The association of Coronary Artery Disease and Female Androgenetic Alopecia in Thai population.

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ABSTRACT :

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Background: There have been many epidemiological studies exhibiting some evidence of association between coronary artery disease and female androgenetic alopecia, only few studies accentuate on the association of coronary angiography results and female androgenetic alopecia.

Objectives: To determine the association of coronary angiography results and severity of female androgenic alopecia.

Materials and Methods: Our study was a cross-sectional study include 203 female participants who underwent coronary angiography due to both emergency and non-emergency conditions. All of the participants were evaluated for the severity of the baldness according to Ludwig' score[1]. Coronary angiography results were reported in standard protocols by interventional cardiologists.

Results: There are 203 female patients, 60.4% (84 in 139) of the patients with female androgenetic alopecia and 56.3% (36 in 64) of the patients without alopecia had at least one significant coronary artery stenosis, the difference was not statistically significant in both univariate (odd ratio 1.12, 95% CI 0.74-1.69, p-value 0.573) and multivariate (odd ratio 0.93, 95% CI 0.49-1.77, p-value 0.833) analytic model.

Conclusion: Our study revealed that there is no significant association between severity of baldness and result of coronary artery angiography in female androgenetic alopecia patients.

Key words: female androgenetic alopecia, female pattern hair loss, coronary artery disease,

             coronary angiography, ischemic heart disease, myocardial ischemia

บทคัดย่อ :

ปวงใจ วราภรพิพัฒน์*, จุลพรรธน์ อินทรศัพท์*, อาทิตย์ นาคะเกศ*, ธรณิศ จันทรารัตน์** ลักษณะหลอดเลือดหัวใจในผู้ป่วยโรคผมร่วงจากพันธุกรรมเพศหญิง วารสารโรคผิวหนัง 2560; 33: 153-160.

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ภูมิหลัง: มีการศึกษาเชิงระบาดวิทยาหลายการศึกษาแสดงถึงความสัมพันธ์ระหว่างภาวะผมร่วงจากพันธุกรรมและโรคหลอดเลือดหัวใจ แต่มีการศึกษาจำนวนไม่มากที่เน้นเรื่อง ความสัมพันธ์ระหว่างโรคผมร่วงจากพันธุกรรมกับภาวะการตีบของหลอดเลือดหัวใจ ที่สามารถตรวจพบได้โดยการตรวจหลอดเลือดหัวใจโดยการใช้สารรังสีทึบแสงโดยตรง

จุดประสงค์: หาความสัมพันธ์ระหว่างผลการตรวจหลอดเลือดหัวใจด้วยวิธีการฉีดสารทึบแสงกับโรคผมร่วงจากพันธุกรรมในผู้ป่วยเพศหญิง

วิธีการวิจัย: จากผู้ป่วยหญิง 203 รายที่ได้รับการตรวจหลอดเลือดหัวใจ ด้วยวิธีการฉีดสารทึบแสงนั้น ผู้ป่วยทุกรายจะได้รับการตรวจภาวะเส้นผมว่ามีโรคผมร่วงจากพันธุกรรหรือไม่ และถ้ามี มีความรุนแรงเพียงใดโดยใช้ วิธีการตรวจให้คะแนนแบบ Ludwig's core

ผลการวิจัย: จากผู้ป่วยหญิง 203 รายพบว่า 60.4% (84 ใน 139 ราย) ของผู้ป่วยที่มีภาวะผมบางทางพันธุกรรมจะตรวจพบว่ามีภาวะเส้นเลือดหัวใจตีบอย่างน้อยหนึ่งเส้นจากการตรวจหลอดเลือดหัวใจด้วยการฉีดสารทึบแสง และ 56.3% (36 ใน 64 ราย) ของผู้ที่ไม่มีภาวะผมบางจากพันธุกรรม จะพบว่าภาวะเส้นเลือดหัวใจตีบอย่างน้อยหนึ่งเส้นจากการตรวจหลอดเลือดหัวใจด้วยการฉีดสารทึบแสง ซึ่งข้อมูลดังกล่าวไม่มีความแตกต่างอย่างมีนัยสำคัญ ทั้งจาก การประเมินด้วยวิธี Univariate (odd ratio 1.12, 95% CI 0.74-1.69, p-value 0.573) และวิธี Multivariate (odd ratio 0.93, 95% CI 0.49-1.77, p-value 0.833)

