Journal of Cranio-Maxillo-Facial Surgery 47 (2019) 1285–1291

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Impact of orthognathic surgery on quality of life: Predisposing clinical and genetic factors

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ARTICLE INFO

Article history:
Paper received 17 January 2019
Accepted 4 May 2019
Available online 9 May 2019

Keywords:
Quality of life
Orthognathic surgery
Questionnaire
Genetic predisposition
Prospective clinical trial

ABSTRACT

Introduction: Dentofacial deformities have an impact on quality of life (QOL). Many factors can influence this perception, including genetic aspects. ANKK1 and DRD2 genes are associated with dopaminergic system and could modulate behavioral dysfunction.
Purpose: The impact of orthognathic surgery and associated factors on QOL of adults was evaluated.
Material and methods: The abbreviated World Health Organization Quality of Life questionnaire (WHOQOL-BREF) was applied to patients from two surgery services one week before (T0) and six months after surgery (T1). The independent variables were age, sex, race, facial pattern, presence of jaw asymmetry and vertical deformities, and polymorphisms associated with ANKK1 and DRD2 genes. Descriptive and bivariate analyses were performed.
Results: There was improvement in the perception of QOL from T0 to T1 in the general score, in the physical and psychological domains, and in the quality of life and general health perception (QOLGHP) ($p < 0.001$). In this interval, individuals aged ≥30 years reported positive impacts on all outcomes ($p < 0.05$), whereas in women this improvement did not occur only for the physical domain ($p = 0.136$). There was an association between the polymorphisms associated with the ANKK1 gene (rs1800497) and the perception of QOL in the social relationship's domain ($p = 0.021$) and QOLGHP ($p = 0.042$). The other clinical conditions were not associated with outcomes ($p > 0.05$).
Conclusion: Perception of QOL of patients improved following orthognathic surgery in physical, psychological, and QOLGHP domains. Aged ≥30 years, being women and polymorphisms associated with the ANKK1 gene were related to positive impacts.

1. Introduction

Several dentofacial deformities have a negative impact on quality of life (QOL) (Mendes de Paula Gomes et al., 2018; Ribeiro-Neto et al., 2018; Sun et al., 2018); however, the concept of QOL is associated with subjectivity and multidimensionality (The WHOQOL Group, 1998a) changes over time (Allison et al., 1997) and includes physical, psychological, and social perceptions (Feu et al., 2017). In this context, the aim of orthognathic surgery is to improve function and aesthetic problems in these patients. The physical and psychological implications of interventions used to correct a range of severity of deformities, from moderate to severe, have been assessed (Alves e Silva et al., 2013; Miguel and Palomares, 2014; Bortoluzzi et al., 2015; Brunault et al., 2016; Cariati et al., 2016; Corso et al., 2016; Kurabe et al., 2016; Silva et al., 2016; Alves et al., 2017; Eslamipour et al., 2017; Feu et al., 2017; Pelo et al., 2017; Song and Yap, 2017; Al-Asfour et al., 2018; Lin et al., 2018; Posnick and Kinard, 2019). The results of combined ortho-surgical treatment can be measured both objectively and subjectively. Both factors influence patients' perception of QOL (Miguel and Palomares, 2014; Song and Yap, 2017) and should be considered by the surgeon (Miguel and Palomares, 2014).

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https://doi.org/10.1016/j.jcms.2019.05.001
1010-5182/

Some factors may predispose to improved or worsened perception of QOL in patients undergoing orthognathic surgery, such as age (Montero et al., 2011; Bortoluzzi et al., 2015; Kurabe et al., 2016) and sex (Corso et al., 2016). The influence of genetic aspects has now been observed; a recent study indicated that dopamine D2 receptor (DRD2) is associated with QOL (Sprangers et al., 2014) and ankyrin repeat polymorphism and kinase domain containing 1 (ANKK1) was associated with a 40% reduction in D2 receptor expression (Neville et al., 2004).

