Original Article

Characterization of phenotypes of skeletal Class III malocclusion in Korean adult patients treated with orthognathic surgery using cluster analysis

Il-Hyung Yang[a]; Jin-Young Choi[b]; Seung-Hak Baek[c]

ABSTRACT

Objectives: To characterize the phenotypes of skeletal Class III malocclusion in adult patients who underwent orthognathic surgery (OGS).

Materials and Methods: The sample consisted of 326 patients with Class III malocclusion treated with OGS (170 men and 156 women; mean age, 22.2 years). Using lateral cephalograms taken at initial visits, 13 angular variables and one ratio cephalometric variable were measured. Using three representative variables obtained from principal components analysis (SNA, SNB, and Björk sum), K-means cluster analysis was performed to classify the phenotypes. Statistical analysis was conducted to characterize the differences in the cephalometric variables among the clusters.

Results: Class III phenotypes were classified into nine clusters from the following four major groups: (1) retrusive maxilla group, clusters 7 and 9 (7.1% and 5.5%; severely retrusive maxilla, normal mandible, severe and moderate hyperdivergent, respectively) and cluster 6 (9.2%; retrusive maxilla, normal mandible, normodivergent); (2) relatively protrusive mandible group, cluster 2 (20.9%; normal maxilla, normal mandible, hyperdivergent); (3) protrusive mandible group, clusters 3 and 1 (11.7% and 15.3%; normal maxilla, protrusive mandible, normodivergent and hyperdivergent, respectively) and clusters 8 and 4 (15.3% and 3.7%; normal maxilla, severe protrusive mandible, normodivergent and hypodivergent, respectively); and (4) protrusive maxilla and protrusive mandible group, cluster 5 (11.4%; protrusive maxilla, severely protrusive mandible, normodivergent). Considerations for presurgical orthodontic treatment and OGS planning were proposed based on the Class III phenotypes.

Conclusions: Because the anteroposterior position of the maxilla and rotation of the mandible by a patient's vertical pattern determine Class III phenotypes, these variables should be considered in diagnosis and treatment planning for patients who have skeletal Class III malocclusion. (*Angle Orthod.* 2022;92:537–546.)

KEY WORDS: Class III; Phenotype

INTRODUCTION

Classification of skeletal Class III malocclusion based on specific morphological features is advantageous to provide differential diagnosis and set up treatment planning in surgical orthodontic treatment.[1,2] To characterize the diverse phenotypes of patients with skeletal Class III malocclusion, numerous previous studies have undergone cluster analysis.[3–10] In a systematic review, de Frutos-Valle et al.[11] reported that the number of Class III clusters ranged from 3 to 14 because of differences in ethnic background, sample size, and severity of malocclusion within the sample. The cluster number can be also changed by subjective decisions of researchers.[3–8] Therefore, before performing cluster analysis, it is necessary to obtain the representative variables in an objective way. Because principal component analysis (PCA) can extract com-

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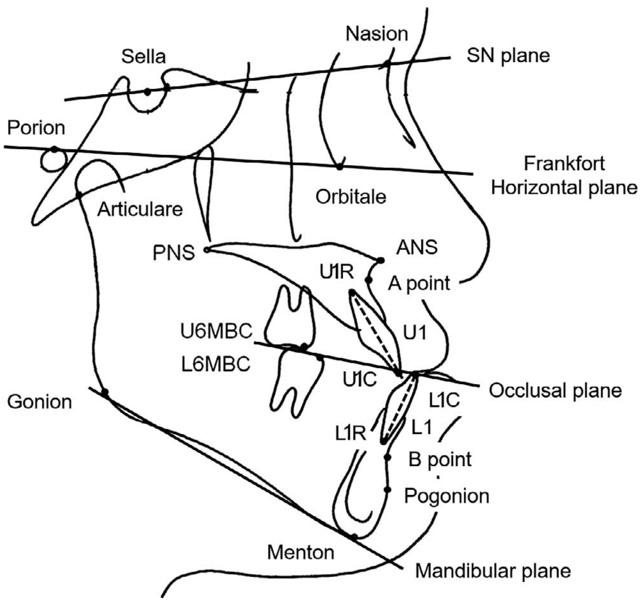

Figure 1. Landmarks and reference lines: sella, nasion, porion, orbitale, articulare, posterior nasal spine (PNS), anterior nasal spine (ANS), A point, B point, the incisor tip and root apex of the maxillary central incisor (U1C and U1R, respectively), the incisor tip and root apex of the mandibular central incisor (L1C and L1R, respectively), mesiobuccal cusp tip of the maxillary and mandibular first molar (U6MBC and L6MBC, respectively), pogonion, menton, gonion, SN plane, Frankfort horizontal (FH) plane, occlusal plane (OP), mandibular plane (MP), and long axis of the maxillary and mandibular central incisors (U1 and L1, respectively).

ponents by grouping cephalometric variables with greatest interaction on each axis, it can help cluster analysis to obtain the least dispersion within each group and the greatest difference between groups.[9,10]

There are several considerations for cluster analysis study on skeletal Class III phenotypes to increase sample purity. First, it is necessary to confine the patients in terms of ethnicity and age to minimize the confounding effects of different ethnicities and remaining facial growth on the cephalometric measurements.[4,6–8] Second, it is necessary to use the skeletal cephalometric variables as the main representative variables in cluster analysis for preventing the interaction with dental compensation and soft tissue variations.[9] Third, it is necessary to use angular and ratio cephalometric variables, not linear cephalometric variables, to avoid the interaction of linear variables between male and female patients.[10] Finally, it is necessary to limit the patients to those who finished presurgical and postsurgical orthodontic treatment and orthognathic surgery to ensure that the patients had real skeletal problems.

There are few cluster analysis studies on skeletal Class III phenotypes, which has limited patients and research methodology in terms of ethnicity, age, cephalometric variables, completion of surgical orthodontic treatment, and large enough sample size.[11] Therefore, the purpose of this study was to classify the phenotypes in Korean adult patients with skeletal Class III malocclusion who underwent presurgical and postsurgical orthodontic treatment and orthognathic surgery using PCA and cluster analysis.