สรุป: การศึกษาของเราไม่พบความสัมพันธ์ระหว่างโรคผมร่วงทางพันธุกรรมในเพศหญิงและการตรวจพบเส้นเลือดหัวใจตีบจากการตรวจด้วยการฉีดสารทึบแสง

คำสำคัญ: โรคผมร่วงจากพันธุกรรม, โรคผมร่วงในเพศหญิง, โรคหลอดเลือดหัวใจ,

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Introduction

Androgenetic alopecia (AGA) has higher prevalence for coronary artery disease (CAD) more than healthy population since 1972 from Cotton et al study found that androgenetic alopecia is a significant risk factor for coronary artery disease[2] and the other study stated that AGA is associated with CAD especially in alopecia at vertex area in young men.[3]

Pathophysiology of the association between AGA and CAD caused by many mechanisms. Elevation of androgen activity is associated with the severity of alopecia by increasing androgen receptors at scalp and increasing testosterone level resulting in miniaturization of hairs. Concurrently, hyperandrogenism can stimulate atherosclerosis pathway as a result of thrombus formation, decreased level of high-density lipoprotein (HDL), increase cholesterol to HDL ratio that are all important risk factors for metabolic complication such as dyslipidemia, hypertension and ultimately coronary artery disease.[4]

Although most of the studies focused on male AGA but many studies also found that female AGA is important risk factor for CAD. For example from Parvin M. study found that female AGA was associated with coronary artery disease especially in women younger than 55 years old.[5]

The objective of our study was to determine the association of coronary angiographic results and severity of female androgenic alopecia in female patients who undergoing coronary angiography regardless the indications.

Methods

Study design and settings

Our study was designed as cross sectional study to determine the association of coronary angiographic results and the severity of androgenetic alopecia in female patients

We conducted this study from June 2014 to March 2015 including all the female patients that were undergoing coronary angiography at the Sirintorn Cardiac Center of Phramongkutklao Hospital.

Participants and inclusion criteria

The eligible patients were the female patients that were admitted for coronary angiography. Exclusion criteria were the patients that unwilling to join the study or the patients that their coronary angiographic results cannot be interpreted. The study protocol had been approved by the institutional review board, Royal Thai Army Medical Department.

Data collection and definition

We collected the data from all of female patients who underwent coronary angiography at Cardiology unit of Phramongkutklao Hospital for both emergency indications, such as acute coronary syndrome or cardiogenic shock, and non-emergency indications, such as abnormal exercise stress test, abnormal echocardiographic

results and preoperative evaluation were recruited. The demographic data including age, sex, body mass index, history of diabetes mellitus, hypertension, dyslipidemia, smoking habit were collected.

The severity of androgenic alopecia was graded and collected according to Ludwig classification[1] by the doctor who were blinded to the coronary angiographic results.

The severity of coronary artery disease was determined by the number of vessels of significant stenosis as single, double or triple vessels stenosis. The significant stenosis of the coronary artery disease was defined by 70% or more stenosis of the coronary arteries, except in left main coronary artery, using the cut-point of 50% or more stenosis, to define significant stenosis.

The exclusion criteria were male sex, accompanied with other type of alopecia, or receiving treatment of androgenetic alopecia both medical and hair transplantation.

Primary end point

Our primary end point of this study was to find the association between presence of coronary stenosis and the severity of female androgenetic alopecia.

Statistical analysis

For the demographic data, we used mean $\pm$ standard deviation and range to represent the quantitative data. We also used number and percent to represent the quantitative data. For comparison between two groups, we used independent t-test for quantitative data and Chi square test for qualitative data. We conducted both univariate and multivariate logistic regression analysis for identify the association between androgenetic alopecia and coronary angiographic results. A value of p<0.05 indicated statistical significance.

Sample size estimation

From the previous paper[5], the prevalence of coronary artery disease in the patients with female androgenetic alopecia were 43% comparing with 19% in the patients without female androgenetic alopecia. At a confidence level of 95% and power of the test at 90% for a two-tailed test. A sample size of 152 participants with the above criteria were required.

