undergoing distraction at a rate of 2 mm/d or greater was significantly younger (9.9 months) compared with those undergoing distraction at a rate of 1 mm/d (38.6 months). These findings suggest that for children younger than 12 months, distraction at a rate of 2 mm/d is safe and effective.  We recommend that because of the more rapid distraction and shorter period of treatment, distraction at a rate of 2 mm/d is safe in children younger than 12 months.  There is a higher incidence of failure with the use of external distractors, and this is most commonly because of technical difficulties that require a return to the operating theater. Scarring is also more common then external distractors are used compared with internal distractors. When possible, internal distractors should be used. |
| Breik et al. 2016 - Feeding and reflux in children | Systematic review | C | The objective of this study is to determine the effects of MDO on feeding and gastro-esophageal reflux. | Inclusion:  All the studies includedwere children with clinical evidence of micrognathia who underwent bilateral MDO. All studies needed to have included the conservative treatment options attempted, reasons for failure, and minimumof 1 year followup.  Syndromic and non-syndromic childrenwere included if therewas clinical evidence of glossoptosis and upper airway obstruction  Exclusion:  Patients with bilateral TMJ ankylosis, unilateral hemifacial microsomia or other conditions that may be contributing to the airway obstruction for reasons other than the micrognathia alone. Also, children with known lower airway abnormalities prior to treatment were also excluded. | Included number of patients:  66 articles overall included,  21 articles on feeding,  4 articles on GERD (gastro-oesophageal reflux disease).  The total numbers of patients included in the feeding analysis were 300 (of 21 papers). | In this review, four out of five patients were able to feed exclusively orally within 12 months after MDO. Most of these children were weaned from gastrostomy or enteric feeding before MDO to oral feeding after MDO. It is hypothesized that this is due to improvement in the upper airway caliber, allowing the child to breathe adequately and maintain oxygenation while feeding. In addition the improved facial skeletal profile will improve lip approximation, facilitating a better sucking reflex after the healing phase is complete.  The mean age of patients included in this study was 7 months with ages ranging from 5 days of age at the time of surgery to 6 years of age. It can be extrapolated however from our findings that early MDO was successful at improving feeding, and this in turn may affect long term growth of the child. |
| Breik et al. 2016 - Mandibular distration for the management of upper airway obstruction | Systematic review | C | This systematic review was conducted to determine the effectiveness of MDO in the treatment of airway obstruction. | Inclusion:  All of the studies in this review included children with clinical evidence of micrognathia who underwent bilateral MDO and also children who had initially undergone conservative treatment options.  This review considered reasons for failure and for the consideration of tracheostomy.  Exclusion:  Some particular conditions such as bilateral TMJ ankylosis, hemifacial microsomia, and oth- er conditions that may contribute to the airway obstruction for reasons other than the micrognathia alone, were excluded. In addition, children with known lower airway abnormalities prior to treatment were also excluded. | Included number of patients:  66 articles overall included.  51 articles on MDO outcomes | Overall, MDO was found to be very successful at preventing tracheostomy in children with micrognathia who have failed conservative treatment. Success in preventing tracheostomy was achieved in 95.5% of neonates and infants. This was supported by statistically significant improvements in the OAHI. The most common reason for failure of MDO to relieve the airway obstruction was undiag- nosed airway obstruction at other levels, such as tracheomalacia, laryngomalacia, or undiagnosed central apnoea.  All children being considered for MDO should have a thorough airway assessment with nasoendoscopy and polysomnography studies to confirm that the apnoea is a primary obstructive apnoea, and to exclude lower airway abnormalities. Lower airway abnormalities and central apnoea are contraindications for early MDO. |
| Ow and Cheung. 2008 | Systematic review | C | This meta-analysis aims to provide evidence-based data on the clinical applications of mandibular distraction osteogenesis for mandibular lengthening and the functional outcomes associated with this technique. | Inclusion:  Studiens on mandibular distraction osteogenesis for lengthening only.  Exclusion:  Articles involving alveolar distraction, mandibular widening, or distraction of segmental defects were excluded. | Included number of patients:  178 articles were included.  Including 1185 patients who underwent MDO.  539 patients underwent unilateral MDO and 646 patients underwent bilateral MDO.  74% (n=399) of the patients had CFM.  Unilateral MDO: At the time of unilateral mandibular distraction osteogenesis, patients were most commonly aged between 6 and 10 years (28.2 percent). | This meta-analysis has provided an overview of the clinical applications of mandibular distraction osteogenesis and its associated aesthetic and functional airway changes. Its success in inducing these changes provides the clinician with an alternative to conventional treatment methods. |
| Paes et al. 2013 | Systematic review | C | The objective of the current study was to systematically review the published data considering this matter, providing a fundament for protocols and a more conscious treatment strategy for infants with Robin syndrome in the near future. | Inclusion:  Prospective and retrospective case series, describing the outcome after external or internal mandibular distraction using resorbable or non-resorbable distraction device, in more than five infants aged <18 months suffering from RS.  Patients with Pierre Robin  Exclusion:  Studies consisting of a mixed group of patients, in which those diagnosed with RS could not be extracted from the whole study group to analyze the outcome separately, were excluded. | Included number of patients:  12 articles,  Total of 212 patients that underwent MDO over the period 2004-2012.  Of the 212 patients, 82 % suffered isolated RS, 8 % Stickler’s syndrome, 2 % Treacher Collins, 1 % Opitz Syndrome, and the rest suffered from varying syndromes.  The mean age of MDO cases varied from 8.6 weeks in external MDO, 9.6 weeks in internal non-resorbable MDO, and 8.3 weeks in resorbable MDO. | In young infants (i.e., younger than 6 months), an internal (resorbable) distractor has shown promising results with regard to immediate airway obstruction relief and also parental acceptance and tolerability in home care. In the older or multi-complex cases, an external distractor might provide benefits over an internal device. Using guided surgery by means of preoperatively planned surgiguides [79] or navigation [80] could eliminate the need for external devices in complex cases and support the utilization of curvilinear internal devices. |
