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Influence of heritability on craniofacial soft tissue characteristics of monozygotic twins, dizygotic twins, and their siblings using Falconer's method and principal components analysis

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Objective: The purpose of this study was to investigate the influence of heritability on the craniofacial soft tissue cephalometric characteristics of monozygotic (MZ) twins, dizygotic (DZ) twins, and their siblings (SIB). **Methods:** The samples comprised Korean adult twins and their siblings (mean age, 39.8 years; MZ group, n = 36 pairs; DZ group, n = 13 pairs of the same gender; and SIB group, n = 26 pairs of the same gender). Thirty cephalometric variables were measured to characterize facial profile, facial height, soft-tissue thickness, and projection of nose and lip. Falconer's method was used to calculate heritability (low heritability, $h^2 < 0.2$; high heritability, $h^2 > 0.9$). After principal components analysis (PCA) was performed to extract the models, we calculated the intraclass correlation coefficient (ICC) value and heritability of each component. **Results:** The MZ group exhibited higher ICC values for all cephalometric variables than DZ and SIB groups. Among cephalometric variables, the highest $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values were observed for the nasolabial angle (NLA, 1.544 and 2.036), chin angle (1.342 and 1.112), soft tissue chin thickness (2.872 and 1.226), and upper lip thickness ratio (1.592 and 1.026). PCA derived eight components with 84.5% of a cumulative explanation. The components that exhibited higher values of $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ were PCA2, which includes facial convexity, NLA, and nose projection (1.026 and 0.972), and PCA7, which includes chin angle and soft tissue chin thickness (2.107 and 1.169). **Conclusions:** The nose and soft tissue chin were more influenced by genetic factors than other soft tissues.
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Key words: Twin study, Craniofacial soft tissue characteristics, Cephalometric analysis, Heritability

INTRODUCTION

It is an important clinical issue to determine which craniofacial structures are influenced by genetic factors and cannot be significantly changed by orthodontic and/or orthopedic treatment. Although there have been numerous previous studies regarding the heritability of craniofacial structures, most investigations have focused on the heritability of skeletal tissue and dentition.[1-8] A recent paradigm in the orthodontic field is soft tissue-based diagnosis.[9,10] However, there has been a lack of heritability research regarding craniofacial soft tissues that determine actual facial appearance. The methodologies frequently used in craniofacial soft tissue studies include two-dimensional (2D) digital photographs, 2D cephalograms, three-dimensional (3D) scanning, 3D digital stereophotogrammetry, magnetic resonance imaging, computed tomography (CT), and/or ultrasound scans.[11-18] However, there are limitations in using "cutting-edge" technology in terms of cost, radiation dosage, and availability of equipment. Therefore, in this study, 2D cephalometric analysis was conducted because of its low cost and ease of use in clinical situations.

In terms of genetic influence on craniofacial structure, Vanco et al.[11] suggested that the shape of the nose and lip might be under strong genetic influences. Naini and Moss[12] reported that the strongest genetic influence was demonstrated on the triangular area of the midface, which encompasses the lateral orbital rims, intercanthal area, and nose. Similarly, Weinberg et al.[16] proposed that the length and width of the central midface exhibited high heritability. To the best of our knowledge, only a single study has been performed regarding the heritability of craniofacial structures in Korean twins and their families. Kim et al.[15] performed factor analysis and extracted three factors (lower face portion, orbital region, and vertical length) that demonstrated low-to-moderate heritability. However, there are several considerations that affect interpretation of their study. First, their samples consisted of individuals from 38 families, rather than twins.[15] Second, they used 2D digital photographs,[15] rather than the cephalometric radiographs that constitute a universal diagnostic tool in the orthodontic field. Third, they only measured linear variables between two landmark points,[15] rather than angular and ratio cephalometric variables, which more clearly describe the shape of the craniofacial region.

Therefore, this study was undertaken to investigate the influence of heritability on craniofacial soft tissue cephalometric characteristics of monozygotic (MZ) twins, dizygotic (DZ) twins and their siblings with linear, angular, and ratio cephalometric variables. The null hypotheses were as follows: (1) there was no significant difference in the heritability of craniofacial soft tissue cephalometric characteristics of MZ and DZ twins and their siblings; and (2) there were no significant differences in the heritability of facial profile, facial height, soft tissue thickness, or projection of the nose and lip.

