Association between androgenetic alopecia and cardiovascular risk factors according to BASP classification in Korean androgenetic alopecia

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ABSTRACT

Association between androgenetic alopecia and cardiovascular risk factors according to BASP classification in Korean androgenetic alopecia

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Background: There have been many studies on the relationships between androgenetic alopecia (AGA) and cardiovascular risk factors; however, the study results are inconsistent, and research on AGA in Asians remains insufficient.

Objectives: This study investigated the relationships between Korean AGA and various cardiovascular risk factors, considering lifestyle, type of hair loss, and sex.

Methods and Results: This study investigated subjects who visited Wonju Severance Christian Hospital for public or industrial health medical examinations between October 2012 and December 2014. We performed anthropometric measurements and a blood test and administered a questionnaire.

Among the 1,884 total subjects, 52.6% had AGA. AGA patients had significantly higher prevalence of hypertension ($p<0.0001$), diabetes mellitus ($p<0.0001$), stroke ($p=0.0026$), dyslipidemia ($p=0.0175$), cardiovascular disease ($p=0.0163$), smoking ($p<0.0001$), and drinking ($p<0.0001$) than did the non-AGA group. Subgroup analysis showed that M-type (71.8%) and L-type (90.7%) were the most frequent basic types in male and female AGA patients, and F-type and FV-type were most common specific types in both AGA group. Higher prevalence rates of hypertension, diabetes, stroke, cardiovascular disease, and smoking were observed in male AGA patients. Late-onset AGA patients had higher prevalence of hypertension ($p<0.0001$), diabetes ($p=0.0026$), and metabolic syndrome ($p=0.0499$). The more severe was the AGA, the higher was the incidence of hypertension ($p=0.0046$), diabetes ($p=0.0278$), and smoking ($p=0.004$). The prevalence rate of metabolic syndrome increased with increasing AGA severity.

According to the analysis results by BASP classification, patients without any specific type AGA showed relatively lower percentage of medical diseases compared to patients of other specific types. Patients with both F-type and V-type AGA displayed a higher prevalence of hypertension (p=0.0289). The risk of hypertension and diabetes were increased for AGA subjects, especially in male, late onset, FV-type and moderate to severe AGA patients. In adjusted model, hypertension, diabetes, dyslipidemia, stroke, and metabolic syndrome had higher risks in AGA patients.

Conclusion: In this large population-based study, cardiovascular disease-related risk was significantly associated with male sex, moderate to severe AGA, and FV-type AGA. Modifications in lifestyle and early screening for cardiovascular disease and metabolic syndrome are suggested in male patients and in those with moderate to severe AGA involving frontal scalp area.

Key Words: Androgenetic alopecia, BASP classification, Cardiovascular disease, Korean, Lifestyle, Metabolic syndrome

I. Introduction

Androgenetic alopecia (AGA) is the most common type of hair loss in males and females and is characterized by gradual decrease in the thickness and length of hair [1-5]. AGA can occur in all races, though the prevalence rate varies by race. In general, the prevalence rate is highest in Caucasians, though the prevalence rate of AGA in Koreans has been reported to range from 14.1 to 50%. The prevalence rate of AGA is gradually increasing in both of these populations, which is consistent with global trends [4, 6-8].

There have been many ongoing studies on the relationships between AGA and cardiovascular risk factors since Cotton et al. first reported that the risk of cardiovascular diseases was increased in male AGA patients [9]. Some studies have suggested that the incidence of cardiovascular disease was increased in early-onset AGA. Others have reported that AGA involving the vertex area of the scalp and more severe baldness was associated with an increased risk of cardiovascular diseases [10-18]. Recent reports have shown that the prevalence of metabolic syndrome, insulin resistance, dyslipidemia, and hypertension increases in patients with more severe AGA and early onset AGA [11, 12, 14, 19-26].

However, some studies have reported that AGA is not correlated with cardiovascular diseases [16, 27-33]. Therefore, there is controversy in the field.

Most prior research was based on Western populations, and there are few studies on Korean AGA. Moreover, these studies did not consider most cardiovascular-related disorders, such as hypertension, diabetes mellitus, insulin resistance, dyslipidemia, and obesity; they also did not include lifestyle and other factors relevant to hair loss [34]. Previous studies on Korean AGA have excluded male patients with female pattern hair loss [34]. Previous studies on Caucasian AGA patients also excluded such patients. This is associated with the limitation of the Norwood-Hamilton classification. The Norwood-Hamilton classification is the most commonly used system to evaluate AGA, but it has limitations when evaluating female pattern hair loss; in addition, some types of AGA cannot be classified with the Norwood-Hamilton classification [6]. Lee et al. have therefore introduced the BASP classification, which can classify all types of hair loss patterns regardless of sex or race [35]. The BASP could be more useful in a study of Korean AGA patients, who have a high proportion of female pattern hair loss [35].

The current study aimed to investigate the relationships between AGA and cardiovascular risk factors, including lifestyles, in Koreans. In addition, we examined the relationships between cardiovascular risk factors and type of hair

loss, severity of hair loss, and sex. We used the BASP classification to evaluate all types of hair loss and to compare male and female AGA.

II. Materials & Methods

1. Subjects

This study investigated subjects who visited Wonju Severance Christian Hospital for a public health medical examination or industrial health medical examination between October 2012 and December 2014. Patients who refused to provide information and participate in the questionnaire were excluded. Patients who completed the anthropometric measurement, medical history, questionnaire, assessment of hair loss by BASP classification, and a blood test were included in the study.

2. Anthropometric measurements

Blood pressure, height, weight, and waist circumference were measured, and BMI was calculated. The blood pressure was measured in the sitting position after 5 minutes of rest. The patients sat on the chair with both feet on the floor and the brachial artery at the same height as the heart. Coffee, exercise, and smoking

were avoided for at least 30 minutes before blood pressure measurement. Waist circumstance was measured between the lowest rib and pelvis. During the measurement, the patients stood with feet 30 cm apart.

3. Questionnaire on lifestyles and medical information

A questionnaire survey was conducted on smoking, drinking, and physical activity. Smoking was divided into current smokers and non-smokers, and drinking was divided according to the current state of drinking habits. Physical activity was classified into ‘sedentary subjects’ and ‘subjects who exercise’ depending on whether the subject regularly exercised more than two times a week. A questionnaire survey on medical history was conducted. The questionnaire included information about the medical history of the patient and their family, any diagnosed diseases, and medication.