The scientific community has sought to develop and validate instruments that determine the subjective perception of the impact of health problems on QOL. There are questionnaires that relate general health and oral health, such as OHIP-14 (Slade, 1997) and the Orthognathic Quality of Life Questionnaire (OQLQ) (Cunningham et al., 2000a, 2000b). Thus, the World Health Organization introduced the World Health Organization Quality of Life (WHOQOL) questionnaire for internationally and cross-culturally comparisons, with a general perception of QOL (The WHOQOL Group, 1998a). Due to WHOQOL being too long, a short version was created, the WHOQOL-BREF (The WHOQOL Group, 1998b). This version includes two general questions of QOL and general perception of health and an additional 24 questions representing four domains: physical, psychological, social relationships and environment (The WHOQOL Group, 1998b). Translation and validation for the Brazilian population was undertaken (Fleck et al., 2000). The questions are answered using four Likert-type scales, depending on the type of question: intensity, capacity, frequency and evaluation (The WHOQOL Group, 1998a; Fleck et al., 2000).

The aim of this study was to evaluate the impact of orthognathic surgery on the perception of patient QOL and identify possible clinical and genetic factors that may be associated with this perception.

2. Material and methods

2.1. Ethical aspects

The research was approved by the Committee of Ethics in Research with Human Beings of Universidade Positivo under register nº 2,423,530.

2.2. Study design and data collection

A prospective observational study design was used; the intended sample size was 102 individuals aged 18 years and over, of both sexes, who underwent orthognathic surgery at the Bucomaxilofacial Surgery Service of the Universidade Federal do Paraná or Universidade Positivo. All participants provided written and informed consent prior to enrolment. The following patients were excluded: those who submitted incomplete (<80% or six questions) (The WHOQOL Group, 1996) or incorrectly-filled consent form, patients who previously received orthognathic surgery, patients undergoing surgical intervention for the treatment of temporomandibular dysfunction and syndromic patients because of the complex constitution regarding the diagnosis, operative time and response to questionnaires.

2.3. Clinical variables

The independent variables were age, sex, facial profile pattern (I, II or III), presence of jaw asymmetry, and presence of vertical deformities in T0. For the association analysis, age was dichotomized (>30 years and ≤30 years). The facial pattern was classified according to Capelozza Filho (2004) whereby pattern I corresponds to facial normality; II is one in which there is a positive step between the maxilla and the mandible; and III is given when this step is negative. Individuals with pattern I may present with skeletal deformities such as excessive or vertical maxillary deficiency, anterior open bite and facial asymmetry; justifying the need for surgical intervention (Reis et al., 2011).

For the evaluation of facial asymmetry, the deviation of the mandibular midline ≥4 mm in relation to the maxillary midline was assessed. The presence or absence of vertical deformity was noted. For patients with a dentofacial deformity, this was classified as vertical maxillary excess, anterior open bite and vertical maxillary deficiency.

2.4. DNA collection and genotyping

DNA was obtained from buccal mucosal epithelial cells according to an established protocol (Trevilatto and Line, 2000) by a single trained operator (JTG) and purified with ammonium acetate at 10 M and 1 mM EDTA (Aidar and Line, 2007). The genetic polymorphisms in DRD2 and in ANKK1, both genes located in 11q23.2, were chosen based on the GENEQOL consortium, the relationship between DRD2 and the social functioning QOL domain (Sprangers et al., 2014) and their minor allele frequency (>30%). Genotyping of polymorphism in ANKK1 (rs1800497 [A/G]) and DRD2 (rs6275 [A/G] and rs6276 [C/T]) was undertaken using real-time PCR (StepOnePlus™ Real-time PCR System) with the TaqMan™ assay (Applied Biosystems, Foster City, CA, USA). The genotyping was performed by a single operator (MNM) with training and a lot experience.

2.5. Statistical analysis

Pre and post-surgery evaluations, in relation to the applied questionnaire scores (general and by domains) were compared using the Wilcoxon non-parametric test. Chi-square was also used to test Hardy–Weimberg equilibrium. To evaluate the association between genetic polymorphism and the perception of QOL in preoperative patients, Kruskal–Wallis and Mann–Whitney tests were used in the co-dominant model and in the recessive model. Statistical significance was indicated if $p < 0.05$. Data were analyzed using SPSS v.20.0 (IBM® SPSS®, Armonk, NY, USA) by an independent statistician.

3. Results

Of the patients, 102 were evaluated for QOL and other clinical variables at T0, of which 59 returned to the postoperative surgery service providing data for QOL in T1. Regarding the clinical variables, the most common facial pattern was type III (56.9%). The mandibular asymmetry and the presence of vertical deformities were found in 24.5% and 21.6% of the sample, respectively. In cases where vertical deformities were present, vertical maxillary excess was identified in 68.2%, anterior open bite in 27.3%, and vertical maxillary deficiency in 4.5% of patients. In T0, the mean age was 30.4 years (SD = 9.9); 52 individuals were in the <30 years-old group and 50 individuals were in the ≥30 years old group, with a predominance of females (60.8%) in T0. In T1, the mean age was 30.69 (SD = 9.18), 30 individuals were in the <30 years group and 29 individuals were in the ≥30 years-old group, with a predominance of females (59.3%). Age group and gender were not statistically different between the groups ($p > 0.05$).