MATERIALS AND METHODS

This retrospective study was performed by using initial samples (553 Korean adult twins and their families) whose lateral cephalometric radiograms were taken at the Samsung Medical Center, Seoul, South Korea. Exclusion criteria were as follows: (1) those who had an edentulous area within the anterior teeth, which could affect facial profile; (2) those who had a removable prosthesis that could affect the vertical dimension of the face; (3) those who had undergone orthodontic treatment, orthognathic surgery, or craniofacial plastic surgery; and (4) those whose age was < 19 years old.[19] The twin study protocol was reviewed and approved by the Institutional Review Board, School of Public Health, Seoul National University, Seoul, South Korea (IRB 2005-08-113-027). Informed consent was obtained from all subjects. The final samples consisted of 150 individuals (75 pairs; MZ twins, n = 36 pairs; DZ twins, n = 13 pairs; and siblings [SIB], n = 26 pairs; Table 1). Among the initial samples, sibling pairs were selected from families with MZ or DZ twins. Pairs of DZ twins and SIBs were matched with respect to gender (Table 1). To minimize the age effect, SIB pairs were selected with an age difference of ≤ 5 years (Table 1).

Lateral cephalograms were taken in the natural head position. Landmarks and reference lines used for cephalometric measurement are illustrated in Figures 1 and 2. To investigate which area was significantly affected

Table 1. Demographic characteristics of the samples

Pairs		Number (%)	Age (yr)
Type			
MZ	Male	16 (21.33)	41.0 ± 7.90 (26–57)
	Female	20 (26.67)	38.6 ± 7.56 (24–58)
DZ	Male	7 (9.33)	42.21 ± 9.15 (34–63)
	Female	6 (8.00)	43.67 ± 4.66 (38–48)
SIB	Male	11 (14.67)	32.18 ± 8.32 (20–47)
	Female	15 (20.00)	42.8 ± 11.64 (20–60)
Sex	Male	34 (45.33)	39.40 ± 9.26 (20–63)
	Female	41 (54.67)	40.88 ± 9.17 (20–60)
Total		75 (100)	39.75 ± 9.26 (20–63)

Values are presented as number (%) or mean ± standard deviation (range).
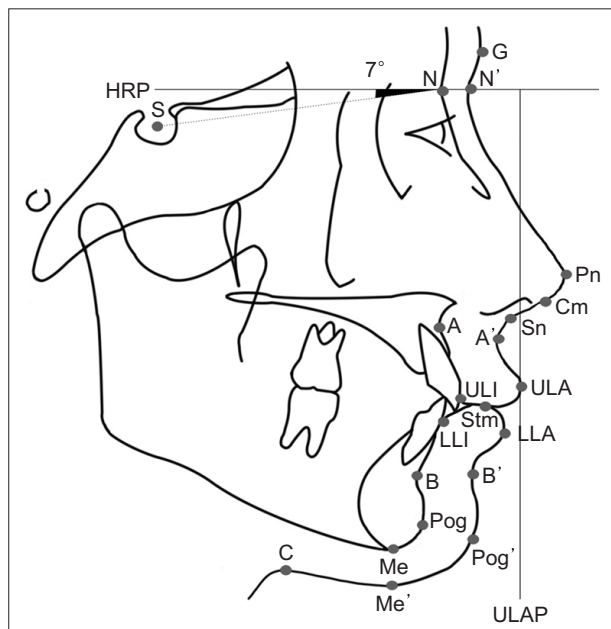MZ, Monozygotic twin; DZ, dizygotic twin; SIB, sibling.

Figure 1. Landmarks and reference planes used in the cephalometric analysis. S, Sella; N, nasion; A, A point; B, B point; Pog, pogonion; Me, menton; G, glabella; N', soft tissue nasion; Pn, pronasale; Cm, columella; Sn, subnasale; A', soft tissue A point; ULA, upper lip anterior; Stm, stomion; ULI, upper lip inside; LLI, lower lip inside; LLA, lower lip anterior; B', soft tissue B point; Pog', soft tissue pogonion; Me', soft tissue menton; C, cervical point; HRP, horizontal reference plane, a horizontal plane angulated 7° clockwise to the SN line passing through Sella; ULAP, ULA perpendicular plane to HRP, a perpendicular line to the HRP passing through ULA.

by heredity, craniofacial soft tissue characteristics were divided into four parts: facial profile, facial height, soft tissue thickness, and projection of the nose and lip. A total of 30 linear, angular, and ratio cephalometric variables were measured to identify the characteristics of the four designated parts. All measurements were performed by a single operator (JMS) with V-Ceph 7.0 program (Cybermed, Seoul, Korea). To verify the reliability of measurement, 20 randomly selected subjects were remeasured by the same operator (JMS) after 4 weeks to calculate intra-correlation, the results of which were valid ($p < 0.01$). Since there were no significant differences between the first and second measurements, we employed the first set of measurements.