질환력(과거력/가족력) 관련 문항

1. 다음과 같은 질환으로 진단을 받았거나, 현재 약물치료 중인가?

	뇌졸중	심장병	고혈압	당뇨병	이상지질혈증	폐결핵	기타
진단여부							
약물치료							

2. 가족 중 다음 질환을 앓았거나 해당 질환으로 사망한 경우가 있는가?

	뇌졸중	심장병	고혈압	당뇨병	기타
진단여부					

흡연관련문항

□예, 현재도 흡연 중 (몇 년째 담배를 피우십니까? 총_____년, 평균 하루 흡연량은? _____개피)
□지금은 끊었음(금연전 담배를 피운 기간? 총_____년, 금연전 평균 하루 흡연량은? _____개피)
□아니오

음주관련문항

1. 1주에 평균 음주 횟수는? □ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7
2. 한번에 얼마나 마십니까? _____잔

신체활동(운동)관련문항

1. 최근 1주일간 숨이 훨씬 찰 정도의 격렬한 활동을 하루 20분 이상 시행한 날은 며칠인가?
□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7
2. 최근 1주일간 숨이 조금 더 찰 정도의 중간정도 활동을 하루 30분 이상 시행한 날은 며칠인가?
□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7
3. 최근 1주일간 한번에 적어도 10분 이상 걸은 경우를 합하여 하루 총 30분 이상 걸은 날은?
□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7

Figure 1. Questionnaire on lifestyles and medical information

4. Assessment of hair loss and classification standard

A well-trained dermatologist used the BASP classification to evaluate hair loss. This classification is based on observed patterns of hair loss. The basic type (BA) represents the shape of the anterior hairline, and the specific type (SP) represents the density of hair in distinct areas (frontal and vertex areas of the scalp). There are 4 basic types (L, M, C, and U) and 2 specific types (F and V). The final type is decided by the combination of the assigned BA and SP types [35]. The subjects who were classified by the BASP system as L, M0, or C0 without a specific type were considered non-AGA patients, and the rest of the BASP types were considered AGA patients. Subjects were classified by onset period of hair loss, and early onset AGA was defined as AGA occurrence before the age of 35. The severity of hair loss was classified by the BASP classification, and the standard was as follows. Mild AGA included basic types L, M0, M1, and C1 and specific types V1 and F1; moderate AGA included basic types M2 and C2 and specific types V2 and F2; and severe AGA included basic types M3, C3, U1, U2, and U3 and specific types V3 and F3.

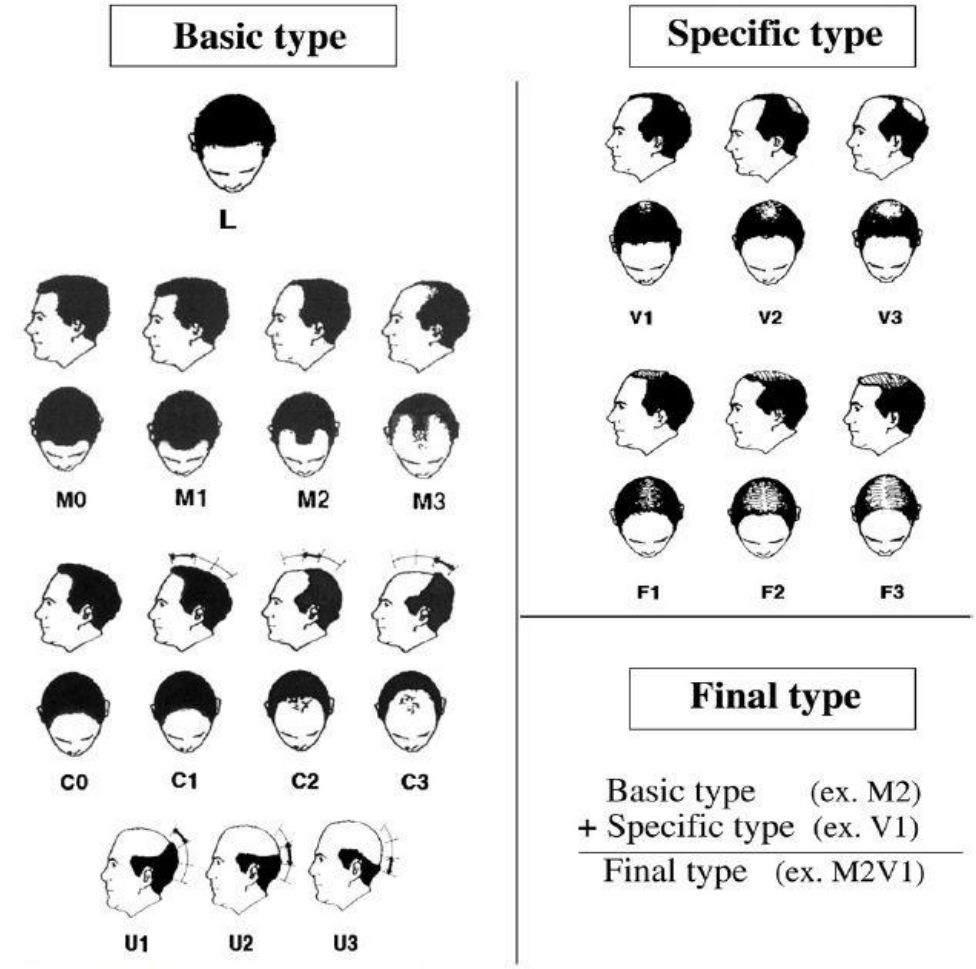

Figure 2. BASP classification

5. Blood test

A blood test was conducted by collecting venous blood after 12 hours of fasting. Fasting glucose, total cholesterol, triglycerides, low density lipoprotein (LDL) cholesterol, and high density lipoprotein (HDL) cholesterol were measured to diagnose metabolic syndrome and evaluate cardiovascular related disorders.

6. Definitions of cardiovascular related disorders

The hypertension, diabetes, dyslipidemia, stroke, and cardiovascular disease were considered as cardiovascular related disorders. The patients who had been diagnosed as or taken medication for hypertension, diabetes, dyslipidemia, stroke, and cardiovascular diseases were considered as having each disorder. In addition, when the systolic blood pressure and diastolic blood pressure were equal to or greater than 140/90mmHg were diagnosed as hypertension. The patients whose fasting glucose was equal to or greater than 126 mg/dl were considered as diabetes. A subject was diagnosed as having dyslipidemia when they met one of the standards below; total Cholesterol $\geq$ 220 mg/dl, LDL-C $\geq$ 140 mg/dl, triglyceride $\geq$ 150 mg/dl, or HDL-C $<$ 40 mg/dl.