Table 1 shows the QOL scores and respective domains for the evaluations at T0 and T1 times. It was observed that the general perception scores, physical and psychological domains, and QOLGHP increased from T0 to T1 ($p < 0.001$), indicating that orthognathic surgery had a positive impact on QOL improvement.

Table 1
Comparison between T0 and T1 of the general score and by domains, in the different times of evaluation of patients submitted to orthognathic surgery (n = 59).

Variable	Evaluation	Median (min–max)	P value
General score	T0	14.8 (9.1–18.5)	
	T1	15.5 (12.3–19.4)	**<0.001**
Physical domain	T0	16.0 (9.1–20.0)	
	T1	16.8 (11.4–20.0)	**<0.001**
Psychological domain	T0	14.7 (4.6–18.7)	
	T1	16.0 (11.3–19.3)	**<0.001**
Social relationships domain	T0	16.0 (8.0–20.0)	
	T1	16.0 (8.0–20.0)	0.075
Environment domain	T0	14.0 (8.6–19.0)	
	T1	14.5 (8.0–19.0)	0.095
QOLGHP	T0	16.0 (8.0–20.0)	
	T1	16.0 (12.0–20.0)	**<0.001**

Note: Bold values are statistically significant.
Wilcoxon test, $p < 0.05$.

In the analysis stratified by age, having ≥30 years resulted in individuals experiencing improved QOL perception after orthognathic surgery in all outcomes analyzed ($p < 0.05$). Patients with <30 years showed an improvement in QOL after surgery only for the psychological domain ($p = 0.031$) and for QOLGHP ($p = 0.033$) (Table 2).

The values of the medians, with respective minimum and maximum, but with significant difference in the times of evaluation, in the age <30 years, for the variable QOLGHP, are explained by means presented here: T0 = 15.6 and in T1 = 16.5. The same is explained for the social relations domain at age ≥30 years, in which: T0 = 15.1 and in T1 = 16.2.

Table 3 shows the results of the association between the outcomes at the time of evaluation, stratified by sex. In this analysis, it was observed that men showed improvement in the perception of QOL in the general score ($p = 0.010$), in the physical ($p = 0.001$) and psychological ($p = 0.004$) and QOLGHP domains ($p < 0.001$). In women, this improvement was noted for all the domains, except for the physical ($p = 0.136$), which shows how women felt the impacts more and in more dimensions.

No association was identified between outcomes and facial pattern, presence of mandibular asymmetry and presence of vertical deformities at the times evaluated ($p > 0.05$).

An association was identified at T0 between the polymorphism associated with the ANKK1 gene (rs1800497) and the perception of QOL of the patients in the social relations domain ($p = 0.021$) and in the QOLGHP ($p = 0.042$). Individuals homozygous for the T allele were found to have a better perception of the QOL than the heterozygous individuals. There was no association with any of the genetic markers and QOL in T1 (Table 4).

In the T0, in the dominant model C, there was an association between the perception of QOL and the ANKK1 gene, in the marker rs1800497 in the general score ($p = 0.025$), the social relations domain ($p = 0.006$) and the QOLGHP ($p = 0.018$). Homozygous T subjects were found to have a better perception of QOL. No associations were found in the other models ($p > 0.05$).

4. Discussion

This study aimed to evaluate the impact of orthognathic surgery on the QOL of adult patients and possible associated factors, with measurements taken in the preoperative and postoperative stages. In general, the findings indicated that surgical intervention promoted the improvement of this perception, as previously observed by other authors (Corso et al., 2016; Kurabe et al., 2016; Silva et al., 2016; Alves et al., 2017; Eslamipour et al., 2017; Feu et al., 2017; Pelo et al., 2017; Mendes de Paula Gomes et al., 2018; Ribeiro-Neto et al., 2018; Sun et al., 2018; Al-Asfour et al., 2018; Lin et al., 2018; Posnick and Kinard, 2019).