| Tsui et al. 2016 | Systematic review | C | To conduct a systematic review to answer the clinical question “What are the effectiveness of mandibular distraction osteogenesis (MDO) and its complications to treat patients with obstructive sleep apnea syndrome (OSAS)?”. | Inclusion:  1. Clinical trial or case series reporting on the treatment outcome of OSA with MDO 2. Human studies 3. The treatment provided clearly described 4. The preoperative and postoperative AHI or respiratory disturbance index (RDI) were reported 5. The duration of the follow-up period of the subjects was reported.  If the study was a case series, the sample size should be more than 10 subjects.  Exclusion:  None | Included number of patients:  12 articles were included,  256 patients were included.  Patients age: 7 days to 60 years with OSA due to retrognathic mandible.  The mandibular advancement achieved was 12 to 29mm.  The mean reported follow-up period ranged from 6 to 37 months.  Children or infants were usually allowed for a shorter latency period of 1 to 5 days, while adult patients were allowed for 5 to 7 days. The protocol of distraction also varied among studies, ranging from 0.8 to 2mm per day in 1 to 4 rhythms. The consolidation period varied from 4 to 28.9 weeks, while the majority was in the range of 2 to 4 months. | This systematic review showed that MDO was highly effective in resolving OSAS in both children and adults with retrognathic mandible. It was found to be an invaluable means in alleviating airway obstructions in children inwhich traditional orthognathic surgery was deemed impossible. It could also help to avoid tracheostomy or help to decannulation in the children/infants population.  It was also showed there were no consensus for the criteria of success/cure for OSAS surgeries in children and infants, and is therefore recommended for their development. There were also no randomized controlled trials to compare MDO and conventional orthognathic surgery to treat patients with OSAS. |
| Verlinden et al. 2015 | Systematic review | C | The aims of this study were (1) to perform a systematic review of the literature on complications of MDO for congenital deformities, and (2) to introduce an index for the classification of complications in (mandibular) DO in general. | Inclusion:  The articles were included if they met the following eligibility criteria: (1) clinical article, (2) mandibular distraction osteo- genesis (MDO), (3) congenital deformity, and (4) a report on complications.  Exclusion:  Studies were excluded if data on complications were insufficient, no translation was avail- able, or the publication was a non-clinical article | Included number of patients:  81 articles were included (on MDO for congenital deformities).  1258 patients | In the present population, an overall complication incidence of 34.4% was found. Infection was seen in 5.8% and device-related problems were present in 7.3% of all patients.  This systematic review shows that MDO can be applied to different indications of DO in congenital deformities and that treatment and treatment outcomes vary widely. |
| Master et al. 2010 | Systematic review | C | The following review outlines documented complications of MDO, presents cases illustrating the more common complications, and offers solutions to prevent these complications. | Inclusion:  None  Exclusion:  None | Included number of patients:  40 articles on complication on craniofacial distraction osteogenesis | Mandibular distraction osteogenesis can be associated with a wide variety of complications. However, all of these complications can be minimized or avoided in most cases with appropriate preoperative planning, meticulous intraoperative technique, and thorough postoperative management. |
| Tahiri et al. 2014 | Systematic review | C | The purpose of the present study was to evaluate the effectiveness of mandibular distraction osteogenesis for the treatment of airway obstruction in pediatric patients (younger than 18 years) with craniofacial defects involving mandibular hypoplasia and its associated complications through a systematic review of the literature. | Inclusion:  Airway obstruction was classified as (1) having an obstructive sleep apnea as proven by polysomnographic studies and/or apnea-hypopnea index, (2) having an adjunctive airway support such as endotracheal or nasopharyngeal/ oropharyngeal airway, or (3) being tracheostomy dependent.  Exclusion:  Cases of simultaneous maxillary and mandibular distraction osteogenesis, midline mandibular distraction osteogenesis, temporomandibular joint ankylosis, alveolar distraction osteogenesis, or orthognathic distraction osteogenesis were excluded. | Included number of patients:  74 articles were included.  711 patients were included that underwent MDO for the treatment of airway obstruction.  The mean age at the time of distraction was 18.1 months (range, 0.1 to 192 months; median, 12 months).  The most frequently cited diagnoses in decreasing order of prevalence were isolated Pierre Robin sequence (52.9 percent), syndromic Pierre Robin sequence (7.0 percent), Treacher Collins syndrome (6.8 percent), Stickler syndrome (3.5 percent), Goldenhar syndrome (3.1 percent), micrognathia (3.1 percent), mandibular hypoplasia (2.5 percent), Nager acrofacial dysostosis (2.5 percent), hemifacial microsomia (2.0 percent), microsomia (1.7 percent), and retrognathia (1.4 percent). Together, these conditions constituted over 85 percent of all cases | Patients in whom external distractors were used also experienced more complications compared with those for whom internal distractors were used (22.1 percent and 8.3 percent complication rates, respectively).  Interestingly, our data suggest that older age at the time of surgery may be associated with an increased complication rate. The mean age of patients who experienced complications was 36.9 months, which is approximately 1.5 years older than the mean age of all patients (18.1 months).  Mandibular distraction osteogenesis is an effective technique for the treatment of upper airway obstruction in the pediatric population, and should be considered in selected patients who have failed conservative airway management efforts before proceeding to tracheostomy. Proper patient selection and workup to rule out associated lower airway anomalies are key to high success rates. |

**Chapter 5.2 – Facial nerve**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| General |  |  |  |  |  |  |
| Luijmes et al. 2017 | Systematic review | A1 | To investigate the effect of a peripheral facial palsy on QoL. | Inclusion:  Literature up to August 2015 was included.  inclusion criteria were either prospective and/or retrospective cohort trials and/or case series measurement of QoL before and after treatment, patients with peripheral facial palsy (irrespective of etiology), and various treatment modalities (medication, physical therapy, botulinum toxin injections, and several types of surgical procedures).  The intervention studied was either medication (antiviral drugs and/or corticosteroids), or botulinum toxin injections, or physical therapy, or surgery. Primary outcome measure was QoL and secondly recovery of facial function.  Exclusion:  None | 12 studies were included.  Of the 12 included studies, nine had a prospective study design,14–22 and three had a retrospective study design.23–25 In total, one study reported the effect of mime therapy (form of physical therapy) on QoL,23 one study reported the effect of corticosteroids,21 two studies reported the effect of treatment with botulinum toxin injections,20,22 and eight studies reported the effect of surgical procedures. | Overall, our findings indicate a significant influence of peripheral facial palsy on QoL, and that after treatment the QoL of patients with a peripheral facial palsy significantly increases. |