7. Diagnosis of metabolic syndrome

Metabolic syndrome was diagnosed based on the standards of the National Cholesterol Education Program's ATP III. A subject was diagnosed as having metabolic syndrome when they met three of the standards below:

1) Abdominal obesity, defined as waist circumference ≥ 90 cm for males or ≥ 85 cm for females (based on the Korean-specific cutoffs for abdominal obesity defined by the Korean Society of Obesity)
2) Hypertriglyceridemia, defined as serum triglyceride concentration ≥ 150 mg/dL (1.69 mmol/L)
3) High blood pressure, defined as systolic blood pressure (SBP) ≥ 130 mmHg, diastolic blood pressure (DBP) ≥ 85 mmHg, or treatment with antihypertensive agents
4) Low serum HDL cholesterol, defined as serum HDL cholesterol concentration < 40 mg/dL for men or < 50 mg/dL for women
5) High fasting glucose, defined as fasting serum glucose ≥ 100 mg/dL or a previous diagnosis of type 2 diabetes

8. Statistical analysis methods

A Chi-square test or Fisher's exact test was performed to compare categorical variables, such as medical history, family history of hair loss, diagnosis of metabolic syndrome, drinking, smoking, and exercising, between AGA patients and subjects without hair loss. A two-sample Student's t-test was performed to compare continuous variables, such as blood pressure, waist circumference, and results of the blood test. AGA patients were divided into subgroups by time of onset of hair loss and sex, and a Chi-square test and two-sample Student's t-test were used for analysis. A one-way ANOVA and Chi-square test (Fisher's exact test) were used to compare the variables by severity of AGA. Logistic regression analysis was used to evaluate the risk factors related to cardiovascular related disorders and metabolic syndrome and to measure the degree of risk of each factor. P-value less than 0.05 were considered statistically significant, and all statistical analyses were performed using SAS 9.2 Ver. (SAS Inc., Cary, NC, USA).

III. Results

1. Characteristics of the subjects

A total of 1,884 patients participated in this study, with 915 (48.6%) males and 969 (51.4%) females. The average age of the subjects was 56.6 years, and the average ages of males and females were 55.7 and 57.5, respectively. Among the total patients, 991 (52.6%) had AGA, 613 (61.9%) males and 378 (38.1%) females (Table 1).

Table 1. Demographic characteristics of subjects

	No. of patient (%)	Age (yr±SD)
Total	1,884 (100.0%)	56.6±12.8
Male	915 (48.6%)	55.7±13.9
Female	969 (51.4%)	57.5±11.5
AGA	991 (52.6%)	53.0±13.0
Male	613 (61.9%)	59.1±12.3
Female	378 (38.1%)	61.1±10.2
non-AGA	893 (47.4%)	53.0±11.6
Male	302 (33.8%)	48.8±14.4
Female	591 (66.2%)	55.2±11.7

2. Comparison between AGA and non-AGA patients

The AGA group had a higher percentage of patients with a family history of hair loss compared to the non-AGA group (39.1% and 19.3%; $p<0.0001$). The AGA group also showed a significantly higher frequency of medical history of hypertension, diabetes, stroke, cardiovascular disease, dyslipidemia and metabolic syndrome. A higher percentage of the AGA group reported smoking, drinking, and regular exercise (Table 2).

Table 2. Comparison between AGA and non-AGA subjects

	non-AGA(n=893)	AGA(n=991)	p-value
Medical history			
HTN	288 (32.3%)	458 (46.2%)	<0.0001
DM	114 (12.8%)	225 (22.7%)	<0.0001
Stroke	11 (1.2%)	33 (3.3%)	0.0026
Cardiovascular dz.	48 (5.4%)	81 (8.2%)	0.0163
Dyslipidemia	464 (52.0%)	569 (57.4%)	0.0175
Metabolic SD	168 (18.8%)	236 (23.8%)	0.0083
Lifestyle			
Smoking	214 (24.0%)	334 (33.7%)	<0.0001
Drinking	314 (35.2%)	436 (44.0%)	<0.0001
Exercise	527 (59.0%)	636 (64.2%)	0.021
AGA FHx	172 (19.3%)	387 (39.1%)	<0.0001

HTN; Hypertension, DM; Diabete mellitus, Cardiovascular dz.; Cardiovascular disease, Metabolic SD; Metabolic syndrome, AGA FHx; Family history of androgenetic alopecia

3. Comparison between male and female AGA groups

Among the total 991 patients in the AGA group, 613 (61.9%) were male and 378 (38.1%) were female. Male patients had a higher frequency of medical history of hypertension, diabetes, stroke, and cardiovascular disease. Smoking and drinking were both significantly higher in the male AGA group (Table 3).

The basic type, specific type, and severity of AGA were significantly different in male and female AGA. Family history of AGA did not show a significant difference in the two groups. M-type (71.8%) and L-type (90.7%) were the most frequent basic types in male and female AGA patients, respectively. In male AGA, F-type (24.8%) and FV-type (20.4%) were most common specific types, and F-type (85.7%) was most common in female AGA. Of the AGA patients, 40.9% of male patients showed moderate severity disease, while 59.0% of female patients had mild disease (Table 3).

Table 3. Comparison between male and female AGA groups

	Male(n=613)	Female(n=378)	p-value
Medical history			
HTN	293 (47.8%)	165 (43.7%)	0.2034
DM	142 (23.2%)	83 (22.0%)	0.6595
Stroke	23 (3.8%)	10 (2.7%)	0.3457
Cardiovascular dz.	55 (9.0%)	26 (6.9%)	0.2425
Dyslipidemia	340 (55.5%)	229 (60.6%)	0.1136
Metabolic SD	137 (22.4%)	99 (26.2%)	0.1679
Lifestyle			
Smoking	319 (52.0%)	15 (4.0%)	<0.0001
Drinking	373 (60.8%)	63 (16.7%)	<0.0001
Exercise	389 (63.5%)	247 (65.3%)	0.548

Be continued

Be continued

AGA factors			
AGA FHx	242 (39.5%)	145 (38.4%)	0.726
Basic type			<0.0001
L	74 (12.1%)	343 (90.7%)	
M	440 (71.8%)	19 (5.0%)	
C	57 (9.3%)	15 (4.0%)	
U	42 (6.9%)	1 (0.3%)	
Specific type			<0.0001
No	248 (40.5%)	12 (3.2%)	
F	152 (24.8%)	324 (85.7%)	
V	88 (14.4%)	17 (4.5%)	
FV	125 (20.4%)	25 (6.6%)	
Severity of AGA			<0.0001
Mild	220 (35.9%)	223 (59.0%)	
Moderate	251 (40.9%)	130 (34.4%)	
Severe	142 (23.2%)	25 (6.6%)	

