

## Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

Joanna Paola Morales Gloria<sup>1</sup>, Laura Leticia Torres Martínez<sup>2</sup>, Omar Alejandro Leal Avalos<sup>3</sup>, Gabriela Rojas Cruz<sup>4</sup>, Ricardo Daniel Flores Altamirano<sup>5</sup>

<sup>1,2,3,4,5</sup> Universidad Nacional Autónoma de México (UNAM). Hospital General Xoco. Ciudad de México, México

### ABSTRACT

Treacher Collins syndrome (TCS) is a rare genetic disorder characterized by craniofacial deformities, resulting from mutations in the TCOF1, POLR1C, or POLR1D genes. These deformities often involve the zygomatic complex, mandible, palate, and external ears, significantly impacting aesthetics and function. This review elucidates the complex pathophysiology, clinical manifestations, and comprehensive surgical management of TCS within the realm of plastic surgery. We emphasize the importance of a multidisciplinary approach, involving otolaryngologists, maxillofacial surgeons, and speech therapists, to optimize functional and cosmetic outcomes. Through detailed analysis of current surgical techniques, including distraction osteogenesis, orthognathic surgery, and ear reconstruction, this article aims to provide a framework for individualized patient care, focusing on improving quality of life and psychosocial integration for patients with Treacher Collins syndrome.

**KEYWORDS:** Treacher Collins Syndrome, Mandibulofacial Dysostosis, Craniofacial Deformities, Plastic Surgery

### ARTICLE DETAILS

**Published On:**  
**30 July 2024**

**Available on:**  
<https://ijmscr.org/>

### INTRODUCTION

Treacher Collins syndrome (TCS), also known as mandibulofacial dysostosis, is a congenital disorder primarily affecting the development of the craniofacial structures. First described by Edward Treacher Collins in 1900, this syndrome presents with a spectrum of anomalies ranging from mild to severe facial deformities. TCS is inherited in an autosomal dominant pattern, with variable expressivity and penetrance. The hallmark features include hypoplasia of the zygomatic arches, micrognathia, malformations of the external ear, colobomas of the lower eyelids, and conductive hearing loss due to ossicular chain abnormalities.<sup>1,2</sup>

The pathogenesis of TCS involves disrupted neural crest cell migration and proliferation during craniofacial development. Mutations in TCOF1, POLR1C, or POLR1D genes lead to reduced ribosomal biogenesis and increased apoptosis of neural crest cells, resulting in the characteristic craniofacial anomalies. The clinical presentation can significantly affect breathing, hearing, speech, and overall aesthetics, necessitating a tailored and often staged surgical intervention plan.<sup>1,2</sup>

Plastic surgery plays a pivotal role in the management of TCS, aiming to correct structural deformities, improve functional outcomes, and enhance the patient's quality of life. A multidisciplinary team approach is essential for addressing the complex needs of TCS patients, involving various specialists to provide comprehensive care. This article reviews the current surgical strategies employed in the treatment of TCS, discusses the timing and sequencing of interventions, and highlights the importance of individualized patient care plans.<sup>1,2</sup>

### Surgical Indications for Treacher Collins Syndrome Craniofacial Deformities and Functional Impairments

Treacher Collins syndrome (TCS) presents with a wide range of craniofacial deformities that often require surgical intervention to improve both aesthetic appearance and functional outcomes. The primary surgical indications include severe hypoplasia of the zygomatic arches and mandible, colobomas of the lower eyelids, and malformations of the external ear structures. Additionally, functional impairments such as airway obstruction, feeding difficulties,

## Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

speech problems, and conductive hearing loss necessitate a comprehensive and staged surgical approach.<sup>1,2</sup>

### 1. Severe Zygomatic and Mandibular Hypoplasia

#### ○ Indications:

■ Patients presenting with significant underdevelopment of the zygomatic arches and mandible, resulting in midface retrusion and compromised facial aesthetics.<sup>3,4</sup>

■ Severe micrognathia causing obstructive sleep apnea or difficulty with feeding.<sup>3,4</sup>

#### ○ Surgical Approaches:

■ **Distraction Osteogenesis:** Gradual lengthening of the mandible and/or zygomatic bones to improve facial symmetry and function.