Results

A total of 203 female patients with mean age of 70.1 years (range 31-93 years), were recruited. Diabetic mellitus was found in approximately one-third of the patients. Hypertension and dyslipidemia were more prevalent approximately in a half of the patients. The other demographic data were shown in table 1.

Table 1 Demographic characteristics of all 203 patients. Emergency conditions* included acute myocardial infarction, unstable angina and cardiogenic shock. Non-emergency conditions** included patients who undergoing coronary angiography due to abnormal non-invasive cardiac test or preoperative evaluation. Androgenetic alopecia grading *** were classified as no alopecia and severity score according to Ludwig score[1].

Characteristic	
Number of patient, Number	203
Age in years (mean ± SD) (range)	70.1 ± 12.0 (31-93)
Sex (Male:Female)	0:203
Underlying disease, Number (%)	
Dyslipidemia	92 (45.3)
Hypertension	93 (45.8)
Diabetes mellitus	62 (30.5)
Cerebrovascular disease	5 (2.5)
Current and Ex-smoker, Number (%)	6 (3.0)
Body mass index, (mean ± SD) (range)	24.6 ± 4.4 (14.7-38.8)
Indication for undergoing coronary angiography, number (%)	
Emergency conditions*	132 (65.0)
Non-emergency conditions*	71 (35.0)
Androgenetic alopecia grading***, number (%)	
No alopecia	64 (31.5)
Grade 1	84 (41.4)
Grade 2	34 (16.7)
Grade 3	13 (6.4)
Grade 4	7 (3.4)
Grade 5	1 (0.5)

From 203 patients, 132 patients (65.0%) underwent coronary angiography due to emergency conditions and 71 patients (35.0%) underwent coronary angiography due to non-emergency conditions. The baldness was classified according to Ludwig classification.[1]

Grade 1 according to Ludwig classification was the most common grade in our patients (84 patients, 41.4%)

We classified our patients into two group. The first group represented the patients who did not have androgenetic alopecia according to

Ludwig's classification. The second group represented the patient who had female androgenetic alopecia according Ludwig's classification in any grades (grade 1-5). The table 2 showed the comparison of the characteristics of both groups.

Table 2 Compare the demographic data of the participants with and without female androgenetic alopecia

	No Female androgenetic alopecia (n=64)	Female androgenetic alopecia (n=139)	p-value
Age (mean ± SD) (range)	56.5 ± 13.9 (23-87)	65.4 ±12.1 (23-97)	<0.001
Diabetes mellitus, Number (%)	16 (25.0)	119 (30.0)	0.42
Hypertension, Number (%)	36 (56.3)	225 (56.7)	0.95
Dyslipidemia, Number (%)	42 (65.6)	243 (61.2)	0.50
Creatinine clearance Less than 60 mL/min/1.73m^2, Number (%)	23 (35.9)	190 (48.2)	0.07
Cerebrovascular diseases, Number (%)	2 (3.1)	16 (4.0)	0.73
Current or Ex smoking, Number (%)	36 (56.2)	267 (67.2)	0.09
Emergency coronary angiography*, Number (%)	37 (57.8)	283 (71.28)	0.03

Regardless of the indication for coronary angiography, 84 from 139 patients (60.4%) of the patients with female androgenetic alopecia and 36 from 64 patients (56.3%) of the patients without female androgenetic alopecia had at least one significant coronary artery stenosis. The percentage of coronary artery stenosis was not significantly higher in alopecia group, (odd ratio 1.1, 95% CI 0.74-1.69, p-value = 0.57)

The patients who underwent coronary angiography due to emergency condition, 67 from 97 patients (69.1%) with female androgenetic alopecia and 25 from 35 patients (71.4%) without female androgenetic alopecia had at least one significant coronary stenosis. The percentage of coronary artery stenosis was not statistically different in both groups, (odd ratio 0.9, 95% CI 0.49-1.73, p-value = 0.79)

The patients who underwent coronary angiography due to non-emergency conditions, 17 in 42 (40.5%) of participants with female androgenetic alopecia and 11 in 29 (37.9%) of the participants without female androgenetic alopecia had at least one coronary stenosis. The percentage of coronary artery stenosis was not

significantly difference in both groups, (Odd ratio 1.07, 95% CI 0.06-1.90, p-value =0.829)

When we considered the incidence of at least one coronary stenosis in our participants, the incidence of coronary stenosis was not significantly higher in the patients with female androgenetic alopecia when compare with the patient without alopecia in both emergency and non-emergency conditions in univariate analysis.