MATERIALS AND METHODS

Patients

The initial sample was Korean adult patients who had undergone presurgical and postsurgical orthodontic treatment and orthognathic surgery at the Department of Orthodontics, Seoul National University Dental Hospital (SNUDH) in Korea between January 2015 and December 2020. The inclusion criteria were (1) patients who completed facial growth (older than the age of 18 years); (2) patients who were diagnosed with skeletal Class III malocclusion (ANB, less than 0°); and (3) patients whose chart, lateral cephalograms, and photographs were available. The exclusion criteria were (1) patients who had degenerative joint disease, tumor, or trauma history in the temporomandibular joints and (2) patients who had clefts and other craniofacial anomalies.

As a result, 326 adult patients were recruited as the final sample (170 men and 156 women; mean age $\pm$ standard deviation [SD] at the initial visit, 22.2 $\pm$ 4.71 years). This retrospective study was reviewed and approved by the Institutional Review Board Committee of SNUDH (ERI21019).

Landmarks and Reference Lines

The landmarks and reference lines are illustrated in Figure 1. The craniofacial characteristics were categorized into anteroposterior (AP), vertical, mandibular, cranial base, and dental characteristics. After the landmarks were identified by a single operator (Dr Yang), 13 angular variables and one ratio variable (Figure 2) were measured using the V-Ceph program (Ostem, Seoul, Republic of Korea).

All variables from 20 randomly selected patients were remeasured by the same operator (Dr Yang) with a 2-week interval. Because there was no significant difference in the values of the measurement variables between the first and second measurements by paired *t*-test ($P > .05$), the first set of measurements was used for further analysis.

PCA With Varimax Rotation

Björk sum in principal component 1 and SNA and SNB in principal component 2 were selected as the representative variables for cluster analysis because they had the highest correlation values in each PC and

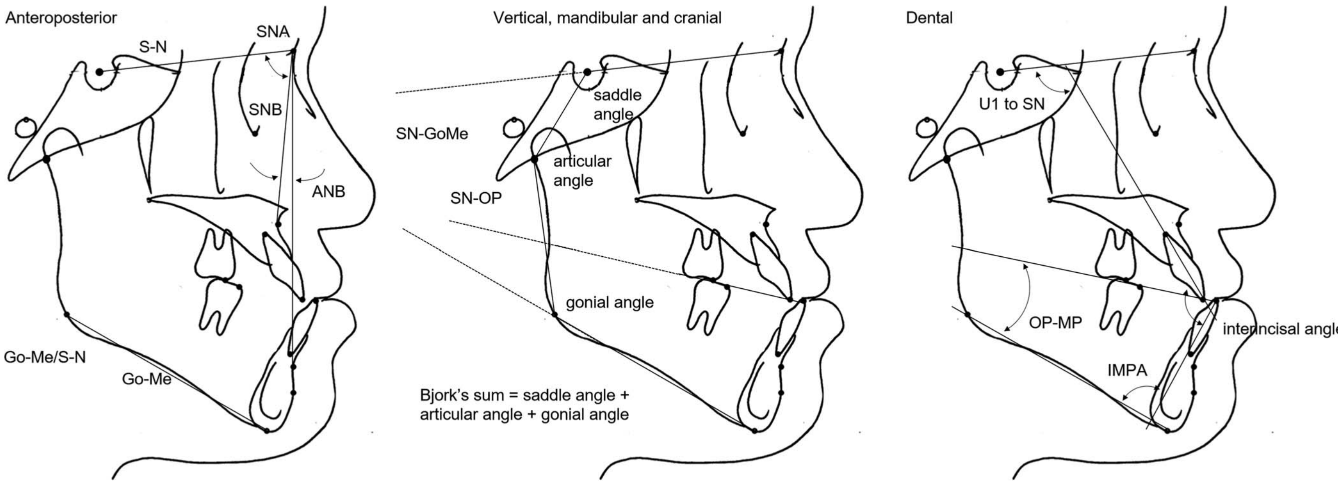

Figure 2. Cephalometric variables. Anteroposterior characteristics are SNA (°), SNB (°), ANB (°), and MBL/ACBL (GoMe/SN). Vertical characteristics are Björk sum (sum of saddle angle, articular angle, and gonial angle [°]), SN-GoMe (°), and SN-OP (°). Mandibular characteristics are articular angle (S-Ar-Go [°]) and gonial angle (Ar-Go-Gn [°]). Cranial base characteristics are saddle angle (N-S-Ar [°]). Dental characteristics are U1 to SN (°), IMPA (°), interincisal angle (°), and OP-MP (°).

could define the vertical pattern and the AP position of the maxilla and mandible, respectively (Table 1).

Cluster Analysis

K-means cluster analysis was conducted to classify the Class III phenotypes using the ordinal scale of three variables (Björk sum in principal component 1 and SNA and SNB in principal component 2) to avoid an unclear cut in the normal distribution of the nominal values. Based on the means and standard deviations (SDs) of the ethnic norm values,[12,13] the degree of these variables was classified into normal (between −1 SD and mean or between mean and 1 SD), moderate (between 1 SD and 2 SD or between −1 SD and −2 SD), and severe (higher than 2 SD or lower than −2 SD; Table 2).

According to the total within-cluster sum of squares, the appropriate number of clusters was considered between six and 10. After analyzing the results of a two-dimensional scatter plot, the final number of Class III clusters was determined to be nine (Figure 3).

Characterization of Class III Phenotype Groups

To characterize the differences in the cephalometric variables among nine clusters with the nominal values, one-way analysis of variance and Kruskal-Wallis test were performed according to satisfaction or no satisfaction of the assumption for parametric statistics, respectively.

Statistical Analyses

All statistical analyses were performed using Language R, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). A *P* value less than .05 was considered statistically significant.