■ **Orthognathic Surgery:** Corrective jaw surgery to reposition the maxilla and mandible, improving occlusion and aesthetic contour.<sup>3,4</sup>

### 2. Colobomas of the Lower Eyelids

#### ○ Indications:

■ Presence of eyelid colobomas leading to exposure keratopathy, dry eyes, or recurrent infections.<sup>3,4</sup>

■ Significant aesthetic concerns due to visible deformities.

#### ○ Surgical Approaches:

■ **Eyelid Reconstruction:** Techniques such as Z-plasty or skin grafting to reconstruct the lower eyelids, protecting the cornea and improving appearance.<sup>3,4</sup>

■ **Canthoplasty:** Procedures to stabilize and reshape the eyelids, ensuring proper closure and function.<sup>3,4</sup>

### 3. External Ear Malformations

#### ○ Indications:

■ Microtia or anotia significantly affecting facial symmetry and causing psychological distress.<sup>3,4</sup>

■ Functional impairment related to conductive hearing loss due to malformed or absent ear structures.<sup>3,4</sup>

#### ○ Surgical Approaches:

■ **Auricular Reconstruction:** Multi-staged procedures utilizing autologous rib cartilage grafts or synthetic implants to construct a natural-looking ear.<sup>3,4</sup>

■ **Osseointegrated Hearing Aids:** Surgical placement of bone-anchored hearing devices to improve auditory function in patients with conductive hearing loss.<sup>3,4</sup>

### Airway and Respiratory Considerations

Airway obstruction is a common and critical concern in patients with TCS due to mandibular hypoplasia and resultant glossoptosis. Surgical interventions are often required to ensure a patent airway and prevent life-threatening respiratory complications.<sup>3,4</sup>

### 1. Mandibular Distraction Osteogenesis

#### ○ Indications:

■ Neonates and infants with severe micrognathia causing upper airway obstruction and respiratory distress.<sup>5,6</sup>

■ Persistent obstructive sleep apnea unresponsive to conservative measures.

#### ○ Surgical Approaches:

■ **Mandibular Distraction Osteogenesis:** Gradual lengthening of the mandible to advance the tongue base

and alleviate airway obstruction, performed using external or internal distractors.<sup>5,6</sup>

### 2. Tracheostomy

#### ○ Indications:

■ Acute airway obstruction that poses an immediate risk to the patient's life.<sup>5,6</sup>

■ Chronic and severe obstructive sleep apnea unmanageable with less invasive interventions.<sup>5,6</sup>

#### ○ Surgical Approaches:

■ **Tracheostomy:** Creation of a direct airway through an opening in the trachea to bypass upper airway obstructions, providing a secure and reliable airway.<sup>5,6</sup>

### Comprehensive Approach to Functional Rehabilitation

Beyond addressing structural deformities, functional rehabilitation is a key component of surgical management in TCS. Speech, feeding, and hearing functions must be restored to enhance the overall quality of life for affected individuals.<sup>5,6</sup>

### 1. Speech and Feeding Interventions

#### ○ Indications:

■ Speech impairment due to velopharyngeal insufficiency or structural anomalies of the oral cavity.<sup>5,6</sup>

■ Feeding difficulties stemming from micrognathia, cleft palate, or other oral deformities.<sup>5,6</sup>

#### ○ Surgical Approaches:

■ **Pharyngeal Flap Surgery:** Procedure to correct velopharyngeal insufficiency, improving speech resonance and articulation.

■ **Palatoplasty:** Surgical repair of cleft palate to facilitate normal speech and feeding functions.<sup>5,6</sup>

### 2. Hearing Restoration

#### ○ Indications:

■ Conductive hearing loss due to malformations of the ossicular chain or external ear canal.<sup>5,6</sup>

■ Need for auditory rehabilitation to support speech and language development.<sup>5,6</sup>

#### ○ Surgical Approaches:

■ **Ossiculoplasty:** Reconstruction of the ossicular chain using autologous or synthetic materials to restore conductive hearing.