HTN; Hypertension, DM; Diabete mellitus, Cardiovascular dz.; Cardiovascular disease, Metabolic SD; Metabolic syndrome, AGA FHx; Family history of androgenetic alopecia

4. Comparison between early onset AGA and late onset AGA

Among the total 991 subjects in the AGA group, 38 (3.8%) had early-onset AGA, with the start of hair loss occurring before the age of 35, and 953 (96.2%) patients had late-onset AGA. The late-onset group had a significantly higher percentage of patients with a medical history of hypertension, diabetes, and metabolic syndrome. The frequency of family history of AGA was higher in early onset AGA. Among the patients with early onset AGA, a higher number of patients were smokers (36.8%) and drinkers (73.7%) (Table 4).

Table 4. Comparison between early-onset AGA and late-onset AGA

	Late onset(n=953)	Early onset(n=38)	p-value
Medical history			
HTN	453 (47.5%)	5 (13.2%)	<0.0001
DM	224 (23.5%)	1 (2.6%)	0.0026
Stroke	33 (3.5%)	0 (0.0%)	0.6334
Cardiovascular dz.	81 (8.5%)	0 (0.0%)	0.0663
Dyslipidemia	550 (57.7%)	19 (50.0%)	0.3457
Metabolic SD	232 (24.3%)	4 (10.5%)	0.0499
Lifestyle			
Smoking	320 (33.6%)	14 (36.8%)	0.676
Drinking	408 (42.8%)	28 (73.7%)	0.0002
Exercise	614 (64.4%)	22 (57.9%)	0.410
AGA FHx	366 (38.4%)	21 (55.3%)	0.037

HTN; Hypertension, DM; Diabete mellitus, Cardiovascular dz.; Cardiovascular disease, Metabolic SD; Metabolic syndrome, AGA FHx; Family history of androgenetic alopecia

5. Comparison by severity of hair loss

Among the 991 AGA patients, 44.7% (443) had mild AGA, 38.4% (381) had moderate AGA, and 16.9% (167) had severe AGA. The severe AGA group displayed a significantly higher frequency of hypertension, and patients with moderate and severe AGA had a significantly higher frequency of diabetes than patients with mild AGA. The prevalence rate of metabolic syndrome increased with increasing severity of AGA. The smoking rate and family history of alopecia showed a significantly increasing trend with severity of AGA (Table 5).

Table 5. Comparison based on severity of AGA

	Mild(n=443)	Moderate(n=381)	Severe(n=167)	p-value
Medical history				
HTN	181 (40.9%)	186 (48.8%)	91 (54.5%)	0.0046
DM	84 (19.0%)	102 (26.8%)	39 (23.4%)	0.0278
Stroke	10 (2.3%)	18 (4.7%)	5 (3.0%)	0.139
Cardiovascular dz.	26 (5.9%)	39 (10.2%)	16 (9.6%)	0.057
Dyslipidemia	263 (59.4%)	218 (57.2%)	88 (52.7%)	0.3297
Metabolic SD	94 (21.2%)	93 (24.4%)	49 (29.3%)	0.1038
Lifestyle				
Smoking	125 (28.2%)	143 (37.5%)	66 (39.5%)	0.004
Drinking	186 (42.0%)	176 (46.2%)	74 (44.3%)	0.477
Exercise	273 (61.6%)	244 (64.0%)	119 (71.3%)	0.086
AGA FHx	143 (32.3%)	155 (40.7%)	89 (53.3%)	<0.0001

HTN; Hypertension, DM; Diabete mellitus, Cardiovascular dz.; Cardiovascular disease, Metabolic SD; Metabolic syndrome, AGA FHx; Family history of androgenetic alopecia

6. Comparison by type of AGA

Among the total AGA patients, 42.1% (417) were L-type, 46.3% (459) were M-type, 7.3% (72) were C-type, and 4.3% (43) were U-type. In a comparison of the basic types of AGA, there was no significant difference in cardiovascular related disorders and metabolic syndrome. The percentages of smoking, drinking and family history of AGA were significantly different between the basic types of AGA. But these factors did not show any distinct trends (Table 6).

The percentage of patients who did not show a specific type of AGA was 26.2% (260) among the total AGA patients, while 17.1% (169) were F-type, 41.6% (412) were V-type, and 15.1% (150) were both F- and V-type. When comparing the specific type groups, patients without any specific type AGA showed relatively lower percentage of medical diseases compared to patients of other specific types. Patients with both F-type and V-type AGA had significantly higher percentages of hypertension. And F-type patients showed higher percentages of smoking and drinking compared to patient groups of other types (Table 7).

Table 6. Comparison based on basic type of AGA

	L(n=417)	M(n=459)	C(n=72)	U(n=43)	p-value
Medical history					
HTN	176 (42.2%)	222 (48.4%)	38 (52.8%)	22 (51.2%)	0.1563
DM	99 (23.7%)	100 (21.8%)	14 (19.4%)	12 (27.9%)	0.6651
Stroke	9 (2.2%)	19 (4.1%)	3 (4.2%)	2 (4.7%)	0.2608
CVD	31 (7.4%)	36 (7.8%)	9 (12.5%)	5 (11.6%)	0.415
Dyslipidemia	239 (57.3%)	272 (59.3%)	39 (54.2%)	19 (44.2%)	0.2584
Met SD	106 (25.4%)	105 (22.9%)	17 (23.6%)	8 (18.6%)	0.6915
Lifestyle					
Smoking	59 (14.1%)	219 (47.7%)	34 (47.2%)	22 (51.2%)	<0.0001
Drinking	101 (24.2%)	277 (60.4%)	39 (54.2%)	19 (44.2%)	<0.0001
Exercise	270 (64.8%)	289 (63.0%)	44 (61.1%)	33 (76.7%)	0.308
AGA FHx	144 (34.5%)	178 (38.8%)	39 (54.2%)	26 (60.5%)	<0.0001

HTN; Hypertension, DM; Diabete mellitus, CVD.; Cardiovascular disease, Met SD; Metabolic syndrome, AGA FHx; Family history of androgenetic alopecia