Table 1. Composition of Principal Components, Percentage of Proportion Variance, and Cumulative Percentage[a]

		Loading of Each Variable								
Principal Component	Cumulative Variance	Björk Sum	SN-GoMe	SNA	SNB	Articular Angle	Gonial Angle	ANB	Saddle Angle	Ratio of MBL to ACBL[b]
1	0.255	**0.952**	**0.952**	−0.216	−0.356	0.017	−0.062	0.068	0.049	0.44
2	0.417	−0.206	−0.206	**0.927**	**0.666**	−0.051	0.091	0.041	−0.33	−0.305
3	0.539	0.024	0.024	0	−0.192	**0.956**	0.07	0.07	−0.349	0.055
4	0.646	−0.035	−0.035	0.062	0.182	0.076	**0.983**	−0.058	0.144	−0.051
5	0.751	0.057	0.057	0.114	−0.178	0.08	−0.06	**0.992**	0.02	0.052
6	0.847	0.049	0.049	−0.194	−0.291	−0.235	0.089	0.015	**0.854**	0.101
7	0.934	0.189	0.189	−0.187	−0.219	0.048	−0.035	0.034	0.096	**0.832**
8	0.98	0.077	0.077	0.051	0.067	−0.11	−0.065	−0.013	−0.084	0.029
9	1	−0.038	−0.038	−0.043	0.438	−0.028	0.022	−0.023	−0.042	−0.04
10	1	0	0	0	0	0	0	0	0	0

[a] PCA with varimax rotation was performed. Dental and soft tissue cephalometric variables were excluded in the PCA.
[b] ACBL indicates anterior cranial base length; MBL, mandibular body length.
The largest loading values of each variable in each principal component were presented in boldface.

Table 2. Comparison of the Cephalometric Variables Among Nine Clusters[a]

				Group		
				Retrusive Maxilla		
Structures	Cephalometric Variables	Ethnic Mean ± SD	Mean ± SD and Median (IQ)	Phenotype Cluster 7 (n = 23, 7.1%)	Phenotype Cluster 9 (n = 18, 5.5%)	Phenotype Cluster 6 (n = 30, 9.2%)
AP	SNA[b]	82.1 ± 3.2	Mean ± SD	74.98 ± 1.44	75.56 ± 1.89	78.46 ± 1.73
			Median (IQ)	75.04 (74.28; 75.44)	75.38 (74.77; 76.18)	78.36 (77.06; 79.56)
	SNB[b]	79.8 ± 3.1	Mean ± SD	76.81 ± 1.40	78.34 ± 1.04	81.27 ± 0.82
			Median (IQ)	76.790 (75.68; 77.93)	78.16 (77.51; 79.47)	81.35 (80.77; 81.97)
	ANB[b]	2.3 ± 1.8	Mean ± SD	−1.83 ± 1.14	−2.78 ± 1.83	−2.82 ± 1.87
			Median (IQ)	−1.47 (−2.51; −1.13)	−2.69 (−3.38; −0.91)	−2.90 (−4.27; −0.78)
Vertical	Björk sum[b]	391.8 ± 5.5	Mean ± SD	405.23 ± 4.21	397.83 ± 3.75	393.36 ± 2.90
			Median (IQ)	405.35 (402.80; 407.62)	398.45 (395.48; 400.64)	394.07 (391.43; 395.68)
	SN-GoMe[b]	31.8 ± 5.5	Mean ± SD	45.23 ± 4.21	37.83 ± 3.75	33.36 ± 2.90
			Median (IQ)	45.35 (42.80; 47.62)	38.45 (35.48; 40.64)	34.07 (31.43; 35.68)
	SN-OP[b]	16.6 ± 4.1	Mean ± SD	24.87 ± 3.28	22.26 ± 3.74	17.80 ± 6.85
			Median (IQ)	24.61 (22.28; 26.74)	21.86 (19.81; 23.88)	20.37 (16.44; 21.24)
Mandible	Articular angle[c]	148.9 ± 6.0	Mean ± SD	147.06 ± 7.57	148.33 ± 6.49	148.07 ± 6.14
			Median (IQ)	144.39 (141.17; 151.86)	147.70 (145.41; 152.98)	147.47 (144.69; 152.69)
	Gonial angle[c]	117.9 ± 6.4	Mean ± SD	132.06 ± 7.84	123.71 ± 7.89	120.12 ± 4.91
			Median (IQ)	133.63 (127.03; 136.43)	124.26 (119.07; 129.49)	119.95 (115.98; 123.94)
	Ratio of MBL to ACBL[c]	1.07 ± 0.06	Mean ± SD	1.13 ± 0.11	1.15 ± 0.10	1.18 ± 0.08
			Median (IQ)	1.10 (1.06; 1.18)	1.16 (1.10; 1.19)	1.21 (1.12; 1.23)
Cranial base	Saddle angle[c]	125 ± 4.7	Mean ± SD	126.11 ± 6.02	125.79 ± 5.53	125.17 ± 4.51
			Median (IQ)	127.70 (121.91; 130.38)	125.56 (122.37; 127.07)	124.35 (122.75; 129.28)
Dental	U1 to SN[c]	107.8 ± 5.9	Mean ± SD	101.90 ± 7.20	108.75 ± 6.56	110.79 ± 5.78
			Median (IQ)	99.54 (97.26; 107.27)	109.63 (107.27; 112.32)	111.54 (108.33; 115.00)
	IMPA[c]	96.3 ± 6.5	Mean ± SD	77.27 ± 9.04	84.48 ± 5.45	85.95 ± 8.03
			Median (IQ)	77.13 (74.47; 82.97)	86.08 (78.02; 88.63)	86.18 (80.24; 91.91)
	Interincisal angle[c]	124.1 ± 8.1	Mean ± SD	135.63 ± 11.08	128.96 ± 9.73	129.93 ± 10.85
			Median (IQ)	135.21 (129.07; 142.07)	127.04 (121.89; 135.61)	129.82 (120.92; 136.46)
	OP-MP[b]	15.2 ± 3.8	Mean ± SD	20.35 ± 4.34	15.56 ± 3.79	15.56 ± 5.68
			Median (IQ)	19.28 (17.49; 22.51)	15.12 (12.86; 18.58)	13.97 (12.25; 17.00)

[a] The K-means cluster analysis was conducted using the variables SNA, SNB, and Björk sum.
[b] Kruskal-Wallis and Conover post hoc tests were conducted.
[c] One-way analysis of variance and Tukey-Kramer post hoc test were conducted.
[d] NS indicates not specific. IQ indicates interquartile range.
* $P < .05$; ** $P < .01$; *** $P < .001$.