■ **Bone-Anchored Hearing Systems:** Implantation of osseointegrated devices to bypass external ear malformations and improve hearing.<sup>5,6</sup>

The successful surgical management of Treacher Collins syndrome requires a multidisciplinary team involving plastic surgeons, otolaryngologists, maxillofacial surgeons, speech therapists, audiologists, and other specialists. This collaborative approach ensures comprehensive evaluation and treatment planning, addressing the unique needs of each patient and optimizing both functional and aesthetic outcomes.<sup>7,8</sup>

In conclusion, the surgical indications for Treacher Collins syndrome are diverse and necessitate a multifaceted approach to address the complex craniofacial deformities and functional impairments. Through coordinated care and

# Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

advanced surgical techniques, patients with TCS can achieve significant improvements in quality of life and psychosocial well-being.<sup>7,8</sup>

## Surgical Contraindications for Treacher Collins

### General Contraindications

When planning surgical interventions for patients with Treacher Collins syndrome (TCS), it is crucial to consider both general and specific contraindications to ensure patient safety and optimize outcomes. General contraindications encompass medical conditions and factors that can pose significant risks during surgery, irrespective of the specific procedure.<sup>9,10</sup>

#### 1. Uncontrolled Medical Conditions

##### ○ Contraindications:

- Patients with poorly managed systemic illnesses such as diabetes mellitus, hypertension, or cardiovascular disease, which can increase the risk of perioperative complications.<sup>9,10</sup>

- Presence of active infections or sepsis, which can complicate surgical healing and increase the risk of postoperative infections.<sup>9,10</sup>

##### ○ Considerations:

- Thorough preoperative medical evaluation and optimization of systemic conditions are essential before proceeding with elective surgical interventions.<sup>9,10</sup>

- Delay elective surgeries until any active infections are adequately treated and resolved.<sup>9,10</sup>

#### 2. Coagulopathies and Bleeding Disorders

##### ○ Contraindications:

- Patients with congenital or acquired coagulopathies, such as hemophilia, von Willebrand disease, or those on anticoagulant therapy, which can lead to excessive bleeding and hematoma formation.<sup>11</sup>

##### ○ Considerations:

- Preoperative assessment of coagulation status and consultation with a hematologist to manage and mitigate bleeding risks.

- Temporary discontinuation or adjustment of anticoagulant medications, with appropriate bridging strategies, may be required.<sup>11</sup>

#### 3. Psychosocial Factors

##### ○ Contraindications:

- Patients with severe psychological or psychiatric disorders, including untreated depression, anxiety, or body dysmorphic disorder, which can affect postoperative compliance and satisfaction.<sup>11</sup>

##### ○ Considerations:

- Comprehensive psychological evaluation and stabilization of any psychiatric conditions before surgery.<sup>11</sup>

- Involvement of a mental health professional to provide ongoing support and counseling throughout the surgical process.<sup>11</sup>

## Specific Contraindications Related to Treacher Collins Syndrome

#### 1. Severe Airway Compromise

##### ○ Contraindications:

- Patients with significant airway obstruction due to severe mandibular hypoplasia or glossoptosis, posing a high risk for perioperative airway management difficulties.<sup>12</sup>

##### ○ Considerations:

- Preoperative assessment by an anesthesiologist specializing in difficult airways and formulation of a detailed airway management plan.<sup>12</sup>

- Elective surgeries may need to be postponed until the airway is adequately secured, potentially requiring interventions such as tracheostomy or mandibular distraction osteogenesis.<sup>12</sup>

#### 2. Inadequate Soft Tissue and Skin Quality

##### ○ Contraindications:

- Patients with insufficient or compromised soft tissue and skin quality at the surgical site, which can hinder wound healing and increase the risk of complications such as dehiscence and infection.<sup>13</sup>

##### ○ Considerations:

- Preoperative planning to ensure adequate tissue availability, potentially involving tissue expansion techniques or staged reconstruction.<sup>13</sup>

- Use of advanced wound care modalities and close postoperative monitoring to promote optimal healing.<sup>13</sup>

#### 3. Previous Radiation Therapy

##### ○ Contraindications:

- History of radiation therapy to the craniofacial region, which can result in fibrotic changes, compromised vascularity, and impaired wound healing.<sup>14</sup>

##### ○ Considerations:

- Detailed assessment of the extent and impact of prior radiation therapy on the surgical field.<sup>14</sup>