| Reddy et al. 2015 | Narrative review | D | Not described | Not described | Not described | The preferred approach requires three stages: (1) cross-facial nerve graft, (2) free tissue transfer, (3) cosmetic balancing procedures. |
| Volk et al. 2010 | Narrative review | D | To develop a standardized approach for diagnosis and treatment of patients asking for facial rehabilitation. | Not described | Not described | Because the first clinical signs of a successful regeneration do not occur before a time of six months and the finial results even needs twelve to 18 months, nerve suture is often combined with static reanimation of the ye closure using a upper lid weight. If the lower lid is suspended due to loss of facial tone, it is recommended to combine upper eye lid surgery with a lower lid plasty |
| Rahman et al. 2007 | Narrative review | D | Not described | Not described | Not described | Tarsorrhaphy is most suited to cases of combined V and VII cranial nerve paresis as corneal sensation may be impaired in such individuals. However, tarsorrhaphy procedures have been criticized for being cosmetically poor and often ineffective. The loss of peripheral vision makes tarsorrhaphy a last resort. |
| Eyelid | | | | | | |
| Baheerathan et al. 2009 | Case-series | C | To describe the experience with 16 consecutive patients who underwent insertion of a predetermined gold weight implant into the upper eyelid to correct lagophthalmos | Inclusion:  patients who had gold weight implantation of the upper eyelid for correction of lagophthalmos  Exclusion:  None | Included number of patients:  16 patients.  The most common cause of facial palsy was radical parotidectomy (69%) followed by one case each of congenital facial palsy, Bell’s palsy, surgery for recurrent choleastotoma, Ramsay Hunt syndrome and neck dissection.  The mean age at operation was 70 years with a range of 42–84 years. There was a striking male predominance with a male to female ratio of 3.2:1. | No relevant conclusions described |
| Hontanilla et al. 2013 | Retrospective study | C | Experience in eye reanimation  with gold weight implants and tendinous suspension during  the last 6 years | Inclusion:  The presence of lagophtalmos, eye dryness, corneal ulcer, epiphora and lower lid ptosis/ectropion was assessed preoperatively.  Exclusion:  None | Included number of patients:  74 patients.  A total of 74 patients underwent 101 procedures, including 58 gold weight implants for the upper lid and 43 tendon slings for the lower lid, with 27 patients having both techniques.  None of the 74 patients had a congenital paralysis. | In conclusion, in light of the results presented in this work, it is fair to say that with static techniques, such as those presented here, the main goals of eye reanimation are addressed and adequately fulfilled. The gold weight implant for lagophtalmos significantly improves eyelid excursion and velocity of blinking without altering the physiological corneal reflex.  Lower eyelid suspension with tendon grafts fully restores lid position correcting ptosis/ ectropion and reversing epiphora in a considerable number of patients. Preoperative assessment of the whole paralysed face, an individualised surgical planning, meticulous surgical technique and a quantitative method of outcomes evaluation are essential to obtain the best possible result |
| Loyo et al. 2015 | Retrospective review | C | We present our experience in the surgical treatment of the periocular complex with patients presenting to the Johns Hopkins Hospital for treatment of paralytic lagophthalmos. | Inclusion:  None  Exclusion:  None | Included number of patients:  101 patients.  mean age was 55 years with range from 15 to 88 years.  The most common causes of facial paralysis were cerebellopontine angle tumors 63/101 (63%) and malignant parotid tumors 27/101 (27%). Table 1 shows all causes. Postoperative radiation was used in 26/101 patients (26%). No congenital origins. | Paralytic lagophthalmos management is not one-size-fits-all. Upper eyelid loading is the mainstay of treatment; however, adjunctive procedures to the lower eyelid and brow are indicated in the majority of patients. |
| Terzis et al. 2010 | Retrospective study | C | To present a retrospective review of the pediatric patients who underwent dynamic procedures aiming at the restoration of the blink reflex performed by the senior author (J.K.T.) as a part of multistage facial reanimation procedures. | Inclusion:  In this study, only the pediatric population is considered.  Inclusion criteria included a complete medical, obstetric, and surgical history; physical, neurologic, and electrophysiologic examination; a detailed examination of the facial musculature; and a follow-up period of 18 months or longer.  Exclusion:  None | Included number of patients:  49 patients.  Group A (n=42) included patients who underwent nerve transfers: cross-facial nerve grafting and subsequent microcoaptations, minihypoglossal nerve transfers, and direct orbicularis oculi neurotization.  Group B (n=14) included patients who underwent eye sphincter substitution techniques: pedicled frontalis, free platysma, mini-temporalis, and a slip of free pectoralis minor transfers.  Seven of the patients included in the groups underwent both nerve and muscle transfer procedures. | Our clinical study offers additional insight into the treatment of young facial paralysis patients by presenting an efficient quantification of blink return after eye reanimation procedures. Treating the still growing patient implies taking well into account future needs and changes in physical and psychological terms. Restoring the neurophysiologic potential of these patients prepares the ground for future adjustments and adaptations and amplifies their contribution in blink restoration. |
| Mouth | | | | | | |
| Chen et al. 2007 | Retrospective study | C | to provide our experience of using surgical resection or botulinum toxin injection for depressor myectomy on the nonparalyzed side as a simple and effective procedure for patients with marginal mandibular nerve paralysis, especially following oromandibular reconstructions or when interventions on the paralyzed side are not feasible. | Inclusion:  The causes of paralysis included the following: congenital causes, such as hemifacial microsomia and Goldenhar syndrome; surgery for oromandibular cancer; surgery for parotid tumors; surgery for intracranial tumors; radiation- related osteonecrosis; and idiopathic facial palsy.  Exclusion:  None | Included number of patients:  76 patients.  25 patients with surgical depressor myectomy.  8 patients with depressor myectomy with subsequent botulinum toxin injection.  43 patients with only botulinum toxin injection in depressor.  There were 28 female patients and 58 male patients in our series. Patient ages ranged from 17 to 68 years, with a mean age of 40.5 years. | Using myectomy for paralysis of the marginal mandibular branch of the facial nerve can be an effective treatment for this significant deformity. Chemical myectomy with botulinum toxin injection is a safe and convenient mode of treatment; however, the disadvantage is that it needs repeated injections and costs more.  Surgical myectomy may still result in recurrence in 24 percent of patients, which necessitates further treatment with botulinum toxin injections. |