Table 7. Comparison based on specific type of AGA

	No(n=260)	F(n=169)	V(n=412)	FV(n=150)	p-value
Medical history					
HTN	109 (41.9%)	71 (42.0%)	194 (47.1%)	84 (56.0%)	0.0289
DM	50 (19.2%)	37 (21.9%)	101 (24.5%)	37 (24.7%)	0.3995
Stroke	5 (1.9%)	8 (4.7%)	13 (3.2%)	7 (4.7%)	0.320
CVD	23 (8.9%)	9 (5.3%)	35 (8.5%)	14 (9.3%)	0.511
Dyslipidemia	147 (56.5%)	92 (54.4%)	238 (57.8%)	92 (61.3%)	0.6465
Met SD	51 (19.6%)	49 (29.0%)	102 (24.8%)	34 (22.7%)	0.1487
Lifestyle					
Smoking	133 (51.2%)	86 (50.9%)	64 (15.5%)	51 (34.0%)	<0.0001
Drinking	158 (60.8%)	108 (63.9%)	100 (24.3%)	70 (46.7%)	<0.0001
Exercise	159 (61.2%)	104 (61.5%)	262 (63.6%)	111 (74.0%)	0.048
AGA FHx	104 (40.0%)	73 (43.2%)	141 (34.2%)	69 (46.0%)	0.039

HTN; Hypertension, DM; Diabete mellitus, CVD; Cardiovascular disease, Met SD; Metabolic syndrome, AGA FHx; Family history of androgenetic alopecia

7. Factors that affect cardiovascular related disorders

Table 8-13 demonstrated the associations between cardiovascular related disorders, metabolic syndrome and AGA. The results were analyzed with and without adjustment for age, gender, smoking, drinking, and exercise.

The risk of hypertension was increased for AGA subjects, especially in male, late onset, FV-type and severe AGA patients in the unadjusted model (1.805, 95% CI 1.496-2.178;1.923, 95% CI 1.556-2.377; 1.903, 95% CI 1.575-2.300; 2.424, 95% CI 1.717-3.420; 2.004, 95% CI 1.568-2.560). The risk of diabetes was similarly increased for AGA subjects with male, late onset, FV-type and moderate AGA in the unadjusted model (2.007, 95% CI 1.569-2.568; 2.060, 95% CI 1.570-2.703; 2.100, 95% CI 1.640-2.688; 1.975, 95% CI 1.315-2.965; 2.498, 95% CI 1.851-3.373). The risks of dyslipidemia, stroke, cardiovascular disease and metabolic syndrome were increased in AGA patients compared with non-AGA (1.247, 95% CI 1.039-1.495; 2.762, 95% CI 1.387-5.498; 1.567, 95% CI 1.083-2.266; 1.349, 95% CI 1.080-1.685).

In adjusted model, diabetes and dyslipidemia had higher risks in AGA patients (1.387, 95% CI 1.058-1.819; 1.248, 95% CI 1.022-1.523). The risks of hypertension, stroke and metabolic syndrome were increased in AGA subjects, but

these findings were not statistically significant (1.201, 95% CI 0.972-1.484; 1.624, 95% CI 0.774-3.408; 1.146, 95% CI 0.898-1.463).

Table 8. Results of multivariate analysis of the factors that affect hypertension

Variables		Crude OR (95%CI)	Adjusted OR (95%CI)
AGA	No	1	1
	Yes	1.805 (1.496 ~2.178)	1.201 (0.972~1.484)
Sex	No AGA	1	1
	Male	1.923 (1.556~2.377)	1.028 (0.754~1.403)
	Female	1.627 (1.271~2.083)	1.360 (1.028~1.799)
Early onset	No AGA	1	1
	Early onset	0.318 (0.123~0.824)	0.729 (0.268~1.980)
	Late onset	1.903 (1.575~2.300)	1.222 (0.987~1.512)
Basic type	L	1	1
	C	2.038 (1.266~3.281)	1.391 (0.829~2.336)
	M	1.708 (1.377~2.118)	1.296 (0.974~1.726)
	U	1.910 (1.039~3.510)	0.965 (0.501~1.857)
Specific type	No specific	1	1
	F	1.380 (0.993~1.917)	0.876 (0.614~1.251)
	FV	2.424 (1.717~3.420)	1.547 (1.067~2.242)
	V	1.695 (1.349~2.130)	1.422 (1.109~1.825)
Severity	No AGA	1	1
	Mild	1.451 (1.146~1.837)	1.166 (0.909~1.497)
	Moderate	2.004 (1.568~2.560)	1.222 (0.931~1.605)
	severe	2.515 (1.799~3.517)	1.288 (0.884~1.875)

AGA; Androgenetic alopecia, OR; Odd ratio, CI; Confidence interval

Table 9. Results of multivariate analysis of the factors that affect diabetes mellitus

Variables		Crude OR (95%CI)	Adjusted OR (95%CI)
AGA	No	1	1
	Yes	2.007 (1.569~2.568)	1.387 (1.058~1.819)
Sex	No AGA	1	1
	Male	2.060 (1.570~2.703)	1.111 (0.751~1.643)
	Female	1.923 (1.406~2.629)	1.660 (1.159~2.378)
Early onset	No AGA	1	1
	Early onset	0.185 (0.025~1.359)	0.414 (0.054~3.187)
	Late onset	2.100 (1.640~2.688)	1.413 (1.076~1.856)
Basic type	L	1	1
	C	1.243 (0.681~2.269)	0.775 (0.405~1.484)
	M	1.435 (1.100~1.871)	0.991 (0.700~1.404)
	U	1.994 (1.008~3.944)	0.924 (0.443~1.927)
Specific type	No specific	1	1
	F	1.690 (1.133~2.522)	1.166 (0.762~1.785)
	FV	1.975 (1.315~2.965)	1.216 (0.788~1.877)
	V	1.958 (1.482~2.588)	1.664 (1.231~2.248)
Severity	No AGA	1	1
	Mild	1.599 (1.175~2.176)	1.316 (0.955~1.814)
	Moderate	2.498 (1.851~3.373)	1.604 (1.154~2.229)
	severe	2.082 (1.383~3.134)	1.087 (0.690~1.711)

AGA; Androgenetic alopecia, OR; Odd ratio, CI; Confidence interval

Table 10. Results of multivariate analysis of the factors that affect dyslipidemia

