The Egyptian Heart Journal 70 (2018) 15–19

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The Egyptian Heart Journal

journal homepage: www.elsevier.com/locate/ehj

Original Article

The degree of hair graying as an independent risk marker for coronary artery disease, a CT coronary angiography study

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ARTICLE INFO

Article history:
Received 22 May 2017
Accepted 1 July 2017
Available online 1 August 2017

Keywords:
Hair graying
Male gender
Coronary artery disease
Computed tomography coronary angiography

ABSTRACT

Background: Cardiovascular disease is a leading cause of death worldwide. Aging is an unavoidable coronary risk factor and is associated with dermatological signs that could be a marker for increased coronary risk. We tested the hypothesis that hair graying as a visible marker of aging is associated with risk of coronary artery disease (CAD) independent of chronological age.

Methods: This cross-sectional study included 545 males who underwent a computed tomography coronary angiography (CTCA) for suspicious of CAD, patients were divided into subgroups according to the percentage of gray/white hairs (Hair Whitening Score, HWS: 1–5) and to the absence or presence of CAD.

Results: CAD was prevalent in 80% of our studied population, 255 (46.8%) had 3 vessels disease with mean age of 53.2 ± 10.7 yrs. Hypertension, diabetes and dyslipidemia were more prevalent in CAD group ($P = 0.001$, $P = 0.001$, and $P = 0.003$, respectively). Patients with CAD had statistically significant higher HWS (32.1% vs 60.1%, $p < 0.001$) and significant coronary artery calcification (<0.001). Multivariate regression analysis showed that age (odds ratio (OR): 2.40, 95% confidence interval (CI): [1.31–4.39], $p = 0.004$), HWS (OR: 1.31, 95% CI: [1.09–1.57], $p = 0.004$), hypertension (OR: 1.63, 95% CI: [1.03–2.58], $p = 0.036$), and dyslipidemia (OR: 1.61, 95% CI: [1.02–2.54], $p = 0.038$) were independent predictors of the presence of atherosclerotic CAD, and only age ($p < 0.001$) was significantly associated with HWS.

Conclusions: Higher HWS was associated with increased coronary artery calcification and risk of CAD independent of chronological age and other established cardiovascular risk factors.

1. Introduction

Aging is a complex process that affects all of us. All organs undergo a series of age related changes, in which the vascular system is prominent.[1] Aging involves various genetic, hormonal, and environmental mechanisms.

Previous studies have found that male pattern baldness, gray hair and facial wrinkles as well as the presence of arcus corneae are all associated with looking old for one's age.[2,3]

Hair graying is one of the natural aging processes.[4] Although it is generally not a medical problem, it greatly concerns many people for esthetic reasons[5] and may be a cause of low self-esteem.[6]

Moreover, because of the strong association between aging and hair graying, many researchers have been concerned that hair graying, especially when occurs prematurely, is a predictor of some severe systemic disease and several studies evaluated the association of premature hair graying (PHG) with osteopenia or coronary artery disease (CAD).[7,8]

Coronary artery disease is a leading cause of morbidity and mortality worldwide. The association of traditional cardiovascular risk factors (CVRFs) with CAD is well established.[9–11] Recently, various reports have indicated the potential association of different cutaneous markers with CAD, so that the population at risk can be identified early.[12–15]

Atherosclerosis and graying of hair share a similar mechanism includes impaired DNA repair, oxidant stress, androgens,

Abbreviations: CAD, coronary artery disease; CCS, coronary calcium score; CI, confidence interval; CTCA, computed tomography coronary angiography; CVRFs, cardiovascular risk factors; HDL, high-density lipoprotein cholesterol; HWS, hair whitening score; LDL, low-density lipoprotein cholesterol; MI, myocardial infarction; OR, odds ratio; PHG, premature hair graying.

Peer review under responsibility of Egyptian Society of Cardiology.

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http://dx.doi.org/10.1016/j.ehj.2017.07.001
1110-2608/

inflammatory process and senescence of functioning cells and the incidence of both increases with age.[16–18]

Accordingly, this study was conducted to determine the prevalence and degree of hair graying among a cohort of males with suspected CAD who underwent CTCA and whether it is an independent marker for CAD.

2. Materials and methods

2.1. Study population

This study recruited 545 adult male patients who underwent a CTCA for suspicion of CAD, patients with evidence of ongoing infection or inflammation, hepatic disease, hematological disorders or known malignancy, renal impairment (serum creatinine >1.4 mg/dl), autoimmune related hair loss or graying disorders and poor CTCA image e.g. severely calcified coronary vessels were excluded from the study. The study protocol was approved by the ethic committees in our university, and all patients willing to participate gave their written informed consent.