Table 2. Extended

Group							
Relatively Protrusive Mandible	Protrusive Mandible				Protrusive Maxilla and Protrusive Mandible		
Phenotype Cluster 2 (n = 68, 20.9%)	Phenotype Cluster 3 (n = 38,11.7%)	Phenotype Cluster 1 (n = 50, 15.3%)	Phenotype Cluster 8 (n = 50, 15.3%)	Phenotype Cluster 4 (n = 12, 3.7%)	Phenotype Cluster 5 (n = 37, 11.4%)	*P* Value	Multiple Comparisons
79.19 ± 1.75	80.11 ± 1.38	82.61 ± 1.72	82.65 ± 1.56	81.08 ± 3.37	86.83 ± 1.35	<.0001***	(7, 9) < (6, 2) < (2, 3) < (3, 4) < (4, 1) < (1, 8) < 5
79.09	80.19	82.84	82.92	80.75	86.50		
(77.97; 80.57)	(79.26; 81.25)	(81.66; 84.12)	(81.71; 83.83)	(78.58; 84.46)	(85.68; 87.52)		
81.85 ± 1.28	84.74 ± 1.15	85.42 ± 1.80	88.21 ± 1.99	87.55 ± 2.99	89.84 ± 2.16	<.0001***	(7, 9) < (6, 2) < (3, 1) < (4, 8) < 5
81.97	84.70	85.31	87.93	87.81	89.88		
(80.79; 82.63)	(83.82; 85.66)	(84.17; 86.00)	(87.22; 88.79)	(84.69; 89.63)	(88.30; 91.54)		
−2.67 ± 1.91	−4.63 ± 2.04	−2.81 ± 2.23	−5.56 ± 2.37	−6.47 ± 4.43	−3.01 ± 1.98	<.0001***	(4, 8, 3) < (5, 6, 1, 9, 2, 7)
−1.98	−4.33	−2.70	−5.68	−5.87	−2.79		
(−3.79; −1.27)	(−5.61; −3.25)	(−3.67; −1.24)	(−7.17; −3.97)	(−8.28; −4.31)	(−3.89; −1.31)		
401.83 ± 3.31	393.37 ± 2.94	398.14 ± 2.67	391.37 ± 2.83	383.12 ± 3.90	390.69 ± 4.03	<.0001***	4 < (5, 8) < (8, 6) < (6, 3) < (9, 1) < (2, 7)
401.27	393.71	398.67	390.48	384.60	391.21		
(399.09; 403.96)	(391.66; 395.83)	(396.20; 399.87)	(389.06; 393.86)	(380.55; 385.91)	(388.62; 393.64)		
41.83 ± 3.31	33.37 ± 2.94	38.14 ± 2.67	31.37 ± 2.83	23.12 ± 3.90	30.69 ± 4.03	<.0001***	4 < (5, 8) < (8, 6) < (6, 3) < (9, 1) < (2, 7)
41.27	33.71	38.67	30.48	24.60	31.21		
(39.09; 43.96)	(31.66; 35.83)	(36.20; 39.87)	(29.06; 33.86)	(20.55; 25.91)	(28.62; 33.64)		
20.99 ± 4.35	16.50 ± 3.80	16.63 ± 3.47	14.43 ± 4.54	10.22 ± 5.10	12.64 ± 3.85	<.0001***	(4, 5, 8) < (8, 3) < (3, 1, 6) < (6, 2, 9) < (9, 7)
20.14	16.52	16.87	14.32	10.57	13.10		
(18.35; 23.93)	(13.22; 18.96)	(13.45; 19.04)	(11.49; 17.10)	(7.70; 13.94)	(10.30; 15.35)		
145.99 ± 6.89	143.64 ± 6.27	146.92 ± 7.38	144.25 ± 6.93	144.09 ± 3.67	145.28 ± 5.44	.0431*	NS[d]
145.27	143.05	147.31	144.33	143.78	144.63		-
(141.71; 150.37)	(139.44; 146.84)	(141.80; 150.53)	(139.69; 147.27)	(141.04; 146.63)	(141.71; 149.24)		
134.17 ± 5.96	127.62 ± 5.94	132.36 ± 6.43	127.22 ± 6.16	116.95 ± 5.62	128.35 ± 5.29	<.0001***	(4, 6, 9) < (9, 8, 3, 5) < (8, 3, 5, 7) < (7, 1, 2)
133.91	127.81	133.20	126.67	117.20	127.48		
(130.59; 137.12)	(124.61; 131.01)	(128.32; 136.05)	(123.26; 132.69)	(115.14; 120.10)	(124.28; 133.02)		
1.15 ± 0.07	1.15 ± 0.08	1.19 ± 0.11	1.20 ± 0.08	1.21 ± 0.08	1.19 ± 0.09	.0015**	(7, 2, 9, 3, 6, 5, 1, 4) < (2, 9, 3, 6, 5, 1, 4, 8)
1.15	1.16	1.21	1.20	1.22	1.20		
(1.11; 1.20)	(1.08; 1.21)	(1.09; 1.27)	(1.15; 1.25)	(1.15; 1.24)	(1.12; 1.25)		
121.68 ± 4.99	122.10 ± 4.71	118.86 ± 5.15	119.90 ± 4.45	122.08 ± 5.74	117.06 ± 4.43	<.0001***	(5, 1, 8, 4) < (1, 8, 4, 2, 3) < (4, 3, 6, 9, 7)
121.61	121.38	119.39	119.52	121.04	116.02		
(118.29; 125.61)	(119.26; 125.54)	(115.81; 121.87)	(116.73; 122.82)	(117.29; 127.82)	(114.14; 120.47)		
109.31 ± 6.53	113.73 ± 6.05	114.18 ± 5.99	114.39 ± 5.10	113.81 ± 4.82	119.04 ± 6.44	<.0001***	7 < (2, 9, 6, 4) < (9, 6, 3, 4) < (6, 3, 1, 8, 4) < (4, 5)
109.14	114.54	113.62	114.67	111.66	117.94		
(106.17; 113.22)	(109.35; 117.80)	(110.21; 119.03)	(110.79; 117.94)	(110.26; 117.70)	(114.30; 124.20)		
77.68 ± 7.31	83.45 ± 7.15	78.81 ± 7.68	79.84 ± 7.19	84.59 ± 6.15	82.81 ± 6.93	<.0001***	(7, 2, 1, 8, 4) < (2, 1, 8, 4, 5, 3) < (1, 8, 4, 5, 3, 9) < (4, 5, 3, 9, 6)
77.85	82.79	79.36	80.43	85.23	84.06		
(74.06; 83.14)	(78.55; 87.69)	(73.58; 84.53)	(74.47; 84.94)	(79.67; 89.25)	(77.70; 88.30)		
131.19 ± 10.90	129.48 ± 9.15	128.89 ± 10.13	134.43 ± 8.97	138.51 ± 8.06	127.48 ± 9.82	.0013**	(5, 1, 9, 3, 6, 2, 7) < (1, 9, 3, 6, 2, 7, 8, 4)
129.29	130.17	129.22	133.61	137.15	127.33		–
(124.27; 137.04)	(121.76; 137.00)	(122.42; 134.59)	(128.96; 138.88)	(130.99; 146.23)	(120.32; 135.00)		
20.86 ± 4.88	16.87 ± 3.61	21.46 ± 3.60	16.57 ± 3.99	12.96 ± 3.73	18.05 ± 3.64	<.0001***	(4, 6, 9, 8, 3) < (9, 8, 3, 5) < (5, 7) < (7, 2, 1)
21.08	16.96	21.84	16.78	11.25	17.73		
(18.36; 23.36)	(14.54; 20.02)	(19.30; 24.03)	(14.89; 18.84)	(10.34; 16.16)	(16.41; 20.56)		

