

Does an ear deformity bring an adverse impact on quality of life of Treacher Collins syndrome individuals?

Fernando Felipe Lodovichi¹
Jessica Pereira Oliveira¹
Rafael Denadai²
Cesar Augusto Raposo-Amaral²
Enrico Ghizoni¹
Cassio Eduardo Raposo-Amaral²

Abstract Treacher Collins syndrome (TCS) is an autosomal dominant disorder with variable expression in which the ear may or may not be absent or with a malformation. Individuals with TCS suffer social stigma that may affect interaction with their peers. Quality of life instruments are stigma identification tools and can enable social adjustment of these individuals. This study aims to assess the quality of life of individuals with TCS and to gauge the impacts of ear deformity on the quality of life. Twelve volunteers with a clinical and genetic diagnosis of TCS answered the WHO quality of life questionnaire and were divided into groups with normal ears ($n = 6$) versus affected ears ($n = 6$), and their results were compared. Siviero's scale was used to stratify the quality of life scores as satisfactory, intermediate and unsatisfactory. The overall score of the normal ears group was 73.13 and 71.81 for the affected ears group, and both were classified as an intermediate quality of life, with no statistically significant differences between them. Ear deformity is not a burden to the quality of life of these individuals, who already show other deformities and overall intermediate quality of life scores.

Key words Treacher Collins Syndrome, Quality of life

¹ Faculdade de Ciências Médicas, Universidade Estadual de Campinas. R. Tessália Vieira de Camargo 126, Cidade Universitária. 13083-887 Campinas SP Brasil. fernando.lodovichi@gmail.com

² Sociedade Brasileira de Pesquisa e Assistência para Reabilitação Craniofacial. Campinas SP Brasil.

Introduction

The Treacher Collins syndrome (TCS), also known as mandibulofacial dysostosis or Franceschetti-Klein¹ syndrome, is a rare syndrome transmitted in an autosomal dominant pattern characterized by the poor development of the supraorbital ridge, maxillary, zygomatic and mandibular hypoplasia and soft tissue of the face². It has an estimated incidence of 1 in 50,000 live births³. Most individuals with TCS are from heterozygotes to a localized mutation in the TCOF1 gene⁴. Although mutation detection rates have been observed to reach 93%, a relevant subset of individuals with the causal mutation syndrome has not yet been identified⁵.

In more recent studies, mutations have also been found in the POLR1D and POLR1C genes in a smaller sample of individuals³. Common clinical features include lower eyelid retraction, corneal exposure, decreased retropharyngeal space, respiratory distress, and hearing loss⁶. Another feature of extreme clinical relevance that may be present is deformity or absence of ears, called microtia or anotia. In these situations, the treatment is even more complicated since it involves the total reconstruction of the ears with the cartilages of the ribs, performed in two to four stages on each side⁷.

The treatment of the most severe forms of TCS requires an average of 5 surgeries until the end of craniofacial growth⁸. In cases of ear deformity (microtia) or total absence of ear (anotia), the number of surgeries increases significantly, which generates a social burden on the individual and their families, with a probable impact on their quality of life. Therefore, there is a need to identify parameters to measure the responses of these individuals to craniofacial surgeries employing quality of life measurement instruments and whether microtia/anotia clinical characteristic leads to a negative impact on the quality of life and, consequently, compromised longitudinal treatment of individuals with TCS.

Interestingly, the quality of life of individuals with TCS and its distinct phenotypes (with normal ear versus deformity or absence of ear) has not yet been measured and compared in the literature. Therefore, it is urgent to evaluate and measure the quality of life of these Brazilians with TCS and to determine whether the deformity or absence of ears has an adverse impact on the quality of life of this group. We hypothesized that deformity or absence of ears can significantly reduce the quality of life of individuals with TCS.