2.2. Clinical evaluation

All studied population underwent full medical history taking and clinical examination. Presence of CVRFs was evaluated, and hypertension was defined as the active use of antihypertensive drugs or documentation of blood pressure more than 140/90 mmHg.[19] Diabetes mellitus is defined as fasting plasma glucose levels over 126 mg/dL or glucose level over 200 mg/dL at any measurement or active use of antihyperglycemic treatment.[20] Smoking (using tobacco at time of evaluation or those stopped smoking within the last year were considered as smokers.). The family history for CAD was defined as a history of CAD or sudden death in a first-degree relative before the age of 55 years for men and 65 years for women. Dyslipidemia, if the patient has a documented history of hypercholesterolemia diagnosed and/or treated by a physician, defined as total cholesterol $\geq$200 mg/dl and/or low-density lipoprotein cholesterol (LDL) $\geq$100 mg/dl and/or high-density lipoprotein cholesterol (HDL) <40 mg/dl.[21]

2.3. Hair graying assessment

Extent of grayness was assessed with two observers using hair whitening score (HWS), defined according to percentage of gray/white hairs (1: pure black; 2: black > white; 3: black = white; 4: white > black; 5: pure white).[7] Patients were divided into different subgroups according to the percentage of gray/white hairs and to the absence or presence of CAD.

2.4. CTCA

CT coronary angiography was performed using 256 slices (Philips ICT, Cleveland, OH) machine using the ECG gated acquisition during a single breath hold. Injection of 75 ml of nonionic contrast material through an anti-cubital vein at a high flow rate (5.3 ml/s) followed by rapid acquisition of ultra-thin sections (0.5 mm) through the heart to evaluate the coronary arteries.

All coronary arteries were studied at 75% and 40% of the cardiac cycle with selective reconstruction of the improperly visualized coronary segments at different phases of the cardiac cycle. The acquired data were used to reconstruct multi-planar reformatted, maximal intensity projections and 2 volume rendering images. Our study population was evaluated for the presence and extent of coexisting atherosclerotic CAD (obstructive or non-obstructive atherosclerotic lesions). Obstructive CAD was defined as coronary wall atheromatous plaques with $\geq$50% luminal reduction in comparison with that of the normal reference segment.

Non-contrast electrocardiogram gated thin sections were carried through the coronary arteries to detect and calculate the coronary calcium score (CCS). Total calcium scores of all patients were calculated with the dedicated software and expressed as volumetric and Agatston scores. Using the sequential axial images; any tissue above the 130 Hounsfield unit occupying a minimum of 0.5 mm^2 that was identified along the anatomical course of a coronary artery was considered as coronary calcification, and hence, highlighted and analyzed using the software.[22]

2.5. Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences, version 18 (SPSS 18). Firstly all variables were tested for normality using Kolmogorov-Smirnov test; if the test was significant, non-normality was accepted otherwise double check using graphs, skewness and kurtosis was required to confirm normality. All of the quantitative variables in this research were normally distributed and accordingly were presented as mean (Standard deviation). Qualitative data are presented as number (percentage).

Comparison analysis was conducted using student *t* test, and One Way ANOVA for quantitative data and chi-square test for qualitative data. Logistic regression analysis was conducted to determine predictors of atherosclerotic coronary artery disease. Multivariate analysis of independent variables which were included if they were significantly different in the univariate analyses. Probability value of <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

This cross-sectional study included 545 male patients with a mean age of 53.2 ± 10.7 years, and baseline characteristics of the study population are presented in Table 1. Hypertension and dyslipidemia were the most frequent traditional CVRFs, and 298

Table 1
Baseline characteristics of the study population.

Variable	No (%)
Age	53.2 ± 10.77
Hypertension	348 (63.9)
Diabetes	203 (37.2)
Smoking	226 (41.5)
Family history	159 (29.2)
Dyslipidemia	317 (58.2)
Hair whitening score	
Pure Black	117 (21.5)
Black > White	130 (23.9)
Black = White	91 (16.7)
White > Black	108 (19.8)
Pure White	99 (18.2)
CTCA result	
Presence of CAD	439 (80.6)
Number of vessels affected	
One vessel	89 (16.3)
Two vessels	95 (17.4)
Three vessels	255 (46.8)
Ectasia	144 (26.4)
Coronary calcification	332 (60.9)

Data are presented as Mean ± SD or number (%).
CTCA: computed tomography coronary angiography.

(54.7%) patients had predominant white hair (HWS ≥ 3). CTCA studies showed that 80.6% had atherosclerotic CAD with 255 (46.8%) presented with multi-vessel disease, and 144 (26.4%) patients had coronary artery ectasia.

3.2. Categorization according to the HWS

Patients were divided into different subgroups according the percentage of gray/white hairs and to the absence or presence of CAD. Table 2 shows that among traditional coronary risk factors, age, hypertension, diabetes were significantly higher in patients with predominant white hair (high HWS) while smoking was significantly higher in patients with lower HWS. Moreover, patients with HWS 3 or more showed statistically significant higher prevalence of CAD and coronary calcification (73.5% vs 45.7%, $p < 0.001$).