RESULTS

Classification of Class III Phenotypes

Four major groups and nine Class III phenotypes were found in the present study (Table 2, Figures 4 and 5).

First, the retrusive maxilla group consisted of three phenotypes according to degree of maxillary retrusion and difference in the vertical pattern: cluster 7 (7.1%; severely retrusive maxilla, normal mandible, and severely hyperdivergent pattern), cluster 9 (5.5%;

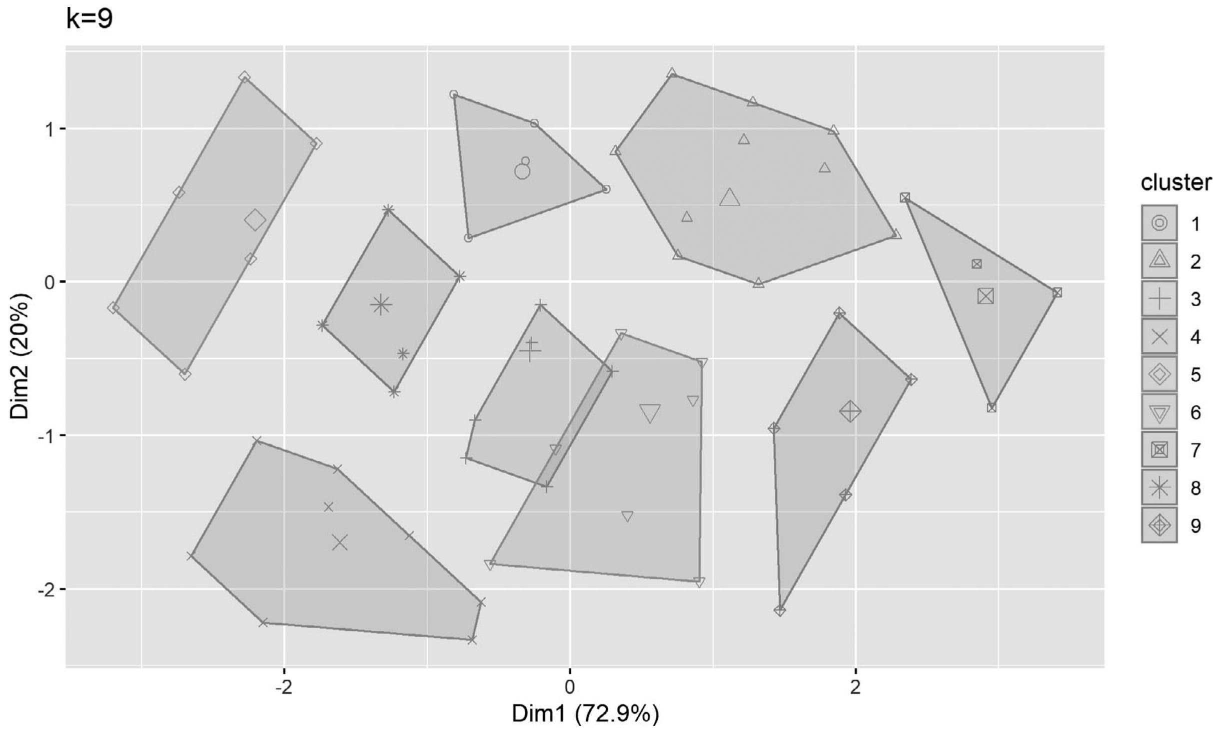

Figure 3. The results of cluster analysis showing nine clusters.