Intraclass correlation coefficient (ICC)

The ICC values of 30 cephalometric variables in the MZ, DZ, and SIB groups were calculated through reliability analysis, as follows.[20]

$$ICC = (MS_{between} - MS_{within}) / (MS_{between} + MS_{within})$$

MS_{within}: the mean-square estimates of within-pair variance

$MS_{between}$: the mean-square estimate of between-pair variance

A particular phenotype appears as a sum of genetic and environmental factors. In a narrow sense, heritability (h^2) can be defined as the proportion of trait variances influenced by genetic factors, rather than by environmental factors.[19] Since MZ twins share identical genes, the genetic effect is equal in MZ twins.[19] DZ twins or their siblings of the same gender share half of their genes.[19] An estimate of heritability is approximately twice the difference in ICC between MZ and DZ or between MZ and SIB.[19-21] A higher ICC value indicates higher concordance of variables in the twin pair. Falconer's method was used to calculate heritability[19-21]; it is simple and easy to apply for calculating the heritability of craniofacial variables because it uses the difference in ICC between MZ and DZ or between MZ and SIB.

$h^2_{(MZ-DZ)} = 2 (ICC_{MZ} - ICC_{DZ})$ and $h^2_{(MZ-SIB)} = 2 (ICC_{MZ} - ICC_{SIB})$, where ICC_{MZ} corresponds to ICC of MZ pairs; ICC_{DZ} corresponds to ICC of DZ pairs; and ICC_{SIB} corresponds to ICC of SIB pairs.

h^2 values close to or below 0 are regarded as low heritability; h^2 values close to or above 1 are regarded as high heritability.[19-21] In the present study, h^2 values < 0.2 were considered low heritability; values > 0.9 were considered high heritability, similar to the criteria of Kim et al.[19]