The impact that oral conditions have on patient QOL is a relevant issue (Haag et al., 2017), with emphasis on the negative influence of dentofacial deformities (Mendes de Paula Gomes et al., 2018; Ribeiro-Neto et al., 2018; Sun et al., 2018). Orthognathic surgeries aim to improve the functional and aesthetic conditions of these alterations (Proffit et al., 2007) and it's physical and psychological impacts have been evaluated (Alves e Silva et al., 2013; Miguel and Palomares, 2014; Bortoluzzi et al., 2015; Brunault et al., 2016; Cariati et al., 2016; Corso et al., 2016; Kurabe et al., 2016; Silva

Table 2
Results of the association between outcomes at different times of evaluation of patients submitted to orthognathic surgery, stratified by age (n = 59).

Age (in years)	Variable	Evaluation	Median (min–max)	*P* value
<30	General score	T0	15.1 (13.5–18.0)	
		T1	15.6 (13,5–18.5)	0.225
	Physical domain	T0	17.1 (13.1–20.0)	
		T1	16.6 (13.7–19.4)	0.819
	Psychological domain	T0	14.7 (10.0–18.0)	
		T1	16.0 (11.3–18.7)	**0.031**
	Social relationships domain	T0	16.0 (12.0–20.0)	
		T1	16.0 (12.0–20.0)	0.715
	Environment domain	T0	14.5 (11.5–17.5)	
		T1	15.0 (11.5–18.5)	0.778
	QOLGHP	T0	16.0 (12.0–20.0)	
		T1	16.0 (12.0–20.0)	**0.033**
≥30	General score	T0	14.5 (9.1–18.5)	
		T1	15.5 (12.3–19.4)	**<0.001**
	Physical domain	T0	14.9 (9.1–18.9)	
		T1	17.1 (11.4–20.0)	**<0.001**
	Psychological domain	T0	14.7 (4.6–18.7)	
		T1	16.0 (11.3–19.3)	**0.003**
	Social relationships domain	T0	16.0 (8.0–20.0)	
		T1	16.0 (8.0–20.0)	**0.048**
	Environment domain	T0	13.5 (8.6–19.0)	
		T1	14.0 (8.0–19.0)	**0.045**
	QOLGHP	T0	14.0 (8.0–18.0)	
		T1	16.0 (12.0–20.0)	**<0.001**

Note: Bold values are statistically significant.
Wilcoxon test, $p < 0.05$.

Table 3
Results of the association between outcomes at different times of evaluation of patients submitted to orthognathic surgery, stratified by sex (n = 59).

Sex	Variable	Evaluation	Median (min–max)	*P* value
Male	General score	T0	14.8 (9.1–18.5)	
		T1	15.5 (12.3–19.4)	**0.010**
	Physical domain	T0	16.0 (9.1–18.9)	
		T1	17.1 (11.4–20.0)	**0.001**
	Psychological domain	T0	14.7 (4.6–18.3)	
		T1	16.0 (11.3–19.3)	**0.004**
	Social relationships domain	T0	16.0 (8.0–20.0)	
		T1	16.0 (8.0–20.0)	0.679
	Environment domain	T0	14.0 (8.6–19.0)	
		T1	14.0 (8.0–19.0)	0.524
	QOLGHP	T0	16.0 (8.0–18.0)	
		T1	16.0 (12.0–20.0)	**<0.001**
Female	General score	T0	14.8 (12.0–18.0)	
		T1	15.8 (13.4–19.2)	**0.006**
	Physical domain	T0	16.6 (13.1–20.0)	
		T1	16.7 (13.7–20.0)	0.136
	Psychological domain	T0	14.7 (10.0–18.7)	
		T1	15.7 (11.3–18.7)	**0.017**
	Social relationships domain	T0	14.7 (12.0–20.0)	
		T1	16.0 (12.0–20.0)	**0.016**
	Environment domain	T0	14.0 (9.5–18.0)	
		T1	14.8 (11.0–19.0)	**0.041**
	QOLGHP	T0	16.0 (8.0–20.0)	
		T1	16.0 (12.0–20.0)	**0.033**

Note: Bold values are statistically significant.
Wilcoxon test, $p < 0.05$.

et al., 2016; Alves et al., 2017; Eslamipour et al., 2017; Feu et al., 2017; Pelo et al., 2017; Song and Yap, 2017; Al-Asfour et al., 2018; Lin et al., 2018; Posnick and Kinard, 2019). Tools such as OHIP-14 (Corso et al., 2016) and it's variations (Kurabe et al., 2016), the OQLQ (Eslamipour et al., 2017; Al-Asfour et al., 2018; Ribeiro-Neto et al., 2018) or a combined questionnaire (Silva et al., 2016; Alves et al., 2017; Feu et al., 2017; Pelo et al., 2017; Mendes de Paula Gomes et al., 2018; Sun et al., 2018), are proposed in this analysis.