Methods

This is a retrospective observational study in which a WHO quality of life questionnaire (WHOQOL-100) was applied to individuals with a clinical and genetic diagnosis of TCS in follow-up at our institution between 2005 and 2013. In the records of the institution, a total of 20 individuals meeting the diagnostic criteria were identified, so all were invited to participate in the study. Those who received any intervention outside the service, and individuals who did not agree to respond to the quality of life questionnaire were excluded. Thus, eight individuals were excluded, all because they chose not to participate in the study since most of them lived far from our center. The remaining 12 individuals with TCS were then divided into two groups. Group 1 consisted of volunteers with normal, unaffected ears ($n = 6$) and group 2 by volunteers with partial or total absence of ears with a clinical diagnosis of microtia or anotia (affected ears) ($n = 6$). (Figures 1 and 2).

All patients were, therefore, under the care of a specialized multidisciplinary center (with psychologists, speech therapists, orthodontists, plastic surgeons, otolaryngologists, and social workers). In the first service, the individuals and relatives visit all the specialties and a detailed diagnosis of each is described in the medical records by each specialty, as well as the immediate priorities and throughout the follow-up. The number and types of surgeries and the ages at which they should occur are outlined for families, as well as the age at which orthodontic treatment begins. The need for follow-up by the



Figure 1. Patient with Treacher Collins syndrome and diagnosis of microtia.



Figure 2. Patient with Treacher Collins syndrome and with normal, unaffected ears.

psychology team is emphasized to the family, as well as the approximate number of sessions, time of each session and average follow-up time. The active interference of the Social Service with the municipality aims to facilitate the obtaining of the aid called Out-of-Home Transportation. The Health Secretariat of the individual's hometown acknowledges that there is no treatment within the area of the municipality and must provide transportation to the specialized center. Thus, the social service promotes assurance of the individual's adherence to the multidisciplinary treatment throughout the follow-up until the final rehabilitation and full insertion in the work environment. All care is performed by the Unified Health System (SUS).

The individuals evidenced hypoplasia of the middle third of the face (bone and muscle), antimongolian rotation of the palpebral cleft, coloboma of the lower eyelids, absence of eyelashes in the medial region of the eyelids. All had hearing loss due to bone conduction regardless of the presence of the ears and alteration of lateral capillary line configuration. Bone deformities were characterized as mandibular retrusion, mandibular ramus shortening, anterior open bite, micrognathia and microgenia. A decreased posterior maxilla height and a decreased posterior airspace was noted. These bone deformities led individuals to respiratory distress. The patients who answered the questionnaire had good hearing ability and communicated very well with the evaluators.

The WHOQOL-100 is a quality of life assessment tool of international acceptance proposed and elaborated by the World Health Organi-

zation. It consists of 100 questions related to 6 realms (physical, psychological, level of independence, social relationships, environment and spirituality/religiosity/personal beliefs), which are divided into 24 facets, each facet consisting of four questions. In addition to the 24 specific facets, the tool has a twenty-fifth facet composed of general questions about the quality of life⁹.

After the application of the questionnaires, socioeconomic data, surgical history and complications were collected from the medical records. Only those events that had permanent and significant repercussions, with the potential to reflect on the quality of life of the evaluated individuals, were established as complications.

The scale of Siviero¹⁰ was adopted to define parameters of quality of life and as a reference to determine the quality of life as satisfactory, intermediate or unsatisfactory. In this perspective, values lower than 25 characterized dissatisfaction (poor quality of life), while values higher than 75 characterized satisfaction (satisfactory quality of life). Values between 25 and 75 characterized the intermediate level of quality of life¹¹.

The questionnaire was applied according to established guidelines so that the volunteers were informed of the purpose of their application and the destination of the data collected. All the individuals attended the institution so that the questionnaire was answered by each one in just one meeting. As a general guideline, it was established that the questionnaire is self-answered, based on the individual interpretation and how the respondent felt in the last two weeks before the research, so he would read and indicate one of the alternatives proposed in the instrument (self-explanatory), without the influence of the applicators in the explanation of the questions. The children were assisted by a parent at certain times during the interview and were also not assessed for sexual life.