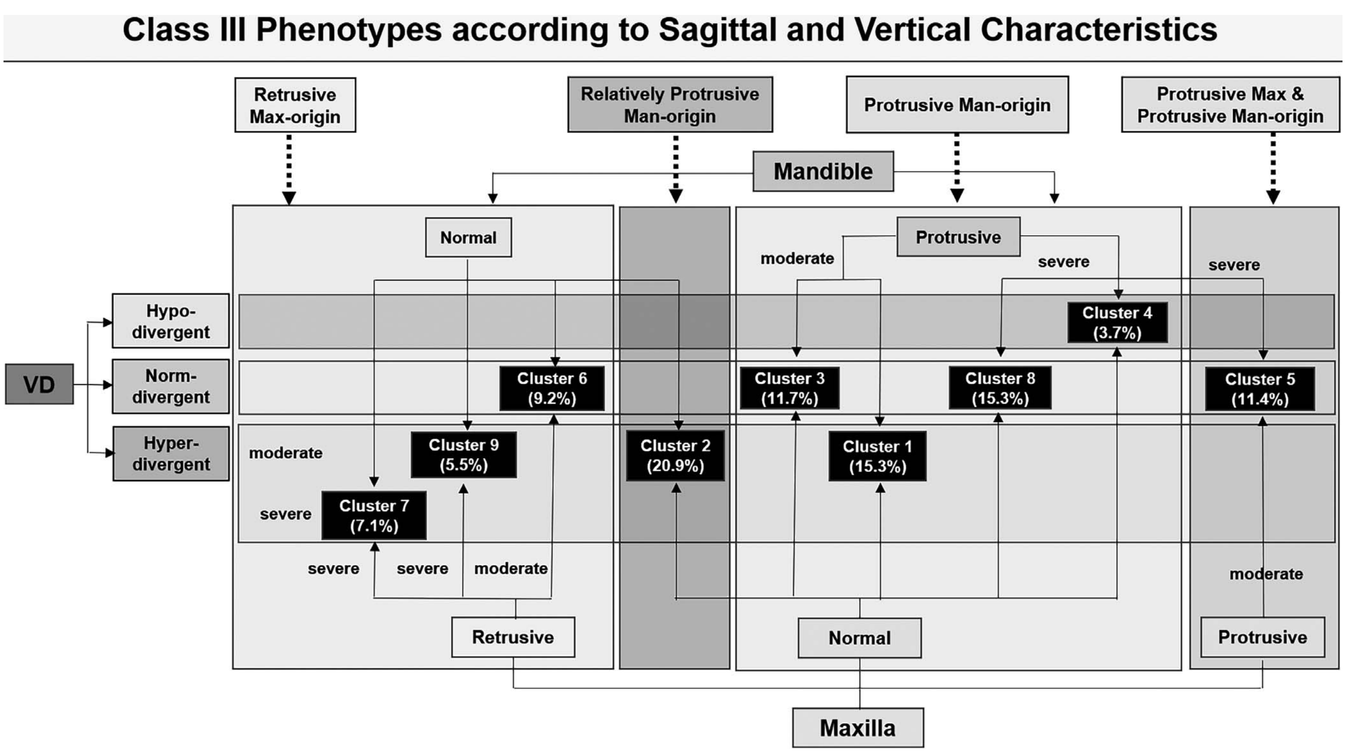

Figure 4. Composition of Class III phenotype clusters.

Class III phenotypes			Cephalometric characteristics						Pre-op Ortho Tx		Orthognathic Surgery			
			SNA (norm, 82.1°)	SNB (norm, 79.8°)	Bjork sum (norm, 391.8°)	SN-OP (norm, 16.6°)	U1-SN (norm, 107.8°)	IMPA (norm, 96.3°)	Maxillary arch	Mandibular arch	Maxilla	Mandible	Chin	Check point
Retrusive Maxilla group		C7	severely retrusive Max (75.0°)	normal Man (76.8°)	Severely hyper-divergent(405.2°)	Severely steep (24.9°)	normal (101.9°)	severely linguoversed (77.3°)	non-ext	Lower incisor : + torque / miniscrews	LF-I or II Advancement with minimal post impaction	minimal setback without or with minimal clockwise rotation	If needed, adv / vert. reduction genioplasty	
		C9	severely retrusive Max (75.6°)	normal Man (78.3°)	Moderately hyper-divergent (397.8°)	moderately steep (22.3°)	normal (108.8°)	moderately linguoversed (84.5°)	non-ext	Lower incisor : + torque	LF-I or II Advancement with minimal post impaction	minimal setback without or with minimal clockwise rotation	If needed, adv / vert. reduction genioplasty	Para-nasal augmentation
		C6	moderately retrusive Max (78.5°)	Normal Man (81.3°)	normo-divergent (393.4°)	normal (17.8°)	normal (110.8°)	moderately linguoversed (86.0°)	non-ext	Lower incisor : + torque	LF-I Advancement with moderate post impaction	minimal setback with minimal clockwise rotation		
Relatively Protrusive Mandible group		C2	normal Max (79.2°)	normal Man (81.9°)	Moderately hyper-divergent (401.8°)	moderately flat (12.0°)	normal (109.3°)	severely linguoversed (77.7°)	Non-ext	Lower incisor : + torque / miniscrews	LF-I with minimal Post impaction or no surgery in the maxilla	minimal setback with clockwise rotation	If needed, adv / vert. reduction genioplasty	
Protrusive Mandible group	Moderate subgroup	C3	normal Max (80.1°)	moderately protrusive Man (84.7°)	normo-divergent (393.4°)	normal (16.5°)	moderately labioversed (113.7°)	moderately linguoversed (83.5°)	P1 or non-ext	Lower incisor : + torque	LF-I with moderate post impaction or no surgery in the maxilla	moderate setback with clockwise rotation		
		C1	normal Max (82.6°)	moderately protrusive Man (85.4°)	Moderately hyper-divergent (398.1°)	normal (16.6°)	moderately labioversed (114.2°)	severely linguoversed (78.8°)	P1 ext	Lower incisor : + torque / miniscrews	LF-I with moderate post impaction or no surgery in the maxilla	moderate setback with clockwise rotation	If needed, adv / vert. reduction genioplasty	
	Severe subgroup	C8	normal Max (82.7°)	severely protrusive Man (88.2°)	normo-divergent (391.4°)	normal (14.4°)	moderately labioversed (114.4°)	severely linguoversed (79.8°)	P1 ext	Lower incisor : + torque	LF-I compensatory advancement with Post impaction and/or ASO	Moderate setback with clockwise rotation		airway
		C4	normal Max (81.1°)	severely protrusive Man (87.6°)	Moderately hypo-divergent (383.1°)	moderately flat (10.2°)	moderately labioversed (113.8°)	moderately linguoversed (84.6°)	P1 or non-ext	Lower incisor : + torque	LF-I compensatory advancement with moderate or large post impaction and/or ASO	Moderate setback with clockwise rotation	If needed, setback / vert. reduction genioplasty	
Protrusive Maxilla and Protrusive Mandible group		C5	moderately protrusive Max (86.8°)	severely protrusive Man (89.8°)	normo-divergent (390.7°)	normal (12.6°)	moderately labioversed (119.0°)	severely linguoversed (82.8°)	P1 ext	Lower incisor : + torque / miniscrews	LF-I setback and moderate or large post impaction and/or ASO	Moderate setback with clockwise rotation	If needed, setback / vert. reduction genioplasty	airway