3.3. Categorization according to the presence of CAD

As shown in Table 3, patients who had significant CAD were significantly older in age. Hypertension, diabetes and dyslipidemia were significantly more prevalent in patients with CAD when compared with those without CAD ($p = <0.001$, 0.001 and 0.003, respectively). Furthermore, patients with CAD had statistically significant higher HWS (predominately white hair) (32.1% vs 60.1%, $p < 0.001$).

3.4. Prediction of atherosclerotic CAD in all patients

Multivariate regression analysis demonstrated that age (OR: 2.40, 95% CI: 1.31–4.39, $p = 0.004$), HWS (OR: 1.31, 95% CI: 1.09–1.57, $p = 0.004$), hypertension (OR: 1.63, 95% CI: 1.03–2.58, $p = 0.036$), and dyslipidemia (OR: 1.61, 95% CI: 1.02–2.54, $p = 0.038$) were independent predictors of the presence of atherosclerotic CAD.

3.5. Prediction of hair whitening score in all patients

Linear regression analysis was performed for evaluating the effect of CVRFs on hair graying, among all studied risk factors only age (<0.001) was significantly associated with HWS, Table 4.

4. Discussion

In this study, we investigated the prevalence and degree of hair graying, as a sign of aging, in relation to established CVRFs, the extent of coronary atherosclerosis among a cohort of male patients who underwent CTCA for suspicion of CAD and whether it is an independent marker for CAD.

We found that patients who had atherosclerotic CAD were older in age and among all CVRFs, hypertension, diabetes and dyslipidemia were more prevalent, and that high hair whitening score was associated with increased risk of CAD independent of chronological age and other established CVRFs.

Table 3
Distribution of studied parameters according to the presence of CAD.

Variable	No CAD ($n = 106$)	CAD ($n = 439$)	*P* value
Age	44.53 ± 9.20	55.29 ± 10.06	<0.001
Risk factors			
Hypertension	52 (49.1)	296 (67.4)	<0.001
Diabetes	24 (22.6)	179 (40.8)	0.001
Smoking	46 (43.4)	180 (41)	0.478
Family history	31 (29.2)	128 (29.2)	0.986
Dyslipidemia	48 (45.3)	269 (61.3)	0.003
Hair whitening score			
Predominant black hair	72 (67.9)	175 (39.9)	<0.001
Predominant white hair	34 (32.1)	264 (60.1)	<0.001

Data are presented as Mean ± SD or number (%).
CAD: coronary artery disease.

Table 4
Relation between CVRFs and hair whitening score.

Variable	Standardized coefficients beta	*P* value
Age	0.578	<0.001
Hypertension	−0.003	0.928
Diabetes	0.052	0.147
Smoking	0.008	0.815
Family history	−0.035	0.329
Dyslipidemia	−0.022	0.547

CVRFs: cardiovascular risk factors.

4.1. The relationship between graying of hair and CAD

Evidence of a possible linkage between premature hair whitening and CAD, myocardial infarction (MI) in men or women comes from several studies with various sample sizes and different patient populations.[5,8,15,23,24] In accordance with these finding, a study by Miric et al.[25] showed that a moderately gray hair yielded a significant relative risk of MI, but only in men under the age of 45 years.

Additional evidence comes from Kocaman et al. who investigated the relationship between hair graying intensity, as a sign of biological aging in humans, and coronary atherosclerotic burden and reported that [7] CVRFs were higher in CAD group especially hypertension, diabetes, hyperlipidemia and family history of CAD which showed statistically significant difference ($p = 0.009$, 0.012, <0.001 and 0.013, respectively). Furthermore, similar to our study, HWS was significantly different between normal coronary arteries and CAD groups.

Table 2
Distribution of studied parameters in different white/gray hair scale.

	Pure Black hair (1) ($n = 117$)	Black > White (2) ($n = 130$)	Black = White (3) ($n = 91$)	White > Black (4) ($n = 108$)	Pure White hair (5) ($n = 99$)	*P* value
Age	43.25 ± 8.89	50.44 ± 8.55	54.96 ± 8.41	58.04 ± 8.49	61.68 ± 9.02	<0.001
Hypertension	64 (54.7)	87 (66.9)	51 (56)	77 (71.3)	69 (69.7)	0.024
Diabetes	24 (20.5)	48 (36.9)	35 (38.5)	56 (51.9)	40 (40.4)	<0.001
Smoking	59 (50.4)	58 (44.6)	43 (47.3)	36 (33.3)	30 (30.3)	0.040
Family history	40 (34.2)	42 (32.3)	25 (27.5)	26 (24.1)	26 (26.3)	0.415
Dyslipidemia	64 (54.7)	74 (56.9)	54 (59.3)	66 (61.1)	59 (59.6)	0.881
Presence of CAD	75 (64.1)	100 (76.9)	80 (87.9)	98 (90.7)	86 (86.9)	<0.001
Ectasia	28 (23.9)	33 (25.4)	24 (26.4)	26 (24.1)	33 (33.3)	0.528
Calcification	46 (39.3)	67 (51.5)	66 (72.5)	77 (71.3)	76 (76.8)	<0.001

Data are presented as Mean ± SD or number (%).
CAD: coronary artery disease.