The calculation of scores and descriptive statistics was performed using the Microsoft Excel instrument developed by the Federal Technological University of Paraná (UFTPR)¹². After the application of the questionnaires, the data were tabulated and, after statistical analysis, the responses were converted to scale from 0 to 100 by the program itself, and the inverted-scale facets were converted to allow comparison with the other facets. Each facet and realm of the questionnaire were compared between the two groups of patients with TCS through the Mann-Whitney Test. The level of statistical significance was set at $p < 0.05$.

Ethical considerations

This project was approved by the Institution's Ethics Committee. All individuals signed the Informed Consent Form as legal documentation. The legal representative signed the document on behalf of individuals under the age of 18. All volunteers could still choose not to participate at any time in the course of the research, and this choice would never entail any harm regarding their current or future treatment plan.

Results

Twelve volunteers with TCS were interviewed – 9 males and three females. The group's mean age was 20 years and seven months, ranging from 6 to 33 years. Meanwhile, the mean per capita household income was R\$ 630.59.

According to the scale defined by Siviero¹⁰, individuals with TCS had satisfactory levels of quality of life for the following realms: level of independence, social relationships and spiritual aspects/religion/personal beliefs (77.43, 76.71 and 80.11, respectively). Responses to the other realms generated intermediate levels of quality of life, and the physical and environmental realms generated the lowest levels (67.88 and 68.36, respectively). Regarding the instrument's overall score, volunteers with TCS have intermediate levels of quality of life (72.47). (Table 1)

When they were divided into two groups; the group of individuals with normal ears consisted of five males and one female. The mean age of the group was 24 years and 10 months, ranging from 15 to 33 years. The mean per capita household income was R\$ 532.55. The group of individuals with affected ears consisted of four males and two females. The mean age was 16 years and four months, ranging from 6 to 32 years. The mean per capita household income in the group was R\$ 728.64.

An average of 5.5 surgical procedures per individual of the group with normal ears was performed. A blood transfusion of one packed red blood cell unit was performed in one of the procedures. All the other individuals evolved without complications or transfusions in this group. In the group with affected ears, the mean was 7.17 surgical procedures per subject. No permanent and significant complications were identified.

In most realms of the WHOQOL-100 questionnaire, the results of volunteers with normal

ears were higher than those with affected ears. In the physical realm, the mean for the group with normal ears was 70.49, while the result was 65.28 in the group with affected ears, both with intermediate levels of quality of life, according to the scale defined by Siviero¹⁰. In the psychological realm, the results were 76.88 for the group with normal ears (satisfactory level of quality of life) and 70.21 (intermediate level of satisfaction) for the group with affected ears. Regarding the realm level of independence, the results were 78.65 and 76.22, in groups 1 and 2, respectively, both scores considered as satisfactory level of quality of life. In the social relationships realm, the normal ears group obtained 77.78 and the group with affected ears 75.64, also considered scores of satisfaction with the quality of life.

In the environmental realm, both groups had an intermediate quality of life scores, although the group with affected ears scored higher (69.40) than the group with normal ears (67.32). In the realm spiritual aspects/religion/personal beliefs, we found that the group with affected ears obtained a score of 81.25 while the group with normal ears obtained 78.75, satisfactory levels in both groups. Finally, in the general assessment of the quality of life, the score of the group of normal ears was 73.13 and 71.81 in the group of affected ears, intermediate levels of quality of life in both groups. (Table 2 and Graph 1).

Finally, we observed that there were no results with a significant difference between the two groups for any compared realm.

Discussion

Bindra *et al.*¹³ emphasized the premise that individuals themselves are the most reliable and accurate observers of their health perceptions and experiences regardless of their age at the time of evaluation. Also, quality of life identification tools through questionnaires provide reliable results¹³ and, therefore, facilitate the multidisciplinary team to develop treatment strategies to benefit the individual.