The WHOQOL-BREF was the questionnaire chosen for this research because it is an instrument that reflects the multidimensionality of the general QOL, being worldwide used, with a version translated and adapted for Brazilian populations (Fleck et al., 2000). This questionnaire has been used infrequently for the assessment of QOL following orthognathic surgery (Brunault et al., 2016; Alves et al., 2017).

Despite using differing methods of assessment, results similar to those presented here reinforce the significant difference in the perception of improved QOL in the postoperative phase (Corso et al., 2016; Kurabe et al., 2016; Silva et al., 2016; Alves et al., 2017; Eslamipour et al., 2017; Feu et al., 2017; Pelo et al., 2017; Mendes de Paula Gomes et al., 2018; Ribeiro-Neto et al., 2018; Sun et al., 2018; Al-Asfour et al., 2018).

Brunault et al. (2016) found an improvement in psychological and social QOL and depression in one year after surgery, as measured by WHOQOL-BREF. The perception of the physical domain was worse in young patients with mild dentofacial deformity and in those with depression; the psychological domain was also worse for the young and for the depressed, whereas the worse perception of social relations was reported by single patients with mild dentofacial deformity and those suffering from depression.

The mean age of 30 years observed in this study indicates that there is a greater demand for orthognathic surgeries in young patients (Alves e Silva et al., 2013; Castro et al., 2013). In the present study, younger individuals (<30 years old) did not show significant improvement in the physical domain after intervention, contrary to findings in older patients. At the times analyzed, these young people only had more perception of the impact in the psychological domain and the QOLGHP. This can be explained by a tendency towards dissatisfaction regarding appearance noted in young people, reflected in worsening perception of QOL and an early search for ortho-surgical procedures (Liddle et al., 2018). Contrastingly, those aged 30 years or older had a significant improvement in all outcomes analyzed at different times. A significantly higher QOL score has been observed in older patients, compared to young people with facial deformities, following orthognathic surgery (Kurabe et al., 2016). Bortoluzzi et al. (2015), in an analysis of the impact of dentofacial deformities on the QOL of patients 12–52 years old, emphasized that the advancement of age negatively compromises this perception, mainly in the aesthetic and functional domains. In another study, patients over 45 years of age, regardless of sex, were more likely to experience negative impact on QOL and less satisfaction with oral health (Montero et al., 2011). Regarding the psychological aspects, perception of the QOL improved in both age groups, but not significantly in the present analysis. Other studies have found similar results regarding the environment domain, to those reported here (Alves e Silva et al., 2013).

The higher proportion of female participants in this study, similar to those in previous studies involving orthognathic surgery (Castro et al., 2013; Corso et al., 2016; Kurabe et al., 2016; Al-Asfour et al., 2018), relates to the fact that they perceive the impacts of QOL intervention more than men, as has been reported by other authors (Corso et al., 2016). In addition, it is recognized that women seek more health services (Green and Pope, 1999; Thompson et al., 2016) and are more concerned with aesthetic issues that motivate them undergo surgery (Johnston et al., 2010; Al-Asfour et al., 2018).

The facial pattern III was the most prevalent in this sample, probably due to the greater presence of women who do not accept the mentioned pattern for aesthetic reasons. The facial profile with mandibular retrusion or the straight profile is considered more aesthetically pleasing in women (Oliveira et al., 2015; Jovic et al., 2016). However, in this study, the facial pattern did not influence the perception of QOL. It is known that the more severe the facial deformities, the greater the postoperative changes in appearance and, consequently, the more impacts in several areas of the subjects' lives (Alves e Silva et al., 2013). In the study in question the

Table 4
Association between genotypes and QOL in T0 and T1 of patients submitted to orthognathic surgery (n = 59).