We also performed multivariate analysis to eliminate the influence of age and other traditional risk factors such as diabetes mellitus, hypertension, dyslipidemia, cerebrovascular disease, smoking and body mass index. After adjusting for all potential confounders, our results still showed that incidence of coronary stenosis was not difference in both groups. The detail was shown in table3.

Table 3 Compare the coronary stenosis between the participants with no alopecia and the participants with female androgenetic alopecia. Adjusted odd ratio was calculated to eliminate the effect of age, body mass index, diabetes mellitus, hypertension, dyslipidemia and smoking.

	No Female androgenetic alopecia	Female androgenetic alopecia	Unadjusted odd ratio (95% CI)	Unadjusted P value	Adjusted* odd ratio (95% CI)	Adjusted P value
All participants, Number (%)	36 (56.3)	84 (60.4)	1.12 (0.74-1.69)	0.57	0.93 (0.49-1.77)	0.83
Emergency group, Number (%)	25 (71.4)	67 (69.1)	0.92 (0.49-1.73)	0.80	0.88 (0.36-1.05)	0.79
Non-Emergency group, Number(%)	11 (37.9)	17 (40.5)	1.07 (0.06-1.90)	0.83	0.54 (0.17-1.75)	0.31

Discussion

Our study can show that the severity of androgenetic alopecia in female was not associated with coronary artery stenosis. Our result did not differ from *Su et al.* study. This study was a prospective cohort study which enrolled 7,960 Taiwanese patients showed that there were no association between mortality from heart disease and androgenetic alopecia after adjusting for age, sex and other significant factors by multivariate analysis.[4] There was also another study that also revealed a negative association.[6] On the other hand, the other studies showed opposite result.[5]

There are many studies revealed the association between coronary artery disease and

androgenetic alopecia. Most of them suggested that the higher androgen activity in the patients with androgenetic alopecia should be the cause of cardiac insults[7-9], but our participants were female, so the increasing of androgen activity may not as much as in men.

There were some limitations in our study. The first limitation was the small sample size in some subgroup of our study. Larger sample size was required to show better correlation. The second limitation of our study was that we did not collect the follow up results so we could not further demonstrate any difference in the outcomes such as mortality or morbidity in short term and long term.

In conclusion, this study revealed that there was no significant association between the degree of female androgenetic alopecia and the coronary artery disease assessed by the coronary angiography regardless of the indications.

References

1. Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. Br J Dermatol 1977;97:247–54.

2. Susan GC, Nixon JM, Carpenter RG, Evans DW. Factors discriminating men with coronary heart disease from healthy controls. Br Heart J 1972;34:458-64.

3. Yamada T, Kazuo H, Hitomi U, Takashi K. Male pattern baldness and its association with coronary heart disease: a meta-analysis. BMJ Open 2013; 3.

4. Su LH, Chen LS, Lin SC, Chen HH. Association of androgenetic alopecia with mortality from diabetes mellitus and heart disease. JAMA Dermatol. 2013;149:601-6.

5. Mansouri P, Mortazavi M, Eslami M, Mazinani M. Androgenetic alopecia and coronary artery disease in women. Dermatology Online J 2015; 11: 2.

6. Schnor P, Nyboe J, Lange P, Jensen G. Longevity and gray hair, baldness, facial wrinkles, and arcus senilis in 13,000 men and women: the Copenhagen City Heart Study. J Gerontol A BiolSci Med Sci 1998; 53:347-50.

7. Ford ES, Freedman DS, Byers T. Baldness and ischemic heart disease in a national sample of men. Am J Epidemiol 1996;143:651-7.

8. Mirić D, Fabijanić D, Giunio L, et al. Dermatological indicators of coronary risk: a case-control study. Int J Cardiol 1998;67:251-5.

9. Lotufo PA, Chae CU, Ajani UA, Hennekens CH, Manson JE. Male pattern baldness and coronary heart disease: the Physicians' Health Study. Arch Intern Med 2000; 160: 165-71.