Studies on the quality of life in children with and without craniofacial anomalies have considered children from five years of age eligible to respond to instruments that measured the quality of life¹⁴⁻¹⁶. Several authors¹⁴⁻¹⁷ has already used the age threshold of five years for the application of the questionnaire WHOQOL-100¹⁴⁻¹⁷. It has even been described that children from this age on can be self-critical¹⁴⁻¹⁶. Therefore, the use of

a validated instrument for the Portuguese language in Brazilian patients with TCS with ages between 6 and 33 years facilitated the retrieval of data that show that these individuals with TCS treated in our Institution have high quality of life scores in all realms and facets. It is very likely that adherence to the well-planned surgical protocol has positively affected the quality of life of these individuals. Furthermore, psychological therapy allowed to obtain tools to strengthen the cognitive repertoire necessary for the handling of peer offenses and insults.

At our center, a group of 14 psychologists provides longitudinal therapy to cope with the many stages of treatment and lays the foundations for the fight against pains of repeated offenses in the social and school environment. Thus, we believe that every individual with craniofacial deformity should be treated in a specialized craniofacial surgery center.

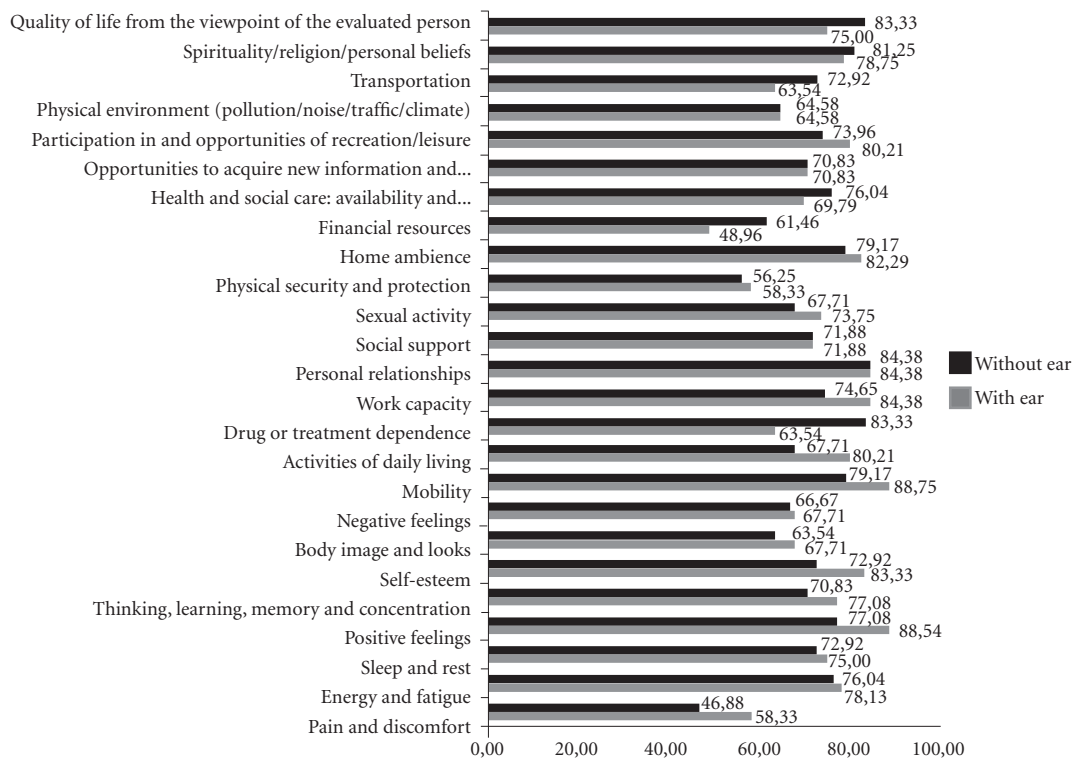
Individuals born with TCS require longitudinal treatment with a multidisciplinary approach in which many surgeries are planned and performed individually according to severity and phenotypic situation from birth. The main anatomical problem is hypoplasia of the middle third of the face and mandibular and chin hypodevelopment. These anatomical alterations are phenotypic characteristics of the genetic alterations inherent to the syndrome and interfere directly with the respiratory function, since the airspace is narrowed in these individuals and, as a consequence, they breathe precariously. Usually, they are fragile individuals, due to the great effort and caloric breathing expenditure. Early surgeries in children less than one year of age may be necessary for the restoration of the posterior airway. The gradual mandibular stretching employing osteogenic distraction was a surgical technique proposed by McCarthy, which enabled