Principal components analysis (PCA) is a useful statistical technique to find a pattern in data with a high number of dimensions; it uses an orthogonal transformation to convert a set of observations of possibly correlated variables into a set of values of linearly uncorrelated variables, known as principal components.[6,15,16,22,23] In recent years, PCA has been applied to gain a more intuitive understanding of craniofacial variables.[6,15,16,22,23] PCA with Kaiser normalization varimax rotation was used to extract factors by grouping 30 cephalometric variables based on statistical correlation (cut-off value, > 1). After the arithmetic means of variable ICC values were calculated as the ICC value of each factor, h^2 was calculated to understand the heritability of the craniofacial soft tissues. All statistical analyses were performed by using SPSS with a significance level of 0.05 (IBM SPSS Statistics version 21, IBM Corp., Armonk, NY, USA).
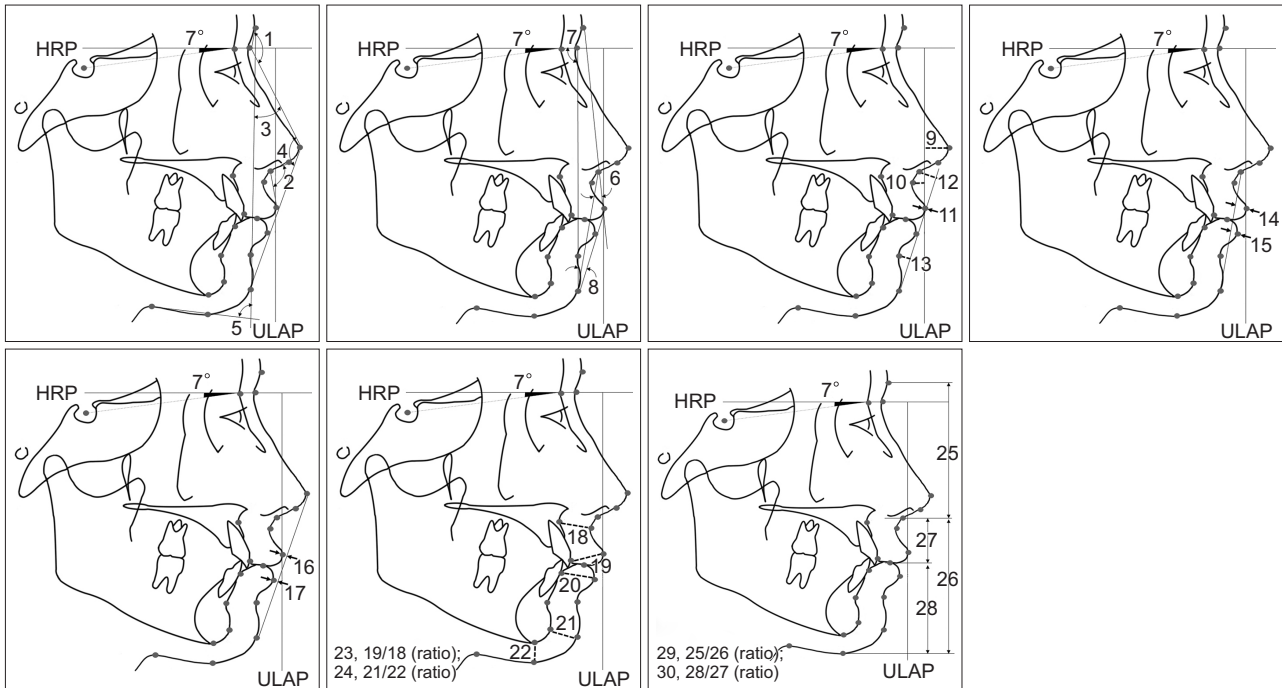
Figure 2. Cephalometric variables.
Facial profile: 1, G-N'-Pn (angle determined by points G, N', and Pn); 2, Cm-Sn-ULA (angle determined by points Cm, Sn, and ULA); 3, GPog'-N'Pn (angle formed by G-Pog' and N'-Pn lines); 4, N'-Pn-Pog' (angle determined by points N', Pn and Pog'); 5, GPog'-Me'C (angle formed by G-Pog' and Me'C lines); 6, G-Sn-Pog' (angle determined by points G, Sn, and Pog'); 7, HRP-N'Pog' (angle formed by HRP and N'Pog' lines); 8, N'-Pog'-ULA (angle determined by points N', Pog' and ULA'). Projection of nose and lip: 9, Pn-ULAP perp (perpendicular distance from point Pn to ULAP in mm); 10, A'-ULAP perp (perpendicular distance from point A' to ULAP in mm); 11, LLA-ULAPog' perp (perpendicular distance from point LLA to ULA-Pog' line in mm); 12, Sn-ULAPog' perp (perpendicular distance from point Sn to ULA-Pog' line in mm); 13, B'-ULAPog' perp (perpendicular distance from point B' to ULA-Pog' line in mm); 14, ULA-SnPog' perp (perpendicular distance from point ULA to Sn-Pog' line in mm); 15, LLA-SnPog' perp (perpendicular distance from point LLA to Sn-Pog' line in mm); 16, ULA-PnPog' perp (perpendicular distance from point ULA to Pn-Pog' line in mm); 17, LLA-PnPog' perp (perpendicular distance from point LLA to Pn-Pog' line in mm). Soft tissue thickness: 18, A-A' (distance between points A and A' in mm); 19, ULI-ULA (distance between points ULI and ULA in mm); 20, LLI-LLA (distance between points LLI and LLA in mm); 21, Pog-Pog' (distance between points Pog and Pog' in mm); 22, Me-Me' (distance between points Me and Me' in mm); 23, ULI-ULA/A-A' (the ratio of the distance between points ULI and ULA to the distance between points A and A'); 24, Pog-Pog'/Me-Me' (ratio of the distance between points Pog and Pog' to the distance between points Me and Me'). Facial height: 25, G-Sn (vertical height between point G and Sn in mm); 26, Sn-Me' (vertical height between point Sn and Me' in mm); 27, Sn-Stm (vertical height between point Sn and Stm in mm); 28, Stm-Me' (vertical height between point Stm and Me' in mm); 29, G-Sn/Sn-Me' (ratio of the distance between points G and Sn to the distance between points Sn and Me'); 30, Stm-Me'/Sn-Stm (ratio of the distance between points Stm and Me' to the distance between points Sn and Stm).
See Figure 1 for definition of each landmark.

RESULTS

ICC values of MZ, DZ, and SIB groups

The MZ group exhibited higher ICC values for all cephalometric variables, compared to the DZ and sibling groups (Table 2), which indicates that soft tissue measurements in each pair were most similar in MZ twins, compared to DZ twins and their siblings. In particular, N'-Pn-Pog' (°, 0.919, $p < 0.001$), G-Sn-Pog' (°, 0.935,

$p < 0.001$), Sn-ULAPog' perp (mm, 0.912, $p < 0.001$), ULA-SnPog' perp (mm, 0.911, $p < 0.001$), Sn-Me' (mm, 0.946, $p < 0.001$), and Stm-Me' (mm, 0.939, $p < 0.001$) showed high ICC values in the MZ group (Table 2).