Variables		Crude OR (95%CI)	Adjusted OR (95%CI)
	No	1	1
	Yes	1.247 (1.039~1.495)	1.248 (1.022~1.523)
Sex	No AGA	1	1
	Male	1.151 (0.937~1.415)	1.035 (0.775~1.382)
	Female	1.421 (1.113~1.815)	1.459 (1.119~1.903)
Early onset	No AGA	1	1
	Early onset	0.925 (0.483~1.770)	0.979 (0.500~1.917)
	Late onset	1.262 (1.050~1.516)	1.268 (1.034~1.555)
Basic type	L	1	1
	C	1.020 (0.634~1.643)	1.050 (0.641~1.722)
	M	1.256 (1.012~1.558)	1.336 (1.020~1.749)
	U	0.684 (0.371~1.260)	0.703 (0.370~1.334)
Specific type	No specific	1	1
	F	1.060 (0.767~1.466)	1.040 (0.741~1.459)
	FV	1.407 (0.993~1.993)	1.382 (0.961~1.987)
	V	1.213 (0.967~1.523)	1.195 (0.941~1.516)
Severity	No AGA	1	1
	Mild	1.351 (1.073~1.701)	1.340 (1.058~1.696)
	Moderate	1.237 (0.971~1.575)	1.210 (0.931~1.572)
	severe	1.030 (0.740~1.434)	1.001 (0.697~1.439)

AGA; Androgenetic alopecia, OR; Odd ratio, CI; Confidence interval

Table 11. Results of multivariate analysis of the factors that affect stroke

Variables		Crude OR (95%CI)	Adjusted OR (95%CI)
AGA	No	1	1
	Yes	2.762 (1.387~5.498)	1.624 (0.774~3.408)
Sex	No AGA	1	1
	Male	3.126 (1.512~6.460)	1.163 (0.454~2.977)
	Female	2.179 (0.917~5.174)	2.407 (0.809~7.168)
Early onset	No AGA	1	1
	Early onset	0.000 (0.000 ~999.9)	0.000 (0.000 ~999.9)
	Late onset	2.876 (1.445~5.726)	1.654 (0.787~3.478)
Basic type	L	1	1
	C	2.805 (0.814~9.666)	1.794 (0.463~6.957)
	M	2.786 (1.473~5.268)	1.996 (0.840~4.741)
	U	3.148 (0.712~13.914)	1.523 (0.300~7.717)
Specific type	No specific	1	1
	F	3.531 (1.487~8.383)	2.285 (0.926~5.638)
	FV	3.479 (1.407~8.599)	1.948 (0.754~5.028)
	V	2.315 (1.104~4.856)	2.040 (0.933~4.463)
Severity	No AGA	1	1
	Mild	1.852 (0.780~4.394)	1.386 (0.573~3.352)
	Moderate	3.976 (1.859~8.502)	2.161 (0.951~4.910)
	severe	2.475 (0.849~7.217)	1.017 (0.320~3.230)

AGA; Androgenetic alopecia, OR; Odd ratio, CI; Confidence interval

Table 12. Results of multivariate analysis of the factors that affect cardiovascular disease

Variables		Crude OR (95%CI)	Adjusted OR (95%CI)
AGA	No	1	1
	Yes	1.567 (1.083~2.266)	0.866 (0.572~1.311)
Sex	No AGA	1	1
	Male	1.735 (1.161~2.593)	0.812 (0.449~1.468)
	Female	1.300 (0.794~2.129)	0.918 (0.524~1.608)
Early onset	No AGA	1	1
	Early onset	0.000 (0.000 ~999.9)	0.000 (0.000 ~999.9)
	Late onset	1.635 (1.130~2.366)	0.874 (0.577~1.323)
Basic type	L	1	1
	C	2.226 (1.068~4.641)	1.244 (0.544~2.846)
	M	1.326 (0.881~1.997)	0.860 (0.505~1.464)
	U	2.050 (0.785~5.354)	0.788 (0.278~2.239)
Specific type	No specific	1	1
	F	0.857 (0.420~1.749)	0.536 (0.253~1.135)
	FV	1.569 (0.861~2.859)	0.827 (0.432~1.586)
	V	1.415 (0.928~2.156)	0.997 (0.631~1.574)
Severity	No AGA	1	1
	Mild	1.098 (0.671~1.794)	0.805 (0.480~1.349)
	Moderate	2.008 (1.292~3.120)	0.993 (0.607~1.624)
	severe	1.865 (1.032~3.371)	0.725 (0.373~1.410)

AGA; Androgenetic alopecia, OR; Odd ratio, CI; Confidence interval

Table 13. Results of multivariate analysis of the factors that affect metabolic syndrome

Variables		Crude OR (95%CI)	Adjusted OR (95%CI)
AGA	No	1	1
	Yes	1.349 (1.080~1.685)	1.146 (0.898~1.463)
Sex	No AGA	1	1
	Male	1.242 (0.964~1.600)	0.898 (0.628~1.284)
	Female	1.531 (1.153~2.035)	1.378 (1.005~1.890)
Early onset	No AGA	1	1
	Early onset	0.508 (0.178~1.450)	0.846 (0.288~2.487)
	Late onset	1.389 (1.110~1.737)	1.159 (0.905~1.484)
Basic type	L	1	1
	C	1.169 (0.668~2.046)	0.983 (0.545~1.773)
	M	1.121 (0.869~1.448)	1.012 (0.729~1.405)
	U	0.864 (0.396~1.884)	0.631 (0.279~1.428)
Specific type	No specific	1	1
	F	1.742 (1.211~2.506)	1.565 (1.065~2.299)
	FV	1.250 (0.830~1.883)	1.047 (0.682~1.609)
	V	1.403 (1.074~1.834)	1.188 (0.896~1.575)
Severity	No AGA	1	1
	Mild	1.162 (0.876~1.542)	1.074 (0.803~1.436)
	Moderate	1.394 (1.045~1.858)	1.162 (0.850~1.589)
	severe	1.793 (1.235~2.603)	1.417 (0.937~2.143)

AGA; Androgenetic alopecia, OR; Odd ratio, CI; Confidence interval

IV. Discussion

AGA is the most common type of hair loss in both sexes. The main characteristic of AGA is hair miniaturization caused by peripheral androgens [1-5, 36]. AGA is an alteration of hair growth or premature aging of the pilosebaceous unit and has a multifactorial and potentially polygenic etiology [5, 37-40]. AGA can occur in all races, though the prevalence rate and type vary. In general, the prevalence rate of AGA is highest in Caucasians, as 30% of white men have AGA by the age of 30 years, and 50% have AGA by the age of 50 [4, 6]. Moreover, premature balding is 4 times more frequent in Caucasians than in other races [7, 8, 41, 42]. In studies of Korean AGA patients, the prevalence rate was approximately 14.1% in males and 5.6% in females. The rate of incidence increased with age in both sexes, but the prevalence rate appeared to be lower than that seen in Europeans. Nonetheless, the prevalence of AGA shows an increasing trend, globally [3, 7].