| Lindsay et al. 2011 | Retrospective chart review | C | to retrospectively review our outcomes after treatment of the asymmetric lower lip, and to propose a progressive, stepwise algorithm for the management of lower lip asymmetry in facial paralysis. | Inclusion:  Retrospective chart review was performed on all patients treated in a multidisciplinary facial nerve center with lower lip asymmetry over an eighteen month period. | Included number of patients:  58 patients.  57 patients had botulinum toxin injections.  4 patients had anterior belly of the digastric transfer.  3 patients had a depressor labii inferioris resection.  The average patient age was 48 years (range, 14–84 years; SD, 14). The average follow-up period was 18.3 months (range, 10–30; SD, 5.9). | No relevant conclusions described |
| Dynamic reanimation | | | | | | |
| Barr et al. 2011 | Review | C | We review the surgical procedures that have been used to treat pediatric facial nerve paralysis and provide therapeutic facial reanimation. | Inclusion:  None  Exclusion:  None | No relevant conclusions described | No relevant conclusions described |
| Roy et al. 2019 | Retrospective review | C | To investigate surgical outcomes of the procedure in terms of complications, secondary revisions, and smile excursion gains | Inclusion:  children with Möbius syndrome who had undergone facial animation surgery with a free segmental gracilis muscle transfer and microneurovascular repair between January 1, 1985, and August 31, 2014.  Exclusion:  Patients who had undergone cross-facial nerve grafting without gracilis muscle transplantation were excluded. | Included number of patients:  A total of 107 patients undergoing 197 reconstructive procedures were included.  The motor nerve branch to the masseter was used in 174 cases of microneurovascular repair, and the hypoglossal nerve was used in four cases.  The study population included pediatric patients with Möbius and Möbius-like syndrome who had undergone facial animation surgery with a free gracilis muscle flap. | Smile animations used free microneurovascular gracilis transfers because of the muscle’s reliable pedicle and minimal associated donor-site morbidity and had low complication (12 percent) and secondary revision rates (3 percent). Smile excursion improved significantly perioperatively for the 37 patients (35 percent of our cohort) with available photographic records.  Midfacial animation procedures in Möbius syndrome pediatric patients using the gracilis muscle led to few early postoperative complications, and provided good smile excursion outcomes and symmetry. The low revision rate must be interpreted with caution considering the geographic distribution of patients treated and subsequent variable follow-up. |
| Banks et al. 2019 | Case-series | C | We describe our early experience in 59 cases using five-to-seven nerve transfer in an attempt to report function and patient-reported outcomes, and to begin to define potential parameters predictive of outcome. | Inclusion:  Criteria used to determine candidacy for nerve transfer included patients with flaccid facial paralysis for less than 4 years, and patients with poor smile excursion following facial nerve insult and recovery into a synkinetic, hypertonic phase with less than 3 mm of oral commissure excursion. All adults with flaccid facial paralysis underwent five-to-seven nerve transfer after denervation of 30 months or less.  Exclusion:  No congenital facial paralysis included | Included number of patients: 60 patients had trigeminal-to-facial nerve branch transfers,  55 patients had masseteric-to-facial nerve transfers,  5 patients had deep temporal-to-facial nerve transfer ("We used the deep temporal donor nerve instead of the masseteric nerve in patients in whom we were concerned about the potential for reinnervation and thus wanted to preserve the masseteric as an option for gracilis if the five-to-seven nerve transfer were to fail.") | Five-to-seven nerve transfer is a viable option in facial reanimation. Our early experience indicates that shorter denervation times and preoperative flaccidity, rather than hypertonicity, are favorable predictors of outcome. The best results were achieved in cases of normal facial function with oncologically indicated facial nerve sacrifice for parotid malignancy, where cable grafting of native facial nerve either is not indicated based on positive margins, or is performed in addition to five-to-seven nerve transfer.  In our series, five-to-seven nerve transfer results are unreliable in postparalysis facial palsy to supercharge existing zygomaticus function. |
| Bianchi et al. 2014 | Case-series | C | The purpose of this paper was to review the indications for the use of the masseteric nerve in techniques for facial animation taking account of the patient’s features, the type of palsy, and the available sources of innervation. | Inclusion:  Patients who had facial animation procedures using the masseteric nerve between 1 January 2003 and 1 January 2013 were evaluated retrospectively.  Exclusion:  None | Included number of patients: 60 patients.  There were 23 male and 37 female patients, mean age 28 (range 6–73) years.  Thirteen patients had recent (less than 18 months’ onset) unilateral facial palsies, 21 had established or congenital unilateral palsies, and the remaining 26 had established or congenital bilateral palsies. | No relevant conclusions described |
| Birgfeld CB et al. 2012 | Narrative review | D | Not described | Not described | Not described | When the physician identifies facial nerve palsy, she must first determine whether the patient can protect and lubricate his cornea. If not, eye drops, lubricant, or a surgical procedure such as a tarsorrhaphy or goldweight with eyelid tendon sling should be considered. |
| Bos et al. 2016 | Systematic review | C | To compare the outcomes of reconstructive surgery for long-standing facial paralysis by gracilis free flap transfer versus lengthening temporalis myoplasty | Inclusion:  Outcomes: Efficacy outcomes were analyzed by assessing mouth symmetry both at rest and upon smiling, as well as the quality and the spontaneanity of the smile.  Randomized controlled trials (RCTs), controlled clinical trials (CCTs), and case series with a sample size > 5 were sought.  Exclusion:  None | 16 articles were included, all retrospective case series | Patients operated on by lengthening temporalis myoplasty reach a lesser extent of smiling in most studies, except those from Labb e himself, with controversial evidence of spontaneity. Thus, there is no real evidence to suggest that LTM might be a better option than gracilis free muscle transfer. |
| Chuang et al. 2018 | Retrospective cohort study | C | The purpose of this study was to comparatively evaluate cross-facial-nerve-graft-, spinal acessory nerve- and masseter nerve-gracilis for facial reanimation, their advantages and disadvantages, from our series. | Inclusion:  All patients treated between 1986 and 2015  Exclusion:  None | Included number of patients:  362 patients,  272 patients with cross-facial nerve graft. 56 patients with a spnal accessory nerve. 22 patients with masseter nerve | The CFNG-FFMT procedure remains our first choice for unilateral facial paralysis reconstruction, especially for children and women patients. However, the effectiveness of using XI-FFMT, a 1-stage procedure, is proven a good alternative. There remain some specific indication for V3-FFMT, such as bilateral facial palsy, failed primary CFNG- or XI-FFMT cases, older patients (>70 years old) and malignant tumor resection patients, but it is generally our third choice. |