Genes	Genotypes	n	Quality of life											
			General score		Physical		Psychological		Social relationships		Environment		QOLGHP	
			Median (min–max)	*P* value	Median (min–max)	*P* value	Median (min–max)	*P* value	Median (min–max)	*P* value	Median (min–max)	*P* value	Median (min–max)	*P* value
T0														
	TT	54	15.5 (9.1–19.1)		16.6 (9.1–20.0)		15.3 (4.6–18.6)		16.0[a] (8.0–20.0)		14.5 (8.6–19.5)		16.0[a] (8.0–20.0)	
ANKK1 rs1800497	CT	36	14.6 (10.8–17.9)	0.077	15.1 (10.2–19.4)	0.164	14.7 (8.7–18.3)	0.307	14.7[b] (10.0–20.0)	**0.021**	13.7 (9.5–18)	0.094	14.0[b] (8.0–18.0)	**0.042**
	CC	4	14.7 (13.8–16.8)		16.6 (14.9–17.1)		12.3 (11.3–18.0)		16[ab] (13.3–16.0)		15.0 (13.5–16)		15.0[ab] (14.0–16.0)	
	TT	43	14.8 (10.8–19.1)		16.6 (10.2–20.0)		14.7 (8.7–18.7)		16.0 (10.0–20.0)		14.0 (9.5–19.5)		16.0 (8.0–20.0)	
DRD2 rs6275	CT	33	15.1 (9.1–18.1)	0.798	16.0 (9.1–20.0)	0.597	15.3 (9.3–17.3)	0.685	16.0 (8.0–20.0)	0.514	14.0 (8.6–18.5)	0.906	16.0 (10.0–20.0)	0.569
	CC	15	15.2 (10.5–17.8)		15.4 (10.9–18.9)		15.3 (4.6–18.0)		16.0 (10.7–20.0)		14.5 (11.5–17.5)		14.0 (8.0–20.0)	
	GG	38	15.1 (11.1–19.1)		16.9 (10.2–20.0)		14.7 (8.7–18.7)		16.0 (10.0–20.0)		14.3 (9.5–19.5)		16.0 (8.0–20.0)	
DRD2 rs6276	AG	37	14.8 (9.1–18.1)	0.968	16.0 (9.1–20.0)	0.508	15.3 (9.3–17.3)	0.997	16.0 (8.0–20.0)	0.906	14.0 (8.6–18.5)	0.906	16.0 (10.0–20.0)	0.606
	AA	15	15.2 (10.5–17.8)		15.4 (10.9–18.9)		15.3 (4.6–18.0)		16.0 (10.7–20.0)		14.5 (11.5–17.5)		14.0 (8.0–20.0)	
T1														
	TT	31	15.4 (13.5–18.9)		16.8 (13.7–20.0)		15.3 (11.3–18.7)		16.0 (12.0–20.0)		14.5 (11.0–19.0)		16.0 (12.0–20.0)	
ANKK1 rs1800497	CT	23	15.5 (12.3–19.4)	-	16.6 (11.4–20.0)	-	16.0 (11.3–19.3)	-	16.0 (13.3–20.0)	-	14.5 (8.0–19.0)	-	16.0 (12.0–20.0)	-
	CC	3	16.5 (12.6–16.8)		18.3 (16.0–18.9)		17.3 (11.3–18.0)		16.0 (8.8–16.0)		14.5 (11.5–15.0)		16.0 (14.0–20.0)	
	TT	29	16.0 (12.3–19.4)		17.1 (11.4–20.0)		16.0 (11.3–19.3)		16.0 (8.0–20.0)		15.0 (8.0–19.0)		16.0 (12.0–20.0)	
DRD2 rs6275	CT	16	15.5 (13.8–17.2)	0.755	16.6 (15.4–19.4)	0.821	15.7 (13.3–17.3)	0.745	16.0 (12.0–20.0)	0.484	14.0 (11.0–15.5)	0.364	16.0 (12.0–20.0)	0.327
	CC	12	15.5 (13.5–18.3)		16.9 (14.3–19.4)		14.7 (11.3–18.7)		16.0 (12.0–20.0)		14.8 (13.0–18.5)		16.0 (12.0–18.0)	
	GG	26	16.2 (12.3–19.4)		17.1 (11.4–20.0)		16.0 (11.3–19.3)		16.0 (8.0–20.0)		15.0 (8.0–19.0)		16.0 (12.0–20.0)	
DRD2 rs6276	AG	18	15.5 (13.8–17.2)	0.719	16.6 (15.4–19.4)	0.705	15.7 (13.3–17.3)	0.696	16.0 (12.0–20.0)	0.541	13.8 (11.0–15.5)	0.268	16.0 (12.0–20.0)	0.404
	AA	12	15.5 (13.5–18.3)		16.9 (14.3–19.4)		14.7 (11.3–18.7)		16.0 (12.0–20.0)		14.1 (13.0–18.5)		16.0 (12.0–18.0)	