A report by Cotton et al. in 1972 was the first to show that the risk of cardiovascular disease increased in male AGA patients [9]. Since then, many studies have been conducted on the relationships between AGA and various risk

factors related to cardiovascular disease, such as hypertension, insulin resistance, dyslipidemia, and metabolic syndrome.

In a large-scale study, Lotofu et al. found that there was a correlation between severity of AGA and coronary artery disease [10], and Kamal et al. reported that the risk of coronary artery disease increased in Asian male AGA patients younger than 45 year with severe vertex AGA [11]. In a study conducted by Matilainen et al., the risk of cardiovascular disease was higher with AGA of grade 3 vertex or more on the Norwood-Hamilton classification scale; in addition, the cardiovascular risk was significantly higher in the early-onset AGA group [12]. Recently, there have been reports that the prevalence of metabolic syndrome, insulin resistance, dyslipidemia, and hypertension increase with more severe and early-onset AGA [10, 12, 14-26, 43-47].

However, Halim et al. and Cooke et al. have reported that male pattern alopecia is not correlated with myocardial infarction or coronary artery disease [27, 28], and Ford et al. reported that AGA does not increase the incidence or mortality of coronary artery disease [16]. Although the Framingham Heart Study did not find baldness to be associated with an increased risk of heart disease, men younger than 55 years who had very rapid onset and progressive AGA were slightly more prone to developing coronary heart disease [29]. Due to various

conflicting results, the effect of AGA on the risk of cardiovascular disease remains controversial.

Although the exact reason for the association between AGA and cardiovascular disease is unclear, several mechanisms have been proposed through different studies. Elevated androgen levels and increased peripheral sensitivity to androgens could be an explanation for the association between AGA and cardiovascular disease [10, 16, 32, 48]. It has long been suspected that excess androgens are related to various aspects of cardiovascular disease through mechanisms such as coronary atherogenesis and vasoconstriction [49-51]. Moreover, elevated androgen levels are related to the pathogenesis of AGA, as the number of androgen receptors is increased in the scalp of AGA patients [1, 5]. Chronic inflammation has been suggested to play a significant role in linking AGA, insulin resistance, and cardiovascular disease [40, 52-54]. Hirsso et al. have suggested that the microinflammation in the hair follicle that causes alopecia might be a local manifestation of systemic inflammation that can predict metabolic syndrome and cardiovascular disease among balding men [55].

Most previous studies on AGA have been conducted in Caucasian populations, and research on Asian AGA patients is sparse. However, AGA characteristics differ between Asian and Caucasian populations [8], as Asian men are more likely to demonstrate preservation of the frontal hairline, later onset of

AGA, and less extensive baldness [4, 6-9, 42]. In previous studies, FPHL was observed in 11.1% of Korean males with AGA, and this type of hair loss is not included in the Norwood classification [7]. Furthermore, in a study on Chinese AGA, MPHL was found in 12% of women with AGA [56, 57]. The Norwood-Hamilton classification, the most commonly used system, cannot classify FPHL. Therefore, clinicians must use distinct methodologies for each sex. However, the BASP classification can classify all hair loss patterns, regardless of sex or race [35]. Moreover, the BASP classification had higher reproducibility and repeatability compared with the Norwood-Hamilton classifications [58].

Therefore, we evaluated AGA using the BASP classification and included measurements of lifestyle such as smoking, drinking, and exercising.

We found that the incidence of hypertension, diabetes mellitus, stroke, cardiovascular, dyslipidemia and metabolic syndrome was higher in the AGA group. However, the total cholesterol and LDLcholesterol were lower in the AGA group. This might be because the AGA group was taking medication for dyslipidemia. The percentage of patients who regularly exercised was also higher in the AGA group, which might be related to the need for weight control to manage hypertension, diabetes, and dyslipidemia. However, the rates of smoking and drinking were higher in the AGA group, suggesting that more intensive lifestyle modification might be required for these patients, who had a higher risk

of cardiovascular related disorder. Furthermore, BMI and waist circumference were higher in the AGA group. Waist circumference is one of the diagnostic factors of metabolic syndrome and is considered to be a cardiovascular risk factor. The AGA group showed a higher waist circumference and a higher incidence of cardiovascular-related disorders, smoking, and drinking. Therefore, intensive lifestyle modifications and early screening of cardiovascular-related disorders might be needed.

In subgroup analysis of the AGA group, the percentage of patients with early onset AGA was extremely low, at only 3.8%. This low rate appears to be related to the 10-year slower onset of AGA seen in Asians compared to Caucasians [42]. Furthermore, most AGA patients recognize that they have alopecia after the hair loss has significantly progressed. The patients who their hair losses have actually begun before the age of 35 might think that it begun after the age of 35. Unlike previous studies, the incidences of hypertension and diabetes were significantly higher in late-onset AGA. This difference appears to be related to the smaller number of early-onset AGA patients in comparison to the number of late-onset AGA patients. The average age of the early-onset AGA and late-onset AGA was 33.67 years and 60.9 years, respectively. The older age of late-onset AGA group might also affect the results of the higher incidence of cardiovascular related disorders in late-onset AGA group.

Male and female AGA patients showed different results in basic type, specific type, and severity of AGA. M-type AGA was the most common basic type in male AGA, but L-type was most common in female AGA. These results were consistent with previous studies that suggested that frontal hairlines recede at the temples in male patients but are preserved in female patients [2]. In the present study, female patients showed a high incidence of F-type AGA involving the frontal scalp, which is consistent with the already known fact that female pattern hair loss typically leads to a diffuse decrease in density over the crown of the head [2]. However, this study showed that F-type and FV-type AGA involving the frontal scalp area had a relatively high frequency in male patients with AGA. These results are consistent with previous studies showing that Korean men tend to have more frontal hairline preservation and show a more female pattern of fair thinning than Caucasians [7]. In general, male patients tend to have more severe AGA. Because the Norwood-Hamilton classification is used to classify male pattern hair loss and the Ludwig classification is used for female pattern hair loss, there are no studies comparing the severity of AGA in both sexes. This comparison may be meaningful and the pathogenesis of these findings might be related to the higher level of androgens in male patients; however, the exact pathogenesis requires further study. Most cardiovascular related disorders

appeared at a higher frequency in male AGA patients, which suggests a relationship with increased androgen levels [5, 49-51].