| Gousheh et al. 2011 | Retrospective study | C | Evaluated independently the recovery of both truly spontaneous  smile and facial muscle movement. | Inclusion:  None  Exclusion:  None | Included number of patients:  655 patients.  505 two-stage gracilis, one rectus abdominis, and 14 single-stage latissimus dorsi microneurovascular muscle transfers, in addition to 28 cross-facial facial nerve neurotization procedures.  All patients had unilateral facial paralysis.  The cause of facial palsy was developmental in 350 (53.4 percent); tumor resection surgery (iatrogenic) in 131 (20.0 percent); trauma in 109 (16.6 percent), including 25 (3.8 percent) war injuries; and Bell palsy in 65 patients (9.9 percent). | Temporalis muscle transposition and lengthening myoplasty are acceptable options for patients who are not good candidates for neurotization by the facial nerve.  For the restoration of both truly spontaneous smile and facial muscle movement, free microneurovascular muscle transfer neurotized by the contralateral healthy facial nerve has become the authors’ first-choice surgical technique.  For the restoration of both truly spontaneous smile and facial muscle movement, free muscle transfer neurotized by the contralateral healthy facial nerve has become our first-choice surgical technique. Based on the results of this retrospective study, temporalis muscle transfer and lengthening myoplasty are acceptable options for patients who are not appropriate candidates for neurotization by the contralateral healthy facial nerve. |
| Harrison et al. 2012 | Retrospective study | C | To describe the experience with 637 cases over a 35-year period | Inclusion:  None  Exclusion:  Patients whithout independent long-term evaluation | Included number of patients:  561 patients.  The pectoralis minor muscle was used in the majority of cases (528). Alternatively the latissimus dorsi (28 cases) or the gracilis (3 cases) or EDB (2 cases) were used in a standard two-stage approach.  The sural nerve is used for gross-facial nerve graft. | Facial reanimation with functional muscle transfers is a complex procedure and provides a significant improvement for the patient to display humour and emotion. |
| Hontanilla et al. 2018 | Retrospective cohort study | C | The purpose of the present study was to compare commissural displacement, contraction velocity, satisfaction, and spontaneity after reanimation of the incomplete facial paralysis using cross-face nerve grafting or masseteric-to-facial transposition. | Inclusion:  patients with incomplete unilateral facial paralysis.  For qualitative evaluation, patients were assessed in our clinic 1 year after the operation  Exclusion:  None | Included number of patients:  28 patients.  All with incomplete unilateral facial paralysis.  10 patients with cross-face nerve grafting.  18 patients with masseteric nerve transfer. | Reanimation of incomplete facial paralysis can be satisfactorily achieved with both cross-face nerve grafting and direct masseteric-to-facial nerve transposition.  However, with the masseteric nerve, better symmetry, a higher degree of recovery, and an increased level of satisfaction are achieved in a one-stage operation.  Furthermore, both nerve sources are able to restore spontaneity in more than 50 percent of the patient’s daily life, with no significant differences between them. |
| Panossian et al. 2016 | Case-series | C | We describe our experience using the lengthening temporalis myoplasty in a largely pediatric population | Inclusion:  None  Exclusion:  None | Included number of patients:  14 patients.  Four patients underwent single-stage bilateral reconstruction, and 10 underwent unilateral procedures. | Lengthening temporalis myoplasty is a safe alternative to free tissue transfer for dynamic smile reconstruction in children with facial paralysis. Limited donor-site morbidity, shorter operative times, and shorter hospital stays are some benefits over free flap options. However, revisions are required frequently secondary to tendon avulsions and adhesions. |
| Terzis et al. 2008 | Retrospective study | C | The purpose of this article is to present the nerves that have been used at our center to function as possible motor donor for dynamic facial reanimation. | Inclusion:  None  Exclusion:  None | No relevant patients described | No relevant conclusions described |
| Terzis et al. 2009 - children | Case-series | C | To evaluate the fate of freemuscle transfer over long follow-up periods in pediatric patients. | Inclusion:  Children with follow-up of 5 years or longer who received a free-muscle transfer for smile restoration.  To better analyze the effect of time, patients were classified into groups based on the length of follow-up: group A, 5 to 6 years; group B, 7 to 10 years; group C, 11 to 15 years; and group D, more than 15 years.  Exclusion:  None | Included number of patients:  32 patients.  Two Mobius patients had bilateral muscle transfers; thus, the number of muscle grafts totaled 34.  Children’s ages on first consultation ranged from 2 to 15 years (mean SD, 7.17 3.91 years) and included 21 girls and 11 boys.  Twenty-one patients presented with developmental paralysis and 11 cases presented with acquired palsies. | These clinical data support the use of free-muscle transfer for smile restoration in children. The transplanted muscle appears to grow harmoniously with the craniofacial skeleton, and muscle function and aesthetic outcomes improved over time. |
| Terzis et al. 2009 - adults | Case-series | C | The purpose of this study was to evaluate the long-term outcomes of this technique in adult patients. | Inclusion:  Inclusion criteria demanded a rigorous follow-up of 5 years or longer.  Exclusion:  None | Included number of patients:  24 patients.  All of the interventions were undertaken by the senior author (J.K.T.), using the same technique of cross-facial nerve grafting and free-muscle transfer described previously. | Cross-facial nerve grafting/free-muscle transfer is an effective technique for restoring a coordinated functional and symmetric smile. A progressive functional recovery over time was demonstrated, with no reduction or weakening of muscle function. |
| MacQuillan et al. 2010 | Cross-sectional study (with controls) | C | To examine the incidence of anterior belly of digastric muscle agenesis in patients with hemifacial microsomia | Inclusion:  All consenting patients presenting to the ear reconstruction clinic at our unit with congenital microtia were included in the study.  Exclusion:  None | Included number of patients: All consenting patients presenting to the ear reconstruction clinic at our unit with congenital microtia were included in the study.  Age range, 5 years to 53 years; 14 female patients and 31 male patients; five cases bilateral involvement. Sixteen unaffected individuals were also imaged | The incidence of anterior belly of the digastric muscle agenesis in patients with hemifacial microsomia is high. Before any attempt to undertake lower lip reanimation using this muscle, the floor of the mouth should be imaged to check for its presence. |