Figure 5. A flowchart for consideration in presurgical orthodontic treatment and orthognathic surgery based on the Class III phenotypes.

severely retrusive maxilla, normal mandible, and moderately hyperdivergent pattern), and cluster 6 (9.2%; moderately retrusive maxilla, normal mandible, and normodivergent pattern).

Second, the relatively protrusive mandible group had one phenotype: cluster 2 (20.9%; normal maxilla, normal mandible, and hyperdivergent pattern).

Third, the protrusive mandible group was divided into the following two subgroups according to the degree of mandibular protrusion: (1) moderately protrusive mandible subgroup, cluster 3 (11.7%; normal maxilla and normodivergent pattern) and cluster 1 (15.3%; normal maxilla and hyperdivergent pattern); and (2) severely protrusive mandible subgroup, cluster 8 (15.3%; normal maxilla and normodivergent pattern) and cluster 4 (3.7%; normal maxilla and hypodivergent pattern). In each subgroup, the vertical pattern was different between clusters 3 and 1 and between clusters 8 and 4.

Fourth, the protrusive maxilla and protrusive mandible group had one phenotype: cluster 5 (11.4%; moderately protrusive maxilla, severely protrusive mandible, and normodivergent pattern).

Comparison of the AP Characteristics

Significant differences in the SNA and SNB values among clusters (all $P < .001$) indicated that adult patients with Class III showed a broad range from severely retrusive, moderately retrusive, normal, to moderately protrusive maxilla and a relatively narrow range from normal, moderately protrusive, to severely protrusive mandible with clear differentiation (Table 2, Figure 4).

Comparison of the Vertical Characteristics

The values of Björk sum, SN-GoMe, and SN-OP clearly differentiated the hypodivergent pattern (cluster 4) and the hyperdivergent pattern (clusters 2, 7, 9, and 1) from the normodivergent pattern (all $P < .001$; Table 2, Figure 4).

Comparison of the Mandibular Characteristics

Articular angle did not show a significant difference among clusters in the post hoc test (Table 2, Figure 4). The values of gonial angle significantly differed among clusters ($P < .001$). Clusters 4 and 6 exhibited the lowest values, but within a normal range, and clusters 2, 1, and 7 showed the highest values.

The ratios of MBL to ACBL significantly differed among clusters ($P < .01$). All clusters had a higher ratio when compared with the ethnic norm.[13] Clusters 4 and 8 showed the highest ratio, but cluster 7 showed the lowest ratio.

Comparison of the Cranial Base Characteristics

The saddle angle exhibited a significant difference among clusters ($P < .001$; Table 2, Figure 4). Cluster 5 showed the smallest value. Clusters 7, 9, and 6 exhibited the highest values but within a normal range.[13]

Comparison of the Dental Characteristics

The values of U1 to SN significantly differed among clusters ($P < .001$; Table 2, Figure 4). Cluster 7 showed the lowest value but within a normal range.[13] Cluster 5 had the most flared maxillary incisor inclination.

IMPA also exhibited a significant difference among clusters ($P < .001$). All clusters showed a lingually inclined mandibular incisor inclination compared with the ethnic norm.[13] Cluster 7 showed the most upright mandibular incisor inclination, but cluster 6 showed the least upright mandibular incisor inclination.

Interincisal angle showed a significant difference among clusters ($P < .01$). Cluster 5 showed normal values,[13] but cluster 4 showed the largest value.

OP-MP significantly differed among clusters ($P < .001$). Clusters 4 and 6 showed values within a normal range,[13] but clusters 1 and 2 showed the largest values because of compensation (counterclockwise rotation) of the OP.

DISCUSSION

Number of Clusters in Skeletal Class III Malocclusion

A number of phenotypes less than four or more than 10 might be impractical for clinical use. In the present study, the Class III phenotypes were classified into nine phenotypes from four major groups.

Morphological Characteristics of Class III Phenotypes

In the retrusive maxilla group, clusters 7, 9, and 6 were differentiated by degree of maxillary retrusion and difference in the vertical pattern (Table 2, Figure 4). Interestingly, in the present study, there was no phenotype that showed a combination of retrusive maxilla and protrusive mandible. The reason might be attributed to ethnic differences between White and Korean patients with Class III malocclusion or inclusion of that phenotype into other clusters as a result of a relatively small sample size.