According to the BASP classification results, cardiovascular disease risk factors did not show a significant trend between basic types. However, F-type AGA patients displayed a significantly higher BMI and waist circumference. And the prevalence of hypertension and diabetes were significantly higher in FV-type AGA patients. This result is significant considering the fact that the percentage of female pattern hair loss was higher in Koreans compared to Caucasians.

The results of logistic regression to assess whether AGA factors might affect the cardiovascular related disorders and metabolic syndrome showed that the risk of hypertension and diabetes were increased for AGA subjects, especially in male, late onset, FV-type and moderate to severe AGA patients. In adjustment model for age, gender, smoking, drinking, and exercise, hypertension, diabetes, stroke, and metabolic syndrome also showed higher risk in AGA subjects.

The percentage of patients who smoked and drunk was higher with male AGA, moderate to severe AGA, and F-type AGA. This corresponds with the higher level of cardiovascular related risk factors with male AGA, severe AGA, and F-type AGA and is consistent with the fact that smoking is a major cardiovascular disease risk factor.

The limitations of the study are that this study was performed at only one center and did not characterize the relationship between AGA and severity of cardiovascular disease.

In view of the results obtained thus far, we suggest modifications in lifestyle and early screening for cardiovascular disease, hypertension, and diabetes. Color Doppler ultrasound of the carotid arteries to assess the level of atheromatosis in addition to laboratory and anthropometric studies can be considered an effective early screening method for cardiovascular disease. These interventions might be suggested for Korean males who show severe AGA involving the frontal area.

V. Conclusion

There have been many studies on the relationships between AGA and cardiovascular risk factors, but study results are inconsistent, and research on AGA in Asians remains insufficient. We investigated the relationships between Korean AGA and cardiovascular risk factors, taking into account lifestyle, type of hair loss, and sex.

AGA patients displayed a significantly higher prevalence of cardiovascular related disorders, metabolic syndrome, smoking, and drinking than subjects without AGA. The prevalence of cardiovascular related disorders and smoking rate were higher in male AGA patients and moderate to severe AGA. Based on the BASP classification, F-type and FV-type AGA patients were more likely to be obese and had higher prevalence of cardiovascular related disorders than other types of AGA patients.

We suggest modifications in lifestyle and early screening for cardiovascular related disorders and metabolic syndrome for AGA patients. These interventions could be recommended for Korean males who show moderate to severe AGA involving the frontal and vertex scalp area.

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Abstract in Korean (국문요약)

한국인 안드로겐성 탈모 환자에서 BASP classification에 따른 안드로겐성 탈모와 심혈관 질환 위험 요소와의 연관성

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안드로겐성 탈모는 남성과 여성의 탈모 중 가장 흔한 유형으로,모든 인종에서 유병률이 증가하는 추세를 보이고 있으며, 한국에서도 안드로겐성 탈모의 유병률은 증가하는 추세이다.

안드로겐성 탈모와 심혈관 질환과의 관련성에 관한 연구들이 다양하게 진행되고 있으나, 연구들마다 서로 상이한 결과들을 보이고 있어 이 둘의 관련성에 대해서 논란의 여지가 있다. 기존에 보고된 대부분의 연구들은 서양인을 대상으로 진행되었으며, 한국인을 대상으로 한 연구는 부족한 실정이다. 특히, 고혈압, 당뇨, 이상지질혈증, 비만을 포함한 다양한 심혈관 질환 관련 위험요소들 및 흡연이나 운동과 같은 생활습관과의 관련성을 전반적으로 살펴본 연구는 전무한 실정이다. 따라서, 이 연구에서는 한국인에서 안드로겐성 탈모와 생활습관을 포함한 다양한 심혈관 질환 위험 요소들과의 관련성을 살펴보았으며, 탈모의 유형이나 성별에 따라 어떠한 경향성을 보이는지를 확인고자 하였다. 2012 년 10 월부터 2014 년 12 월까지 연세대학교 원주세브란스기독병원에 내원한 건강검진 수검자를 대상으로 하였으며, 설문조사, 신체계측 및 혈액검사를 실시하고, 연구에 참여할 의사가 있는 대상자를 연구에 포함하였다. 총 1884 명 중 52.6%가 안드로겐성 탈모 환자였으며, 안드로겐성 탈모 환자는 비 탈모군에 비해 고혈압 ($p<0.0001$), 당뇨 ($p<0.0001$), 뇌졸중 ($p=0.0026$), 이상지질혈증 ($p=0.0175$), 심혈관 질환 ($p=0.0163$), 대사증후군

(p=0.0083)의 유병률 및 흡연률 (p<0.0001)이 높았다. 성별에 따른 분석 결과, 남성 안드로겐성 탈모 환자에서 고혈압, 당뇨, 뇌졸중, 심혈관질환 및 대사증후군의 유병률이 더 높았으며, 여성 안드로겐성 탈모 환자에 비해 흡연률이 더 높았다. 심한 안드로겐성 탈모 환자에서 고혈압 (p=0.0046), 당뇨 (p=0.0278)의 유병률이 높고, 흡연률 (p=0.004)이 높았다. 또한, 안드로겐성 탈모의 중등도가 심할수록, 대사증후군의 유병률이 높아지는 경향을 보였다. BASP classification에 따른 분석 결과, specific type이 없는 탈모 환자에서 specific type의 탈모가 있는 환자에 비해 다양한 질환의 유병률이 더 낮았으며, FV-type을 보이는 안드로겐성 탈모 환자에서 고혈압 (p=0.0289)의 유병률이 높게 나타났다. 고혈압과 당뇨의 위험도는 비탈모군 보다는 탈모가 있는 환자에서, 특히 남성, FV-type, 중등도의 안드로겐성 탈모 환자에서 더 높았다. 여러 가지 인자를 보정한 분석에서도 안드로겐성 탈모 환자에서는 고혈압, 당뇨, 이상지질혈증, 뇌졸중, 대사증후군의 위험성이 더 높게 나타났다.

연구 결과는 중등도의 남성 안드로겐성 탈모 환자와 전두부를 침범하는 안드로겐성 탈모 환자에서 심혈관계 질환의 조기 검진을

고려할 수 있으며, 이와 더불어 생활습관의 변화가 필요함을 시사하고 있다.

핵심 되는 말 : 안드로겐성 탈모, BASP 분류법, 심혈관 질환, 대사 증후군, 한국인, 생활습관

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