**Chapter 5.3 – Soft tissue**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Denadai et al. 2017 | Prospective cohort study | C | The purposes of this study were to assess fat graft retention in patients with craniofacial contour deformities and to identify independent predictors of 12-month fat graft retention. | Inclusion:  None  Exclusion:  None | Not described | No relevant conclusion described |
| Birgfield & Heike et al. 2012 | Review | C | Not described | Not described | Not described | Soft tissue augmentation with dermal fat grafts is another, well proven technique. Dermal fat grafts can provide adequate bulk in moderate and mild deformities, but are prone to some degree of resorption and patients may require additional augmentations.102 Donor site morbidity and scarring are also risks, and the selected donor site should not be constrained by vascular anatomy or angiosomes to make it easier to conceal scars. |
| Sinclair et al. 2019 | Systematic review | C | The aim of the present systematic review was to assess the surgical techniques used to address the soft tissue deformity seen in hemifacial microsomia | Inclusion:  Case reports, case–control studies, retrospective cohort studies, and non-randomized prospective studies were included.  Only data regarding patients with hemifacial microsomia was collected.  Exclusion:  None | Not described | No relevant conclusion described |
| Tanna et al. 2011 | Retrospective cohort study | C | Instead of undertaking soft-tissue reconstruction after skeletal correction, small gains in improving facial contour can be made earlier. To study this alternative soft-tissue treatment strategy, we performed volumetric outcome comparison of patients who underwent serial autologous fat grafting and/or microvascular free flap surgery. | Inclusion:  Patients with craniofacial microsomia who underwent soft-tissue reconstruction with serial autologous fat grafting or free flap reconstruction with an inframammary extended circumflex scapular flap.  All patients had at least 1-year follow-up.  Exclusion:  Excluded from the study were patients with incomplete records (examinations, photographs, or documentation) and inadequate follow-up. | Not described | No relevant conclusion described |

**Chapter 5.4 – Microtia**

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| Study reference | Type of study | Evidence | Aim of the study | Inclusion/exclusion criteria | Patient population | Conclusion |
| Mandelbaum et al. 2017 | Retrospective study | C | In this study, we review characteristics and variables in patients with craniofacial microsomia affecting the external ear and hearing apparatus that affect 3 long-term outcomes measures: wound complications complications, total number of surgeries, and psychosocial development. | Inclusion:  Patients over 13 years of age with craniofacial microsomia treated between 2008 and 2014 at the University of California Los Angeles (UCLA) Craniofacial Clinic were included.  Exclusion:  Patients were excluded if unidentified operative interventions before entry into the craniofacial clinic were performed, other craniofacial syndromes were diagnosed, and if the patients were lost to follow-up before completion of surgical plan. | Included number of patients:  68 patients,  62 patients with auricular abnormalities (91.2%).  All patients started ear reconstruction between ages 5 and 18 years. First-stage ear reconstructions were performed using a modified Nagata/Firmin technique as described previously.3,4,6,17 Six months or more after first-stage reconstruction, the cartilage construct was elevated using banked costal cartilage.  67.7% of patients with microtia were male, and 63.8% occurred on the right side in unilateral cases; 24.2% of patients had bilateral microtia, usually of varying severity  75.3% of external ear abnormalities were categorized as grade III microtia. | Although one may expect that severity of the ear deformity, bilaterality, deformities of other associated structures, total complications, total number of surgeries, or aesthetic ratings may affect psychosocial outcomes, we found that none of these variables predicted psychosocial outcomes in a statistically significant manner. In fact, treatment of hearing impairment, regardless of the unilaterality or bilaterality, was the only factor that had any bearing on psychosocial outcomes. |
| Park et al. 2018 | Retrospective study | C | To provide further information for coverage techniques in microtia reconstruction, the authors have reviewed and analyzed patients who underwent surgery at their center.  In microtia reconstructions of hemifacial microsomia patients, the skeletal deformity affects the location and size of the reconstructed ear, but not the coverage techniques. In this article, we assessed postoperative outcomes of patients who underwent reconstruction with three coverage techniques by considering the severity of five deformed external features of hemifacial microsomia: mastoid atrophy, low hairline, size, and location of the ear vestige. | Inclusion:  Hemifacial microsomia patients who underwent microtia reconstruction between 2006 and 2016 were involved in the study.  Exclusion:  Patients showing minimal asymmetric faces that fell in the normal range were excluded from our study. | Included number of patients:  52 patients.  Follow-up: between 6 months and 10 years (average, 40.3 months; median, 33 months) | When the patient has a mild (no hair) to moderate degree of low hairline and usable remnant vestiges, and enough mastoid skin volume is available, the embedding technique should be used with the addition of laser hair removal.  In cases with severe degrees of hemifacial microsomia, mastoid depression, low hairline, small ear vestiges (anotia or small lobule type), and/or remarkably low-set ear vestiges, the fascia flap technique should be used.  The expansion technique, which is slow and cumbersome, yielded the poorest results and in most patients should be avoided. |
| Qian et al. 2017 | Retrospective study | C | The aim of this study was to investigate the clinical application of an expanded two-flap method for auricular reconstruction in hemifacial microsomia. | Inclusion:  Hemifacial microsomia patients with microtia who underwent auricular reconstruction with expanded retroauricular mastoid skin and autogenous costal cartilage.  Exclusion:  Patients with Treacher-Collins syndrome and Goldenhar syndrome were excluded. | Included number of patients:  111 patients.  The mean age of patients was 9.2 years (range, 5 to 27 years). All patients were unilateral, including 53 left-side (47.7 percent) and 58 right-side (52.3 percent). | In both the Nagata method and the expanded two-flap method a shrinking phenomenon was observed, especially in Pruzansky-Kaban-Mulliken26,27 type 3 hemifacial microsomia.25 In our early experience, several cases of the shrinking phenomenon and framework deformation were encountered after ear reconstruction with the Nagata technique. Similar to other authors, we believe that the reason could be a poor vascular supply and deficient skeletal support in severe hemifacial microsomia. Thus, in patients ith severe hemifacial microsomia, especially in those with taut retroauricular skin, a low hairline, and depressed temporal bone, we selected the expanded two-flap method. |