In the relatively protrusive mandible group (cluster 2), clockwise rotation of the mandible by a hyperdivergent pattern seemed to place the mandible into a normal range of the AP position rather than a protrusive position. However, a relatively more protrusive position of the mandible in relation to the maxilla resulted in a skeletal Class III malocclusion.

In the protrusive mandible group, four phenotypes were allocated into the moderately protrusive mandible subgroup (clusters 3 and 1) and the severely protrusive mandible subgroup (clusters 8 and 4), which were subdivided by a difference in the vertical pattern. In cluster 1, clockwise rotation of the mandible by a hyperdivergent pattern seemed to place the mandible into a moderately protrusive position rather than a severely protrusive position. In cluster 4, counterclockwise rotation of the mandible by a hypodivergent pattern seemed to place the mandible into a severely protrusive position rather than a moderately protrusive position. Therefore, clockwise or counterclockwise rotation of the mandible by a patient's vertical pattern made a difference in the degree of mandibular protrusion.

In the protrusive maxilla and protrusive mandible group, cluster 5 showed a moderately protrusive maxilla, severely protrusive mandible, and normodivergent pattern. This phenotype is unique in Korean patients with Class III malocclusion, which has not been reported in previous studies.[3–8]

Comparison of the AP Characteristics

It was quite interesting that some of the patients with Class III malocclusion (cluster 5) showed a moderately protrusive maxilla and severely protrusive mandible, which might indicate that skeletal Class III malocclusion can occur by more growth of the mandible compared with that of the maxilla (Table 2, Figure 4). In a study on prognosis prediction after growth modification therapy for growing patients with Class III malocclusion, Kim et al.[14] reported that, when the patients had an acute AB-MP angle and more protrusive maxilla at the age of 8 years, a poor prognosis was predicted at the age of 17 years. Because a lower value of AB-MP angle in conjunction with a more protrusive maxilla means a more forward positioning of B point than A point, the values of SNA and SNB in cluster 5 (86.8° and 89.8°) might be reasonable.

In terms of ANB, clusters 4 and 3, which commonly belonged to the protrusive mandible group, showed large negative ANB values. However, the reason might be different between them. In cluster 4, the hypodivergent pattern might play a role in increasing the negative value of ANB (–6.5°). In cluster 3, a relatively more retrusive maxilla compared with other clusters in the protrusive mandible group might be a major factor in increasing the negative value of ANB (–4.6°).

Comparison of the Vertical Characteristics

All three vertical variables could differentiate the hypodivergent pattern (cluster 4) and the hyperdivergent pattern (clusters 2, 7, and 9) from the normodivergent pattern (all $P < .001$; Table 2, Figure 4). In addition, Björk sum and SN-GoMe showed the same result in the post hoc test, which indicated that these two variables might be used interchangeably in determining the vertical pattern, at least in patients with skeletal Class III malocclusion.

Comparison of the Mandibular Characteristics

Although the gonial angle might be related with the shape of mandible, it showed a similar result as the vertical variables (Björk sum, SN-GoMe, and SN-OP; Table 2, Figure 4). For example, cluster 4 (117.0°) and cluster 7 (132.1°) showed the same result with Björk sum in cluster 4 (383.1°, hypodivergent pattern type) and cluster 7 (405.2°, hyperdivergent pattern type), respectively.

In terms of MBL/ACBL, clusters 4 and 8, which belonged to the severely protrusive mandible subgroup, showed the largest ratio (1.21 and 1.20), indicating a longer MBL compared with ACBL. Although clusters 7 and 9 showed the lowest ratios (1.13 and 1.15), a severely retrusive maxilla might induce a skeletal Class III relationship.

Comparison of the Cranial Base Characteristics

When the saddle angle got smaller as in cluster 5 (the smallest among the nine phenotypes), the mandible might move more forward, resulting in a severely protrusive position (Table 2, Figure 4). When the saddle angle got larger as in clusters 7, 9, and 6 (the largest among the nine phenotypes), the mandible might move more backward, resulting in a normal position rather than a protrusive position.

Comparison of the Dental Characteristics

Because cluster 5 showed a moderately protrusive maxilla (SNA, 86.8°) and significantly flared maxillary incisor inclination (U1 to SN, 119.0°; Table 2, Figures 4 and 5), extraction of the maxillary premolars, posterior impaction, and total setback of the maxilla would be necessary.[15–17] However, because clusters 7 and 9 showed a severely retrusive maxilla (SNA, 75.0° and 75.6°) and normal maxillary incisor inclination (U1 to SN, 101.9° and 108.8°), a nonextraction approach in the maxillary arch and advancement of the maxilla would be preferred.

In terms of IMPA, cluster 7 showed significant lingual inclination of the mandibular incisor (77.3°). Therefore, upside-down bonding of the mandibular incisor brackets and/or total mesialization of the mandibular dentition using orthodontic miniscrews and elastomeric chains would be necessary during preoperative orthodontic treatment.[18,19]

Considerations for Presurgical Orthodontic Treatment and Surgical Planning According to the Class III Phenotypes

SNA, SNB, Björk sum, SN-OP, U1 to SN, and IMPA can be used to set up appropriate treatment planning for presurgical orthodontic treatment and orthognathic surgery (Figure 5). A flow chart is proposed (Figure 5) for consideration in presurgical orthodontic treatment and surgical planning based on the Class III phenotypes.[15,20,21]

Although this study provided meaningful results, it is mandatory to confirm the findings from this study using multicenter studies with a larger sample size and sophisticated statistical analyses. Further studies would be necessary to investigate the relationship between the genotype and phenotype in patients with skeletal Class III malocclusion.

CONCLUSIONS

- The results from this study suggest that the AP position of the maxilla and rotation of the mandible according to the patient's vertical pattern might be the main key factors in determining Class III phenotypes.

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