- Implementation of specialized surgical techniques and postoperative care protocols to enhance healing in irradiated tissues.<sup>14</sup>

## Age-Related Considerations

#### 1. Neonates and Infants

##### ○ Contraindications:

- Elective surgeries in neonates and infants with TCS may be contraindicated due to their limited physiological reserves and higher susceptibility to anesthesia-related complications.<sup>14</sup>

##### ○ Considerations:

- Careful evaluation of the risk-benefit ratio for any surgical procedure in this age group.<sup>14</sup>

- Preference for non-surgical management options, such as non-invasive airway support, until the child reaches a more stable physiological status.<sup>14</sup>

#### 2. Elderly Patients

##### ○ Contraindications:

- Elderly patients with TCS may have multiple comorbidities and decreased physiological resilience,

## Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

increasing the risk of perioperative complications and prolonged recovery.<sup>14</sup>

### ○ **Considerations:**

- Comprehensive geriatric assessment to evaluate the overall health status and suitability for elective surgery.<sup>5,6,14</sup>
- Prioritization of minimally invasive procedures and enhanced recovery protocols to reduce surgical stress and facilitate quicker recovery.

### **Immunocompromised State**

#### ● **Contraindications:**

- Patients with immunocompromised states, such as those on chronic immunosuppressive therapy or with conditions like HIV/AIDS, are at an increased risk of infections and poor wound healing.<sup>15</sup>

#### ● **Considerations:**

- Preoperative optimization of immune function and consultation with an immunologist or infectious disease specialist.<sup>15</sup>
- Enhanced aseptic techniques and postoperative infection prophylaxis to mitigate risks.

Understanding and addressing the contraindications for surgical interventions in patients with Treacher Collins syndrome is essential to ensure safe and effective management. A thorough preoperative evaluation, including medical, psychosocial, and specific considerations related to TCS, allows for the identification and mitigation of potential risks. By adopting a comprehensive and multidisciplinary approach, plastic surgeons can optimize surgical outcomes and enhance the quality of life for patients with Treacher Collins syndrome.<sup>16</sup>

### **Current Surgical Techniques for Treacher Collins Syndrome in Plastic Surgery**

Treacher Collins syndrome (TCS), also known as mandibulofacial dysostosis, is a rare congenital disorder characterized by craniofacial deformities that significantly impact aesthetics and function. Surgical management of TCS requires a comprehensive and multidisciplinary approach, leveraging various advanced techniques to address skeletal, soft tissue, and sensory deficits. This article delves into the current surgical techniques employed in the treatment of TCS, highlighting the complexities and innovations that define modern craniofacial surgery.<sup>17,18,19</sup>

### **Distraction Osteogenesis**

**Distraction osteogenesis (DO)** is a cornerstone technique for the correction of severe mandibular and maxillary hypoplasia in TCS. This procedure involves the gradual mechanical lengthening of bone through a controlled surgical process.<sup>19</sup>

#### ● **Procedure:**

- **Osteotomy:** An initial surgical cut is made in the bone, typically the mandible or maxilla.<sup>19</sup>
- **Application of Distractor:** A distraction device is affixed to the bone segments. Devices can be internal (subcutaneous) or external.<sup>19</sup>

- **Distraction Phase:** Post-surgery, the device is gradually adjusted to separate the bone segments, allowing new bone to form in the gap.

- **Consolidation Phase:** The newly formed bone is allowed to consolidate and harden over several weeks to months.<sup>19</sup>

#### ● **Indications:**

- Severe micrognathia leading to airway obstruction or significant aesthetic concerns.<sup>19</sup>
- Midface retrusion affecting dental occlusion and facial harmony.

#### ● **Outcomes:**

- Improved mandibular and maxillary projection.
- Enhanced airway patency and occlusal relationships.

### **Orthognathic Surgery**

Orthognathic surgery corrects jaw deformities and malocclusion by repositioning the jaws.