Heritability values in $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$

For cephalometric measurements, the highest $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values were observed at the nasolabial angle (Cm-Sn-ULA [°], 1.544 and 2.036), chin angle (GPog'-

Table 2. Intraclass correlation coefficients (ICCs) in the monozygotic (MZ), dizygotic (DZ), and sibling (SIB) groups

Variable	ICC$_{MZ}$	ICC$_{DZ}$	ICC$_{SIB}$
Facial profile			
G-N'-Pn (º)	0.750***	0.441	0.695***
Cm-Sn-ULA (º)	0.864***	0.092	−0.154
GPog'-N'Pn (º)	0.893***	0.676*	0.599*
N'-Pn-Pog' (º)	0.919***	0.485	0.618**
GPog'-Me'C (º)	0.811***	0.140	0.255
G-Sn-Pog' (º)	0.935***	0.013	0.651**
HRP-N'Pog' (º)	0.880***	0.711*	0.541*
N'-Pog'-ULA (º)	0.871***	0.513	0.680**
Projection of nose and lip			
Pn-ULAP perp (mm)	0.878***	0.768**	0.400
A'-ULAP perp (mm)	0.865***	0.557	0.580*
LLA-ULAPog' perp (mm)	0.826***	0.364	0.033
Sn-ULAPog' perp (mm)	0.912***	0.671*	0.507*
B'-ULAPog' perp (mm)	0.842***	0.223	0.572*
ULA-SnPog' perp (mm)	0.911***	0.643*	0.505*
ULA-PnPog' perp (mm)	0.886***	0.653*	0.638**
LLA-SnPog' perp (mm)	0.876***	0.597	0.326
LLA-PnPog' perp (mm)	0.889***	0.562	0.443**
Soft tissue thickness			
A-A' (mm)	0.882***	0.858**	0.825***
ULI-ULA (mm)	0.733***	0.721*	0.542*
LLI-LLA (mm)	0.692***	0.711*	0.578*
Pog-Pog' (mm)	0.851***	−0.585	0.238
Me-Me' (mm)	0.832***	0.066	0.550*
ULI-ULA/A-A' (ratio)	0.806***	0.010	0.293
Pog-Pog'/Me-Me' (ratio)	0.703***	0.348	0.578*
Facial height			
G-Sn (mm)	0.889***	0.401	0.524*
Sn-Me' (mm)	0.946***	0.518	0.743***
Sn-Stm (mm)	0.868***	0.553	0.610*
Stm-Me' (mm)	0.939***	0.397	0.800***
G-Sn/Sn-Me' (ratio)	0.839***	0.586	0.409
Stm-Me'/Sn-Stm (ratio)	0.790***	0.304	0.685**

ICCs are positive and large when variation within the pairs is much lesser than variation between the pairs.
*$p < 0.05$, **$p < 0.01$; ***$p < 0.001$.
See Figures 1 and 2 for definitions of each landmark or measurement.

Table 3. Heritability values in $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$

Variable	$h^2_{(MZ-DZ)}$	$h^2_{(MZ-SIB)}$
Facial profile		
G-N'-Pn (º)	0.618	0.110
Cm-Sn-ULA (º)	1.544*	2.036*
GPog'-N'Pn (º)	0.434	0.588
N'-Pn-Pog' (º)	0.868	0.602
GPog'-Me'C (º)	1.342*	1.112*
G-Sn-Pog' (º)	1.844*	0.568
HRP-N'Pog' (º)	0.338	0.678
N'-Pog'-ULA (º)	0.716	0.382
Projection of nose and lip		
Pn-ULAP perp (mm)	0.220	0.956*
A'-ULAP perp (mm)	0.616	0.570
LLA-ULAPog' perp (mm)	0.924*	1.586*
Sn-ULAPog' perp (mm)	0.482	0.810
B'-ULAPog' perp (mm)	1.238*	0.540
ULA-SnPog' perp (mm)	0.536	0.812
ULA-PnPog' perp (mm)	0.466	0.496
LLA-SnPog' perp (mm)	0.558	1.100*
LLA-PnPog' perp (mm)	0.654	0.892
Soft tissue thickness		
A-A' (mm)	0.048	0.114
ULI-ULA (mm)	0.024	0.382
LLI-LLA (mm)	−0.038	0.228
Pog-Pog' (mm)	2.872*	1.226*
Me-Me' (mm)	1.532*	0.564
ULI-ULA/A-A' (ratio)	1.592*	1.026*
Pog-Pog'/Me-Me' (ratio)	0.710	0.250
Soft tissue thickness		
G-Sn (mm)	0.976*	0.730
Sn-Me' (mm)	0.856	0.406
Sn-Stm (mm)	0.630	0.516
Stm-Me' (mm)	1.084*	0.278
G-Sn/Sn-Me' (ratio)	0.506	0.860
Stm-Me'/Sn-Stm (ratio)	0.972*	0.210