Table 1. Results and descriptive statistics of Treacher Collins patients by WHOQOL-100 realm.

Realms	0-100	Mean	Median	Standard deviation	CV	Min	Max	N
Physical realm	67.88	14.86	15.3	2.10	14%	11.0	18.3	12
Psychological realm	73.54	15.77	15.9	2.21	14%	11.8	19.6	12
Level of independence	77.43	16.39	17.0	2.19	13%	11.7	20.0	12
Social relationships	76.71	16.27	16.8	1.94	12%	12.7	19.1	12
Environment	68.36	14.94	15.0	1.57	10%	12.4	18.6	12
Spiritual aspects/religion/personal beliefs	80.11	16.82	17.0	2.48	15%	14.0	20.0	11
General	72.47	15.59	15.9	1.66	11%	12.4	17.9	12

Table 2. Results and descriptive statistics between groups with and without ears by realm of WHOQOL-100.

Realms	Group	0-100	Mean	Median	Standard deviation	N	CI	P-value
Physical realm	With ear	70.49	15.28	15.3	2.18	6	1.75	0.628
	Without ear	65.28	14.44	15.0	2.13	6	1.70	
Psychological realm	With ear	76.88	16.30	16.0	1.85	6	1.48	0.749
	Without ear	70.21	15.23	15.9	2.58	6	2.06	
Level of independence	With ear	78.65	16.58	16.8	0.88	6	0.70	0.629
	Without ear	76.22	16.19	17.1	3.12	6	2.50	
Social relationships	With ear	77.78	16.44	17.0	1.94	6	1.55	0.629
	Without ear	75.64	16.10	16.3	2.12	6	1.69	
Environment	With ear	67.32	14.77	15.0	0.90	6	0.72	0.936
	Without ear	69.40	15.10	14.9	2.12	6	1.70	
Spiritual aspects/religion/ personal beliefs	With ear	78.75	16.60	17.0	2.07	5	1.82	0.711
	Without ear	81.25	17.00	17.0	2.97	6	2.37	
General	With ear	73.13	15.70	15.9	1.03	6	0.83	0.873
	Without ear	71.81	15.49	15.9	2.22	6	1.78	



Graph 1. Results between groups with and without ears by WHOQOL-100 facets.

these individuals to stop receiving tracheostomy by allowing changes in the anatomy of the mandible and re-adaptation and increased posterior airspace and significant improvement in breathing^{18,19}.

Another relatively prevalent clinical feature in these individuals is hearing impairment and deformity/absence of the ears.

Some degree of bilateral conductive hearing loss is always found in all individuals with the syndrome, regardless of the presence or deformities of the outer ear. The middle ear is small, with hypoplasia of the antrum and mastoid cells. The hammer, anvil and stapes ossicles are evidenced with relevant anatomical changes. However, if patients are diagnosed and treated correctly, it is possible to restore hearing ability by employing a bone-anchored hearing aid. Individuals treated at our center with significant hearing loss retrieve conductive hearing ability through the implantation of these devices. Therefore, the hearing of the individuals studied allows them to perform daily tasks (such as talking on the phone without difficulty) and social interaction and dialogues

with proper understanding and communication in a low noise environment. All the patients communicated well, without help for hearing impairment during the interviews.