#### ● **Procedure:**

- **Le Fort Osteotomy:** Used for maxillary advancement or repositioning.
- **Bilateral Sagittal Split Osteotomy (BSSO):** For mandibular advancements, setbacks, or asymmetry corrections.<sup>19</sup>
- **Genioplasty:** Adjustments to the chin to enhance facial balance.<sup>19</sup>

#### ● **Indications:**

- Functional impairments due to malocclusion.
- Aesthetic concerns related to jaw discrepancies.

#### ● **Outcomes:**

- Improved dental occlusion.
- Enhanced facial aesthetics and symmetry.

### **Auricular Reconstruction**

Auricular reconstruction addresses the malformations of the external ear, commonly seen in TCS.

#### ● **Procedure:**

- **Autologous Rib Cartilage Grafting:**
  - **Harvesting:** Rib cartilage is harvested and sculpted into the shape of an ear framework.<sup>19</sup>
  - **Implantation:** The framework is implanted under the skin at the site of the ear.<sup>19</sup>
- **Medpor Implants:**
  - **Synthetic Framework:** Utilization of porous polyethylene implants shaped to mimic ear anatomy.<sup>19</sup>
  - **Tissue Coverage:** Covered with local tissue flaps or skin grafts.

#### ● **Indications:**

- Microtia or anotia impacting facial symmetry and function.<sup>19</sup>

#### ● **Outcomes:**

- Aesthetic restoration of the external ear.
- Enhanced psychosocial well-being and self-esteem.<sup>19</sup>

### **Eyelid Reconstruction**

Eyelid deformities, particularly colobomas, are addressed through various reconstructive techniques.<sup>19</sup>

## Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

- **Procedure:**
  - **Z-Plasty:** A technique used to rearrange and lengthen the eyelid tissues.
  - **Skin Grafting:** Use of autologous skin grafts to reconstruct deficient areas.<sup>19</sup>
  - **Canthoplasty:** Surgical tightening and repositioning of the eyelid canthus to improve function and appearance.<sup>19</sup>
- **Indications:**
  - Eyelid colobomas causing exposure keratopathy or aesthetic concerns.
- **Outcomes:**
  - Improved eyelid function and corneal protection.
  - Enhanced facial aesthetics.

### Tracheostomy and Airway Management

For severe airway compromise, tracheostomy is often performed to secure a patent airway.<sup>19</sup>

- **Procedure:**
  - **Tracheostomy:** A surgical opening created in the trachea to establish a direct airway.<sup>19</sup>
  - **Mandibular Distraction Osteogenesis:** Used as an adjunct to tracheostomy to alleviate airway obstruction long-term.<sup>19</sup>
- **Indications:**
  - Neonates and infants with life-threatening airway obstruction.
  - Persistent obstructive sleep apnea unmanageable with non-surgical interventions.<sup>19</sup>
- **Outcomes:**
  - Immediate and reliable airway access.
  - Potential for decannulation following mandibular advancement procedures.<sup>19</sup>

### Palatoplasty

Cleft palate repair is crucial for addressing feeding and speech difficulties associated with TCS.

- **Procedure:**
  - **Vomer Flap:** Utilizes tissue from the nasal septum to close the cleft palate.<sup>19</sup>
  - **Furlow Double Opposing Z-Plasty:** A technique that repositions and lengthens the soft palate to improve speech outcomes.<sup>19</sup>
- **Indications:**
  - Cleft palate affecting speech and feeding.
- **Outcomes:**
  - Improved speech articulation and resonance.
  - Enhanced feeding and nutritional intake.

### Bone-Anchored Hearing Systems (BAHS)

Conductive hearing loss in TCS patients is often managed with bone-anchored hearing systems.<sup>19</sup>

- **Procedure:**
  - **Implantation:** A titanium implant is surgically placed in the skull bone behind the ear.<sup>19</sup>

- **Attachment:** An external sound processor is attached to the implant, bypassing the external and middle ear to transmit sound directly to the inner ear.<sup>19</sup>
- **Indications:**
  - Conductive hearing loss due to external and middle ear malformations.
- **Outcomes:**
  - Improved auditory function.
  - Enhanced speech and language development.