Note: Bold values are statistically significant. Different letters indicate statistical significance.
Kruskal–Wallis and Mann–Whitney test, $p < 0.05$.

patients' discrepancy was not quantified, so patients with 3 mm or 13 mm of discrepancy were in the same group. It is known that the heterogeneity of the deformities is considered as a limitation, as it is suggested that homogeneity promotes more reliable results (Zhou et al., 2001). The lack of association between the clinical variables facial profile, asymmetry and vertical deformities with the outcomes analyzed in this research may also be related to the absence of a control group.

Regarding the genetic aspects, we found an association between the polymorphism in the ANKK1 gene and the QOL perception in the domain of social relations and QOLGHP. In the general score and in the environment domain, the values were borderline, reinforcing the existence of this association. ANKK1, which is considered a gene proximal to DRD2, may influence the expression of the latter. In addition, an association was found between QOL and DRD2 (Sprangers et al., 2014), which is related to depression (Opmeer et al., 2010; Kao et al., 2011), anxiety (Lawford et al., 2003), and positive behaviors (Lawford et al., 2013). ANKK1 has been associated with an approach to motivation in patients with schizophrenia (Alfimova et al., 2018) and individual sensitivity to reward and response to social cues and reinforcements (Marino et al., 2004), which may justify the association found between the best perception of QOL found in individuals at T0.

Among the limitations of the present research is the difference in the number of patients evaluated at T0 and T1. This was due to non-return after six months of intervention. The same difficulty was observed by other researchers (Corso et al., 2016), since the two services of outstanding surgery are public and of reference in the state, so many patients may travel a long distance for the procedure and are therefore not available for post-operative assessment. However, this time frame has been considered relevant for a prospective analysis of the cases, since patient recovery is more advanced, results can be visualized due to the reduction of edema and social interaction has returned to normal (Choi et al., 2010; Alves e Silva et al., 2013; Kurabe et al., 2016; Silva et al., 2016). In this study, we chose to apply the questionnaire in the preoperative phase, a week prior to the procedure. This may have had an impact on the results, since the patients evaluated here were undergoing conventional preparation, consisting of orthodontic treatment prior to the surgical procedure with the intention of decompensating them, which promotes a worsening in their condition. This prior analysis is discouraged by some authors (Meade and Inglehart, 2010) because the patient is generally still physically and psychologically affected. An alternative approach has been to apply the questionnaire on the day prior to the procedure (Alves e Silva et al., 2013).Previous studies have shown that psychological aspects strongly influence the patients' QOL (Miguel and Palomares, 2014; Song and Yap, 2017). Not only postoperative evaluations must be done, but psychological analysis prior to orthognathic surgery are necessary, once this would allow that disorders such as anxiety, depression and panic syndrome be investigated, increasing the chance of successful surgery (Bellucci and Kapp-Simon, 2007). In general, surgeons focus on the clinical aspects (functional and aesthetic changes) that initiate the patient to investigate orthognathic surgery as well as on the planning of the procedure, and forget to evaluate the individual as a whole (Miguel and Palomares, 2014; Storms et al., 2017). The absence of consideration of the psychological aspects of the surgery may compromise the patient's acceptance, perception and expectations regarding the procedure.

5. Conclusion

In this study, orthognathic surgery improved the QOL reported by patients in physical, psychological, and QOLGHP domains. Older aged (≥30 years old), women and polymorphisms in *ANKK1* gene were related to positive impacts.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

M. Gabardo: None declared. J. Zielak: None declared. G. Tórtora: None declared. J. Gerber: None declared. M. Meger: None declared. N. Rebellato: None declared. E. Küchler: None declared. R. Scariot: None declared.

Contribution to the study

M. Gabardo: Study conception and design, drafting of manuscript.

J. Zielak: Study conception and design, drafting of manuscript.

G. Tórtora: Acquisition, analysis and interpretation of data.

J. Gerber: Acquisition, analysis and interpretation of data.

M. Meger: Acquisition of data, drafting of manuscript.

N. Rebellato: Study conception and design, revising manuscript.

E. Küchler: Study conception and design, revising manuscript.

R. Scariot: Study conception and design, acquisition of data, final approval of manuscript.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.05.001.

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