A recent study by Amitesh et al.[26] disclosed an association between PHG and development of CAD in smokers as well as non-smokers. They postulated that the presence of cutaneous clinical markers as hair graying can be used as preliminary evidence by clinicians for identifying patients at risk for premature CAD particularly in smokers.

We tried to determine the predictors of atherosclerotic CAD in our population, interestingly, we found that only age, hypertension, dyslipidemia and HWS were independent predictors of atherosclerotic CAD.

Similarly, multiple logistic regression analysis in previous study conducted by Kocaman et al.[7] demonstrated that only diabetes mellitus (OR: 3.24, 95% CI: 1.017–10.31, $p = 0.047$), LDL cholesterol (OR: 1.01, 95% CI: 1.00–1.02, $p = 0.029$) and HWS (OR: 1.51, 95% CI: 1.05–2.17, $p = 0.025$) were independently related to the presence of CAD. On the other hand, in a study conducted by Christoffersen et al.[27] graying of hair did not associate with risk of ischemic heart disease or MI after multi-factorial adjustment (baldness, earlobe crease, and xanthelasmata), although in the 12-year follow-up of the same study, an association with MI was found in men.[8]

4.2. The relationship between graying of hair and CVRFs

Today, it is known that CVRFs, especially in combination, cause premature atherosclerosis. Similar to their effects on endothelium and circulating progenitor stem cells they may possibly lead to premature and intense hair graying by through interactions on follicular epithelium and resident stem cells. The common factors associated with hair graying and systemic diseases have not been fully explored.

Currently, CTCA has an important advantages over conventional coronary angiography concerning the accurate detection of coronary calcification. To best of our knowledge, the association of coronary artery calcification (as a marker of atherosclerosis) with intensity of hair graying has not been tested before.

In this study, the relationship of degree of hair graying with well-established conventional CVRFs was examined. The results of our study not only confirm an association between hypertension, diabetes, smoking and hair graying but also shows that coronary calcification detected by CTCA was significantly higher in patient with high HWS. In converse to our findings,

Zayed et al. found no significant association between hair graying and fasting blood glucose or high blood pressure.[28]

Interestingly, when we studied the effect of CVRFs on hair graying, linear regression analysis showed that among all studied risk factors only age was significantly associated with high HWS, which differs from the findings of Kocaman et al.[7] who reported that age ($p < 0.001$), family history of CAD ($p = 0.004$), hyperlipidemia ($p = 0.02$) and creatinine ($p = 0.019$) were independent factors associated with HWS,

In a relatively recent Indian study[29], they noticed that with increasing age, the frequency of individuals with gray hair also increased. This could be explained on the basis that, with age, the production of free radicals increases, while the endogenous defense mechanisms decrease. Moreover, a significant increase in the frequency of individuals with gray hair was observed in individuals with a habit of smoking tobacco, chewing tobacco, or using both when compared with the control nonsmokers group ($P < 0.05$).

This was in accordance with the findings of Jo et al.[30] who tested the hypothesis that either hair graying pattern depend on gender, age and excessive smoking or not, they concluded that age was significantly correlated with hair graying, and found that the prevalence of gray hair by age was 51.5% in their thirties, 81.1% in their forties, and 95.3% in their fifties in addition to that the risk of hair graying increased by 14.9% each year ($P < 0.001$) and the risk in smokers was 1.99 times higher than that in non-smokers ($P = 0.008$). Surprisingly, in our population, only 40% were smokers and they had significantly lower HWS, and we could not prove that smoking is an independent risk marker for hair graying.

4.3. Study limitations

Women were not evaluated in this study. Much of the information needed in this study depended on "subjective evaluation" we tried to overcome this limitation by making the HWS done by two independent observers. Study population consisted of patients with known CVRFs, which may produce relatively higher risk population than age and gender-matched individuals, and this selection bias is likely to affect the predictive power of HWS for CAD.

5. Conclusion

In our population, high HWS was associated with increased risk of CAD and coronary calcification independent of chronological age and other traditional known CVRFs.

Funding

None.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The authors gratefully acknowledge Dr. Heba Farouk, MD for her assistance in drafting the manuscript.

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