### MULTIDISCIPLINARY APPROACH

Successful management of TCS necessitates collaboration among various specialties including plastic surgery, otolaryngology, maxillofacial surgery, audiology, and speech therapy. This integrated approach ensures comprehensive care, addressing the multifaceted needs of TCS patients.<sup>20,21</sup> The surgical management of Treacher Collins syndrome involves a variety of complex and specialized techniques tailored to address the unique craniofacial deformities and functional impairments associated with the disorder. Advances in surgical methods, coupled with a multidisciplinary approach, have significantly improved outcomes for TCS patients, enhancing both aesthetics and quality of life. Through continuous innovation and refinement of surgical techniques, the future of TCS management holds promise for even greater advancements in patient care.<sup>20,21</sup>

### CONCLUSION

The surgical management of Treacher Collins syndrome (TCS) represents a remarkable convergence of medical innovation, meticulous planning, and multidisciplinary collaboration. Treacher Collins syndrome, a rare congenital disorder characterized by distinctive craniofacial anomalies, poses significant challenges that require a comprehensive and individualized approach to treatment. The overarching goal of surgical intervention in TCS is not only to correct anatomical deformities but also to restore function, improve quality of life, and facilitate psychosocial integration for affected individuals.

The complexities of TCS necessitate the use of advanced surgical techniques that have evolved over decades of clinical practice and research. Distraction osteogenesis, a pivotal technique in the armamentarium of craniofacial surgeons, allows for the gradual elongation of hypoplastic bones, such as the mandible and maxilla, thereby addressing both functional deficits and aesthetic concerns. This method has proven particularly effective in mitigating airway obstructions and correcting midface retrusion, ultimately enhancing respiratory function and facial symmetry.

Orthognathic surgery remains a cornerstone for the correction of jaw discrepancies and malocclusion in TCS patients. Procedures such as Le Fort osteotomy and bilateral sagittal split osteotomy enable precise repositioning of the maxilla and mandible, resulting in improved occlusion and

## Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

harmonious facial proportions. When combined with genioplasty, these interventions provide comprehensive solutions for achieving optimal functional and aesthetic outcomes.

The intricate task of auricular reconstruction in TCS patients, often plagued by microtia or anotia, underscores the importance of personalized and staged surgical planning. Utilizing autologous rib cartilage grafts or Medpor implants, surgeons can meticulously reconstruct the external ear, significantly enhancing facial symmetry and patient self-esteem. The integration of bone-anchored hearing systems further addresses the conductive hearing loss commonly associated with TCS, facilitating auditory rehabilitation and improving communication abilities.

Eyelid reconstruction techniques, including Z-plasty and canthoplasty, are essential for correcting colobomas and ensuring proper eyelid function. These procedures not only protect the cornea from exposure-related complications but also contribute to the overall aesthetic enhancement of the periocular region. Similarly, the surgical repair of cleft palates through palatoplasty techniques, such as vomer flap and Furlow double opposing Z-plasty, plays a critical role in improving speech and feeding capabilities.

The management of severe airway compromise in TCS patients often necessitates early and aggressive interventions. Tracheostomy provides immediate airway relief in neonates and infants with life-threatening obstructions, while mandibular distraction osteogenesis offers a long-term solution for advancing the tongue base and alleviating airway obstruction. The judicious use of these techniques, in conjunction with thorough preoperative assessment and perioperative care, ensures the safety and efficacy of surgical interventions.

The success of surgical management in TCS hinges on the collaborative efforts of a multidisciplinary team. Plastic surgeons, otolaryngologists, maxillofacial surgeons, audiologists, and speech therapists must work in concert to develop and implement tailored treatment plans that address the unique needs of each patient. This integrated approach not only optimizes surgical outcomes but also fosters a holistic framework for patient care, encompassing medical, functional, and psychosocial dimensions.

In conclusion, the surgical management of Treacher Collins syndrome epitomizes the advancements and achievements of modern craniofacial surgery. Through the application of sophisticated techniques and a commitment to multidisciplinary collaboration, healthcare providers can significantly improve the lives of individuals with TCS. Continued research and innovation in this field hold the promise of even greater strides in the future, offering hope and enhanced quality of life to those affected by this challenging congenital disorder.