h^2, Heritability; MZ, monozygotic twin; DZ, dizygotic twin; SIB, sibling; MZ-DZ, difference between MZ and DZ; MZ-SIB, difference between MZ and SIB; $h^2_{(MZ-DZ)}$, 2 (ICC$_{MZ}$ − ICC$_{DZ}$); $h^2_{(MZ-SIB)}$, 2 (ICC$_{MZ}$ − ICC$_{SIB}$).
*h^2 values > 0.9 were considered high heritability.
See Figures 1 and 2 for definitions of each landmark or measurement.

Me'C [º], 1.342 and 1.112), lower lip to H line (LLA-ULAPog' perp [mm], 0.924 and 1.586), soft tissue chin thickness (Pog-Pog' [mm], 2.872 and 1.226), and up- per lip thickness ratio (ULI-ULA/A-A' [ratio], 1.592 and 1.026) (Table 3).

Table 4. Principal components analysis (PCA) after varimax rotation

Variable	PCA1	PCA2	PCA3	PCA4	PCA5	PCA6	PCA7	PCA8
LLA-PnPog' perp (mm)	**0.941**	−0.054	0.006	0.152	0.203	0.047	0.091	0.055
LLA-ULAPog' perp (mm)	**0.931**	0.102	0.085	−0.025	−0.116	−0.011	−0.092	−0.004
LLA-SnPog' perp (mm)	**0.930**	−0.179	0.203	0.052	0.121	0.069	0.020	0.004
ULA-PnPog' perp (mm)	**0.619**	−0.229	−0.077	0.300	0.517	0.115	0.263	0.117
B'-ULAPog' perp (mm)	**0.609**	0.212	0.081	−0.258	−0.218	−0.400	−0.309	−0.030
ULA-SnPog' perp (mm)	**0.582**	−0.524	0.118	0.175	0.454	0.203	0.185	0.056
Sn-ULAPog' perp (mm)	**−0.530**	0.509	−0.154	−0.172	−0.521	−0.162	−0.216	−0.068
A'-ULAP perp (mm)	0.194	**−0.890**	0.205	−0.038	0.043	0.164	0.132	0.015
Pn-ULAP perp (mm)	−0.245	**0.839**	−0.008	0.100	−0.019	−0.047	−0.145	−0.019
Cm-Sn-ULA (°)	0.009	**0.735**	−0.023	0.195	−0.021	−0.080	0.092	0.013
HRP-N'Pog' (°)	−0.338	**−0.668**	0.319	−0.008	−0.353	0.089	−0.014	0.016
G-Sn-Pog' (°)	0.345	**0.598**	−0.139	0.487	0.262	0.131	0.011	0.128
ULI-ULA/A-A' (ratio)	0.036	**−0.491**	−0.376	−0.263	0.206	0.447	−0.097	−0.299
Sn-Me' (mm)	0.173	−0.127	**0.929**	−0.023	0.092	0.182	0.030	−0.124
Stm-Me' (mm)	0.137	−0.165	**0.866**	−0.057	−0.266	0.226	0.060	−0.105
G-Sn/Sn-Me' (ratio)	−0.011	0.474	**−0.618**	−0.163	−0.099	0.225	−0.046	0.415
GPog'-N'Pn (°)	0.121	0.212	0.013	**0.881**	0.123	−0.014	0.052	−0.102
N'-Pn-Pog' (°)	−0.164	−0.408	0.093	**−0.810**	−0.163	−0.079	−0.019	−0.035
G-N'-Pn (°)	0.213	0.325	−0.295	**−0.651**	0.200	−0.062	0.020	0.170
N'-Pog'-ULA (°)	0.533	−0.003	−0.108	**0.587**	0.411	0.225	0.188	0.203
Stm-Me'/Sn-Stm (ratio)	−0.031	−0.138	0.167	−0.088	**−0.887**	0.181	0.070	0.020
Sn-Stm (mm)	0.166	−0.005	0.650	0.047	**0.701**	0.027	−0.037	−0.106
ULI-ULA (mm)	−0.061	−0.214	0.085	0.103	−0.033	**0.881**	0.020	−0.173
LLI-LLA (mm)	0.210	−0.144	0.168	0.054	−0.041	**0.685**	0.139	−0.222
A-A' (mm)	−0.112	0.237	0.448	0.369	−0.245	**0.534**	0.099	0.100
G-Sn (mm)	0.174	0.447	0.253	−0.250	−0.024	**0.499**	−0.026	0.390
Pog-Pog' (mm)	−0.025	−0.142	0.343	−0.070	−0.009	0.106	**0.789**	0.088
GPog'-Me'C (°)	0.076	0.026	−0.176	0.125	0.005	0.004	**0.766**	−0.076
Pog-Pog'/Me-Me' (ratio)	0.049	−0.039	−0.151	−0.047	0.007	−0.218	0.068	**0.857**
Me-Me' (mm)	−0.086	−0.031	0.379	−0.001	0.002	0.261	0.507	**−0.643**