| Long 2013 | Systematic review | C | In this systemic review, we aim to (1) calculate the kinds and overall rate of complications in autologous ear reconstruction with costal cartilage and (2) identify the complication rate related with certain surgical methods, including fascia type, with/without preexpansion, and surgical stages. | Inclusion:  Inclusion criteria were English-language publication, human subjects, ear reconstruction, extractable outcomes on complications, and full-tekst availability.  Exclusion:  Exclusion criteria were systematic reviews and meta-analyses, case reports and case series with fewer than 15 patients, and nonrelated with surgery | Included number of patients:  60 articles were included,  A total of 9415 patients.  1525 patients had complications (mean overall complication incidence of 16.2%, range 0-72.9%) | There is significant variability in the literature regarding complication rates in autologous cartilage ear reconstruction of patients with microtia. By providing a comprehensive review of different complications with different surgical techniques, this study could help plastic surgeons adequately take measures to minimize the complication rates in their future operations. |
| Younis 2010 | cross-sectional study | C | This study examines different aspects of patient satisfaction using an eighteen-point postal questionnaire to measure patient outcomes against a Likert rating scale. | Inclusion:  The questionnaire (self-developed) was sent to 33 patients who completed prosthetic ear reconstruction over a 16 year period at a specialist plastic surgery unit in the United Kingdom.  Inclusion criteria; age 16 years at the time of surgery, completion of the ear reconstruction procedure and at least six months lived post surgery.  Exclusion:  None | Included number of patients:  20 patients (response rate 61%).  average age of 37 years (range 17-56 years).  All respondents underwent a unilateral reconstruction.  In ten patients, surgery was performed for a congenital deformity. Nine had surgery after traumatic loss and one after malignancy. In 14 cases, implant surgery was performed after a failure of at least one attempt at autologous reconstruction.  The mean follow up time was 31 months (range 7-108 months).  The case note review found that 20 of the sample of 33 patients had undergone previous attempts at auricular reconstruction although none had received radiotherapy. | Our survey suggests that the patients in our sample were dissatisfied with or at best ambivalent towards prosthetic reconstruction of their ear using a Branemark-type retention device. This contrasts with the findings of a larger satisfaction survey conducted in Sweden, which showed much higher patient satisfaction rates.8 The most obvious reason for the poor satisfaction rates obtained in our study were the high rates of past and current skin complications experienced by our sample. The majority of respondents (15 out of 20) had experienced skin problems in the past and half of the sample (10 out of 20) continued to have problems with the skin. |
| Braun et al. 2010 | Cross-sectional study | C | We initiated the present study to analyze not only the outcome but also the subjective patient benefit in our own patient population (Figs. 1 through 4) using questionnaires well validated for measuring the effect of otorhinolaryngologic interventions, including plastic surgery, on health-related quality of life. | Inclusion:  Patients who had received a plastic auricular reconstruction with porous polyethylene (Medpor; Porex Surgical, Newnan, Ga.) in our department between July of 2003 and January of 2009 were included in the study.  All patienst received a questionnaire  Exclusion:  None | Included number of patients:  65 patients who had received a plastic auricular reconstruction with porous polyehtylene (Medpore).  The mean follow-up time was 2.9 years (median, 2.4 years; range, 0.5 to 6.0 years).  The median of the patients’ age at the time of the operation was 18 years; the youngest patient was aged 4 years and the oldest was aged 68 years.  Fifty-five patients (84.6 percent) suffered from congenital microtia. Forty-four patients had an auricular dysplasia Weerda grade III, and 11 patients had an auricular dysplasia Weerda grade II.7 | This study’s conclusion that auricular reconstruction with porous polyethylene can significantly increase the patient’s health-related quality of life and lead to a high rate of patient satisfaction holds true considering both patient collectives. It must be noted that 75.6 percent of the adults and 100 percent of the children took benefit from the intervention (Tables 1 and 5 and Figs. 5 and 9), but a few (adult) patients also yielded negative total Glasgow Benefit Inventory scores (17.8 percent), indicating an adverse effect. |
| Constantine 2014 | Retrospective record study | C | To evaluate and compare the outcomes of reconstruction of microtia using porous polyethylene implants and rib cartilage grafts. | Inclusion:  Patients who underwent microtia repairbya single surgeon(J.L.) fromJanuary1, 2001, through December 31, 2011.  Grading of the preoperative and postoperative photographs by the 2 blinded observers was analyzed with a Wilcoxon signed rank test for protrusion, ear definition, shape, size, location, and colormatch.  Exclusion:  None | Included number of patients:  35 patients (36 ears),  polyethylene implants (17 ears), rib cartilage grafts (17 ears), and bothmaterials (2 ears).  We included only those patients who underwent complete microtia repair.  Age: Porous polyethylene implant mean age 6.9 (SD 3.0); Rib cartilage graft mean age 8.0 (SD 3.8).  Porous polyethylene implant mean total procedures: 3.35 (SD 1.27).  Rib cartilage graft mean total procedures 4.88 (SD 1.54).  Follow-up in the cartilage group ranged from2 to 11 years, whereas follow-up in the polyethylene group ranged from 2 to 6 years. | Although complicationswith either technique are uncommon, infection and extrusion only occurred with polyethylene implants. This risk should be weighed carefully with the possible benefit of a better cosmetic result should the surgeon and family of the patient decide to proceedwith the polyethylene implant technique.  The decision regarding which technique to pursue is a personal one for the patient and the surgeon performing the procedure. |
| Fu et al 2019 | Retrospective study | C | To provide comprehensive knowledge regarding the occurrence, development, prognosis, risk factors, and treatment of complications. | Inclusion:  Patients who underwent autologous cartilage microtia reconstruction at a single auricular plastic and reconstructive center between March 2005 and June 2016.  The inclusion criterion was patients with microtia who underwent autologous cartilage microtia reconstruction (at least stage I) using the Brent or Nagata technique.  Exclusion:  None | Included number of patients:  470 procedures (stage I) were performed on 429 patients.  The mean (±SD) age at surgery was 12.27 ± 5.01 years (range, 6–32 years).  The mean time to follow-up was 3.67 ± 2.45 years (range, 1–11 years). | The framework of the Nagata technique is more complicated and stereoscopic, and the earlobe translocation was completed in the first stage of the Nagata―but not the Brent―technique. The Brent technique minimizes the risk for vascular compromise of the skin flap. Although the Nagata technique results in more complications, the Brent technique requires three or four stages, while the Nagata technique requires only two. Therefore, despite the higher risk for complications, it is advisable to use the Nagata technique. |