The absence of the external ear is an additional morphological aspect (unrelated to the degree of deafness) that can lead to a tremendous individual stigma with loss of cognitive behavioral function, retraction, and social isolation. The surgery for the reconstruction of the ears in these individuals is extremely complex and involves the removal of three ribs, preparation of the cartilaginous scaffold and insertion in the mastoid region⁷. The ideal age for ear reconstruction is 10 years. However, as these individuals are usually underdeveloped and thin, the need to delay surgery to adulthood is not uncommon. However, growing with ears and facing the periods of childhood and adolescence can bring severe damage and sequelae to psychic development, since this clinical feature may enhance or elicit offenses and jokes from their peers in school settings. Therefore, our study was designed to clarify and identify the impact of microtia/anotia on the quality

of life of individuals with TCS and to anticipate ear reconstruction surgeries for the earliest possible age eventually or to develop a temporary ear prosthesis until ideal age for surgery.

Interestingly, TCS individuals with microtia/ anotia had no quality of life distinct from those with normal ears, contrary to our initial hypothesis. The data of this study showed that other facial deformities characteristic of the phenotype could negatively impact and with higher intensity the quality of life of individuals with TCS. Also, as these individuals and their legal guardians are advised that ear reconstruction surgeries are performed on a scheduled basis from the age of 10, they end up hoping to get an ear close to normal, decreasing anxiety and affecting the quality of life positively. Individuals with TCS in the group of affected ears older than 10 years showed up at our center late or are awaiting clinical conditions for surgery and have already entered the protocol of psychological therapy.

While this study was the first in Brazil to attempt to identify the quality of life of individuals with TCS and the impact of microtia/anotia on their quality of life, it is not free of limitations. This is a quality of life evaluation with a reduced sample. However, we believe that increasing numbers of individuals would probably not change the results obtained in the two different groups since all p-values were above 0.6 for all realms, which significantly weakened our initial hypothesis. Another significant limitation was the absence of a control group and the absence of other instruments that could compare the data obtained by the WHOQOL-100 instru-

ment. Future studies in progress should compare the data of this study to the quality of life of a control group of individuals not affected by the syndrome.

Conclusions

Interestingly, the individuals measured in our study are a small sample of individuals with TCS found in Brazil. Most probably, the vast majority of these are not being followed up in specialized centers and, therefore, without the opportunity for global treatment.

It may be that many individuals with TCS who have not received treatment or received treatment outside the centers will have a lower quality of life than those with a follow-up in a specialized craniofacial surgery center. Thus, any generalization of our data is limited to individuals with TCS accompanied in centers of recognized excellence in the treatment of craniofacial deformities and cannot be extrapolated to other scenarios.

Thus, although it is unclear whether the results apply to all individuals with the syndrome, contrary to our initial hypothesis, both groups with TCS (with or without deformity of ears) in our study had high levels of quality of life, suggesting that they have acquired a repertoire to address adverse situations of daily living, which contributes to justify our approach to these individuals, as well as consolidate the need to ensure access to specialized centers even to those with rare syndromes.

Collaborations

FF Lodovichi worked on the application of the questionnaires, on the review of medical records, on the drafting of the paper and had a central role in the bibliographical survey and the final discussion. JP Oliveira worked on the application of the questionnaires, on the review of medical records, on the drafting of the paper and had a central role in the data survey and the statistical analysis. R Denadai worked on the application

of the questionnaires and the project design. CA Raposo-Amaral worked the Review of the final text and the project design. E Ghizoni worked on the discussions of the results and the Review of the final text. CE Raposo-Amaral worked on the planning, the project design and the discussion of results, as well as guided all the stages and reviewed the final text.

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