perp, Perpendicular.
See Figures 1 and 2 for definitions of each landmark or measurement.

Principal components analysis

PCA derived eight components (Table 4), and its cumulative explanation was 84.5% (Table 5). The components that exhibited higher values of $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$, compared with other components, were PCA2, which depicts facial convexity, nasolabial angle, and nose projection (1.026 and 0.972, respectively), and PCA7, which depicts chin angle and soft-tissue chin thickness (2.107 and 1.169, respectively) (Table 5).

DISCUSSION

ICC values of MZ, DZ, and SIB groups

High ICC values were found in all cephalometric variables of the craniofacial soft tissue in the MZ group compared to those in the DZ and sibling groups (Table 2). These findings were similar to those of Vanco et al.,[11] which suggested that the MZ twins resembled each other to a higher degree than DZ twins, with respect to anterior and vertical aspects of cephalometric measurements.

Table 5. Intraclass correlation coefficients (ICCs) and heritability (h^2) for each of the principal components analysis (PCA)

Principal components	Variance explanation rate (%)	Cumulative rate (%)	ICC_{MZ}	ICC_{DZ}	ICC_{SIB}	$h^2_{(MZ-DZ)}$	$h^2_{(MZ-SIB)}$
PCA1	23.36	23.36	0.877	0.53	0.432	0.694	0.891
PCA2	18.54	41.90	0.871	0.359	0.385	1.026*	0.972*
PCA3	12.18	54.08	0.908	0.5	0.651	0.815	0.515
PCA4	8.97	63.05	0.858	0.529	0.648	0.659	0.421
PCA5	6.78	69.83	0.829	0.429	0.648	0.801	0.363
PCA6	5.37	75.20	0.799	0.673	0.617	0.253	0.364
PCA7	4.94	80.14	0.831	−0.223	0.247	2.107*	1.169*
PCA8	4.38	84.52	0.768	0.207	0.564	1.121*	0.407

MZ, Monozygotic twin; DZ, dizygotic twin; SIB, sibling; $h^2_{(MZ-DZ)}$, 2 (ICC_{MZ} – ICC_{DZ}); $h^2_{(MZ-SIB)}$, 2 (ICC_{MZ} – ICC_{SIB}).
*h^2 values > 0.9 were considered high heritability.

Heritability values in $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$

Nasolabial angle (Cm-Sn-ULA; inclination of the upper lip in relation to the nose) showed high $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values (1.544 and 2.036, Table 3) similar to the findings of Weinberg et al.,[16] who reported that the principal component containing the nasolabial angle showed a relatively high degree of heritability. The upper lip thickness variables showed relatively low $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values (A-A'[mm], 0.048 and 0.114; ULI-ULA [mm], 0.024 and 0.382; Table 3), similar to the results of Tsagkrasoulis et al.,[24] who suggested a relatively low heritability of the lip area. However, the upper lip thickness ratio (ULI-ULA/A-A', indicating the degree of upper lip strain) and the distance from the lower lip to the H line (LLA-ULAPog' perp, mm) showed high $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values (1.592 and 1.026; 0.924 and 1.586; Table 3). Because the distance from the lower lip to the E-line showed higher $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ (LLA-PnPog' perp [mm], 0.654 and 0.892, Table 3) than the distance from the upper lip to the E-line (ULA-PnPog' perp [mm], 0.466 and 0.496, Table 3), lower lip prominence may be more influenced by genetic factors than upper lip prominence. These findings were similar to those of Baydaş et al.,[13] who reported moderate heritability in the distance from the lower lip to the E line and low heritability in the distance from the upper lip to the E line (0.53 vs. 0.3). Djordjevic et al.[25] also suggested that lower lip prominence, in relation to the chin, was under a dominant genetic influence. The anterior middle one-third of facial height (G-Sn) had a higher $h^2_{(MZ-DZ)}$ value than upper lip height (Sn-Stm) (0.976 vs. 0.630; Table 3), which was similar to the findings of Naini and Moss[12] and Weinberg et al.[16] Taken together, these findings suggested that nose length was under a strong genetic influence. However, this result contrasted with the findings reported by Amini and Borzabadi-Farahani.[8]