| Roos 2015 | Retrospective study | C | Our objective was to determine if the reconstructed ear grows and to compare the growth with the normal ear. | Inclusion :  To evaluate the growth of the reconstructed ear, the inclusion criteria were as follows: (1) unilateral microtia, (2) completed reconstruction with postoperative photographic documentation before the age of 12.5 years and (3) a final photograph after the age of 14.5 years  Exclusion:  None | Included number of patients:  22 patients  An initial photograph had been taken after the reconstruction at a median of 11.2 years (range 8.0–12.5 years) of age and a second photograph at a median of 16.3 years (range 14.5–21.6 years).  The median follow-up time was 5.6 years (range 2.1–10.6 years).  In the validation series, the random error of the length measurements was 0.63 mm for the reconstructed ear and 0.79 mm for the normal ear. The systematic error for this method was negligible. | We found that the reconstructed ears grew as much as the normal ears, and hence it is reasonable to use the normal ear as a template at the time of the first reconstructive stage. Our results also support commencing the reconstructive series as early as at the age of 7 years. |
| Kadah et al. 2018 | Retrospective study | C | The aim of this study was to depict a single-institution experience with patients who underwent auricle reconstruction with porous polyethylene or silicone prostheses with a long-term followup of at least 24 months. | Inclusion:  Patients who underwent auricular reconstruction by means of porous polyethylene or silicone rubber prosthesis in the Department of Otolaryngology, Head and Neck Surgery, University Clinic of Homburg/Saar, Germany between 2002 and 2013 were retrospectively analyzed.  Only patients with a minimum follow-up of 2 years were enrolled in our study.  Endpoints included the etiology leading to a necessity of reconstruction, the type of prosthesis, the rate of postoperative complications and the necessity of revision.  Exclusion:  No patient who has previously been treated by means of porous polyethylene implant or silicone prosthesis was included in this study. | Included number of patients:  39 patients, 43 implants,  Porous polyetylene group (medpore): 18 paients (mean age 19 (range 8-56),  Silicon prosthesis group (external): 21 patients, mean age 41.3 years (range 6-84) | Porous polyethylene and silicone prostheses are valuable tools for the auricular reconstruction of patients with auricular deformities. Our study shows that porous polyethylene prostheses rarely demonstrate complications in terms of skin reactions, while silicone prostheses present acceptable complication rates, so that both techniques constitute interesting alternatives to the traditional but complicated ear reconstruction by rib cartilage. |
| Si et al 2012 | Retrospective study | C | To evaluate the complication rate and patient satisfaction of reconstruction of acquired auricular deformities and failed previous reconstruction by the osseointegration technique. | Inclusion:  Patients who had auricular defects diagnosed at Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, were selected based on the following criteria: they had a whole auricular defect caused by trauma, burn or failed reconstruction; they were able to attend a regular follow-up; informed consent was obtained before treatment was started.  Exclusion:  None | Included number of patients:  Twenty-five ears (24 patients) were implanted.  Age at implant placement ≤16 years: 10; >16 years: 14.  The median patient age was 28 years (range, 9–46 years).  The first follow-up visit was 1 week after prosthesis delivery. Subsequent follow-up visits were scheduled every 2 months for 6 months, every 3 months in the following 6 months, and once every year afterward. | No relevant conclusions described |
| Wright 2008 | Case-series | C | The objective of this study was to report on the survival rate of 16 patients treated with extraoral implants in the auricular region, analyze treatment outcomes, and discuss important clinical variables encountered during treatment. | Inclusion:  All patients treated for auricular defects with implant-retained auricular prostheses at Columbia’s Maxillofacial Center were included in the report.  Exclusion:  None | Included number of patients:  A total of 39 implants were placed in sixteen patients between 1987 and 2003.  Ten of these defects were diagnosed as congenital anomalies, two were related to trauma, and four were secondary to tumor resection.  Age distribution was as follows: 12.5% (2/16) younger than 18 years; 50% (8/16) between the ages of 19 and 40 years; 12.5% (2/16) between the ages of 41 and 69 years; and 25% (4/16) 70 years or older. The average age of the 16 patients at the time of stage I surgery as 40.6 years (range: 6 to 76 years). | This retrospective clinical study revealed 100% cumulative implant (n = 39) and prosthesis (n = 16) survival rate in 16 patients. The efficacy of skin-penetrating osseointegrated implants used to restore the auricular defects in this study was excellent. Complications were seen where the surrounding soft tissues were not thin and exhibited mobility or when hygiene compliance was inconsistent. Generally, hygiene compliance required constant monitoring to maintain soft tissue health at the implant sites. Tissue complications were resolved when hygiene compliance was improved. |
| Vijverberg et al 2019 | Case-series | C | The aim of this study is to evaluate the surgical procedure, clinical outcome, and satisfaction of the patient of osseointegration-retained auricular prosthesis using VXI implants (Vistafix ® system) | Inclusion:  All patients who received an auricular prosthesis with Cochlear Vistafix VXI300 implants (Cochlear Bone Anchored Solutions AB, Mölnlycke, Sweden) at our clinic between December 2012 and November 2017 were identified.  Exclusion:  None | Included number of patients:  31 implants were placed in 11 patients.  Minimal follow-up time was 7 months and the average follow-up time was 2 years and 7 months.  The average age of the patients at implantation is 44 years and 6 months. The youngest patient was 13 years and 4 months old and the oldest patient was 85 years old at implantation.  Three of the patients who had their auricle amputated due to a malignancy had received radiotherapy treatment prior to the implantation of the VXI implants. One of these three patients received additional radiotherapy treatment post implantation. | This study describes the work-up of patients with a missing auricle opting for implant-retained prostheses. No implants were lost in our total cohort of patients with an absent auricle due to microtia, trauma or cancer of the auricle and/or external auditory meatus. No revision surgery was needed in an average follow-up period of more than 2.5 years. The VXI implants used are a safe and reliable treatment option for retaining auricular prostheses in patients with an absent auricle.  Adverse skin reactions appeared in 32.2% of the implants and in 27.2% of the patients, resolving after treatment with an antibiotic ointment. |