## REFERENCES

- I. Treacher Collins Syndrome Collaborative Group. Positional cloning of a gene involved in the pathogenesis of Treacher Collins syndrome. *Nat Genet* 1996;12:130–6.
- II. Treacher Collins E. Cases with symmetrical congenital notches in the outer part of each lower lid and defective development of the malar bones. *Trans Ophthalmol Soc UK* 1900;20:190–2.
- III. Thomson A. Notice of several cases of malformation of the external ear, together with experiments on the state of hearing in such persons. *Monthly J Med Sci* 1846;7:420–4.
- IV. Toynbee J. Description of a congenital malformation in the ears of a child. *Monthly J Med Sci* 1847;1:738–9.
- V. Scully C, Langdon J, Evans J. Marathon of eponyms: 20 Treacher Collins syndrome. *Oral Dis* 2011;17:619–20.
- VI. Franceschetti A, Zwahlen P. Un syndrome nouveau: la dysostose mandibulo-faciale. *Bull Schweiz Akad Med Wiss* 1944;1:60–6.
- VII. Franceschetti A, Klein D. The mandibulofacial dysostosis: a new hereditary syndrome. *Acta Ophthalmol (Copenh)* 1949;27:143–224.
- VIII. Kobus K, Wójcicki P. Surgical treatment of Treacher Collins syndrome. *Ann Plast Surg* 2006;56:549–54.
- IX. Trainor PA, Dixon J, Dixon MJ. Treacher Collins syndrome: etiology, pathogenesis and prevention. *Eur J Hum Genet* 2009;17:275–83.
- X. Pun AH, Clark BE, David DJ, Anderson PJ. Cervical spine in Treacher Collins syndrome. *J Craniofac Surg* 2012;23:e218–20.
- XI. Posnick JC, Tiwana PS, Costello BJ. Treacher Collins syndrome: comprehensive evaluation and treatment. *Oral Maxillofac Surg Clin North Am* 2004;16:503–23.
- XII. Jabs EW, Li X, Lovett M, et al. Genetic and physical mapping of the Treacher Collins syndrome locus with respect to loci in the chromosome 5q3 region. *Genomics* 1993;18:7–13.
- XIII. Gonzales B, Henning D, So RB, Dixon J, Dixon MJ, Valdez BC. The Treacher Collins syndrome (TCOF1) gene product is involved in prerRNA methylation. *Hum Mol Genet* 2005;14:2035–43.
- XIV. Valdez BC, Henning D, So RB, Dixon J, Dixon MJ. The Treacher Collins syndrome (TCOF1) gene product is involved in ribosomal DNA gene transcription by interacting with upstream binding factor. *Proc Natl Acad Sci U S A* 2004;101:10709–14.
- XV. Dixon J, Ellis I, Bottani A, Temple K, Dixon MJ. Identification of mutations in TCOF1: use of molecular analysis in the pre- and post-natal

## Comprehensive Surgical Management of Treacher Collins Syndrome in Plastic Surgery: A Multidisciplinary Approach

- diagnosis of Treacher Collins syndrome. *Am J Med Genet A* 2004;127A:244–8.
- XVI. Dixon J, Jones NC, Sandell LL, et al. *Tcof1/Treacle* is required for neural crest cell formation and proliferation deficiencies that cause craniofacial abnormalities. *Proc Natl Acad Sci U S A* 2006;103:13403–8.
- XVII. Posillo D. The pathogenesis of the Treacher Collins syndrome (mandibulofacial dysostosis). *Br J Oral Surg* 1975;13:1–26.
- XVIII. Dixon J, Dixon MJ. Genetic background has a major effect on the penetrance and severity of craniofacial defects in mice heterozygous for the gene encoding the nucleolar protein Treacle. *Dev Dyn* 2004;229:907–14.
- XIX. Teber OA, Gillessen-Kaesbach G, Fischer S, et al. Genotyping in 46 patients with tentative diagnosis of Treacher Collins syndrome revealed unexpected phenotypic variation. *Eur J Hum Genet* 2004;12:879–90.
- XX. Fisher E. Exploring the genetic origins of Treacher Collins syndrome. *Clin Genet* 2011;79:330–2.
- XXI. Dauwerse JG, Dixon J, Seland S, et al. Mutations in genes encoding subunits of RNA polymerases I and III cause Treacher Collins syndrome. *Nat Genet* 2011;43:20–2.