The finding that soft tissue chin thickness showed higher $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values than lower lip thickness (Pog-Pog' [mm], 2.872 and 1.226 vs. LLI-LLA [mm], −0.038 and 0.228; Table 3) was in agreement with the report by Baydaş et al.,[13] who described a high degree of heritability of chin thickness in Turkish siblings. Several previous studies demonstrated differences in facial soft tissue thickness according to sex, Angle's classification, and mandibular plane angle.[26-28] Moreover, Amini and Borzabadi-Farahani[8] and Šidlauskas et al.[22] reported high heritability in SNB, saddle angle (N-S-Ar), gonial angle (Ar-Go-Me) and mandibular shape (Dc-Xi-Pm, Co-Go-Me, and Ar-Go-Me). Interestingly, the chin angle (GPog'-Me'C, °) showed higher $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ values (1.342 and 1.112, Table 3). Because this angle could decrease based on forward and/or downward placement of the chin, the chin angle might be affected by anteroposterior position of the mandible, facial hyper- or hypodivergent pattern, or chin thickness.

Principal components analysis

PCA1 consisted of lip protrusion variables. This finding was similar with the results reported by Djordjevic et al.,[25] which extracted lip protrusion variables as first and second factors in scaled and unscaled PCA (heritability; 1.015 and 0.783, respectively). It is important to note that lip protrusion variables, which comprise one of the main issues in orthodontic diagnosis and treatment planning, were extracted as an initial factor in the present study. PCA2 and PCA7, which described facial convexity, nasolabial angle, nose projection, chin angle, and soft tissue chin thickness, exhibited higher values of $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ (1.026 and 0.972; 2.107 and 1.169, respectively; Tables 4 and 5). PCA6, including lip thickness variables, showed the lowest values of $h^2_{(MZ-DZ)}$ and $h^2_{(MZ-SIB)}$ (0.253 and 0.364, Tables 4 and 5). These findings indicate that the shape of facial profile, nose projection, and thickness and shape of the soft tissue chin

were more influenced by genetic factors than were lip thickness variables; this was consistent with the results of Djordjevic et al.,[25] who suggested that the prominence and height of nose and the prominence of lower lip, in relation to the chin, are dominantly influenced by genetic factors.

The heritability data of the craniofacial soft tissue cephalometric variables obtained from this study could be used as basic guidelines for orthodontic diagnosis and treatment planning and/or prediction of soft tissue changes after completion of growth. However, there are some limitations in this study: First, since this study used a relatively small sample size, it is necessary to increase the number of twins and match the numbers of MZ, DZ, and SIB pairs in future studies. Second, since soft tissue chin was more strongly influenced by genetic factors, further studies are necessary to investigate heritability correlations among chin thickness, mandibular shape, and facial vertical pattern, based on diverse skeletal patterns. Third, since this study was performed with 2D cephalometric radiographs, it is necessary to perform further analysis with 3D-CT or facial scanning. Fourth, since this study investigated heritability in facial soft tissue solely in Korean twins, it is necessary to compare our results with those from twin studies in other populations. Lastly, this study was performed by using a cross-sectional study design, and the mean age of samples was 39.8 years (Table 1). Therefore, to observe the effect of aging on changes in craniofacial soft tissue, a longitudinal follow-up study is necessary.

CONCLUSION

- The first hypothesis, that there was no significant difference in the heritability of craniofacial soft tissue cephalometric characteristics of MZ twins, DZ twins and their siblings, was rejected. Soft tissue measurements in each pair were most similar between MZ twins, compared to DZ twins and their siblings.
- The second hypothesis, that there was no significant difference in the heritability of facial profile, facial height, soft tissue thickness, and projection of the nose and lip, was rejected. The nose and soft tissue chin were more strongly influenced by genetic factors, compared to other soft tissues.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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