

Association between coronary artery disease and the diagonal earlobe and preauricular creases in men*

*Associação entre doença arterial coronariana e as pregas lobular diagonal e anterotragal em homens**

Hélio Amante Miot¹

Letícia de Chiara Cardoso⁴

Luciane Donida B. Miot⁷

Luciana Molina de Medeiros²

Juliana Hammoud Gumieiro⁵

Caio Roberto Shwafaty de Siqueira³

Marco Antônio Pandini Filho⁶

Abstract: BACKGROUND - Several dermatologic findings have been associated with coronary artery disease and represent easily visualized signs that may contribute to classify cardiac risk by a non-invasive technique.

OBJECTIVES - To evaluate the prevalence of some dermatologic findings in patients with or without coronary artery disease.

METHODS - A case-control study involving male patients submitted to coronary angiography was performed. We included patients with greater than 50% obstruction of at least one coronary artery. Both groups were assessed as to presence of diagonal earlobe crease and preauricular crease, alopecia and thoracic hairiness. The results were adjusted for known cardiac risk factors: age, body mass index, diabetes, hypertension, dyslipidemia and smoking.

RESULTS - One hundred and ten individuals were evaluated (80 patients, 30 controls). The prevalence of diagonal earlobe crease in patients (60%) was greater than controls (30%) ($p < 0.05$). Androgenetic alopecia and thoracic hairiness were not associated to coronary artery disease. The odds ratio for diagonal earlobe crease was 3.1 (1.2-8.3) and for preauricular crease was 5.5 (1.9-16.3). The simultaneous finding of diagonal earlobe crease and preauricular crease resulted in a positive predictive value of 90.0%.

CONCLUSIONS - The study detected a positive association between bilateral diagonal earlobe crease and bilateral preauricular crease with coronary artery disease. The simultaneous finding of both folds had high predictivity for coronary artery disease.

Keywords: Coronary arteriosclerosis; Ear, external; Male; Risk factors

Resumo: FUNDAMENTOS – Diversas alterações dermatológicas foram associadas à doença arterial coronariana, representando achados de fácil constatação que podem contribuir na estratificação não invasiva do risco cardíaco.

OBJETIVOS – Avaliar comparativamente a prevalência de certos achados dermatológicos em pacientes com ou sem doença arterial coronariana.

MÉTODOS – Estudo caso/controle envolvendo pacientes do sexo masculino submetidos à cineangiogramia. Foram considerados aqueles casos com obstrução de mais de 50% em pelo menos uma coronária. Avaliou-se a presença da prega lobular diagonal, prega anterotragal, alopecia e presença de pêlos no tórax nos dois grupos. Os resultados foram ajustados para os fatores de risco: tabagismo, hipertensão, diabetes, idade, dislipidemia e índice de massa corporal.

RESULTADOS – Analisaram-se 110 pacientes (80 casos e 30 controles). A prevalência da prega lobular diagonal nos casos (60,0%) foi maior do que no grupo controle (30,0%) ($p < 0,05$). Alopecia androgenética e distribuição de pêlos no tórax não demonstraram associação positiva com coronariopatia neste estudo. O Odds Ratio (IC 95%), da prega lobular diagonal foi de 3,1 (1,2-8,3) e para prega anterotragal foi de 5,5 (1,9-16,3). A verificação simultânea da prega lobular diagonal e prega anterotragal representou valor preditivo positivo de 90%.

CONCLUSÕES – Detectou-se associação positiva entre a presença da prega lobular diagonal bilateral e prega anterotragal bilateral com doença arterial coronariana, sendo que a presença simultânea das duas pregas apresenta alta preditividade para doença arterial coronariana.

Palavras-chave: Arteriosclerose coronária; Fatores de risco; Masculino; Orelha externa

Received on December 28, 2005.

Approved by the Consultative Council and accepted for publication on January 27, 2006.

* Work done at Departamento de Dermatologia e Radioterapia da Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

Conflict of interests: None

¹ Ph.D. Substitute Lecturer at the Department of Dermatology, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

² Resident physician, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

³ Resident physician, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

⁴ Resident physician, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

⁵ Medical student, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

⁶ Medical student, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

⁷ Dermatologist of the Departamento de Dermatologia da Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp. Post-graduate student in Pathology, Faculdade de Medicina de Botucatu - Universidade Estadual Paulista - FMB/Unesp - Botucatu (SP), Brazil.

INTRODUCTION

Coronary artery disease (CAD) is still one of the highest causes of mortality and morbidity in the adult population, with significant age-associated increased prevalence. The adoption of atherosclerosis prevention methods and early clinical detection are priority public health actions.¹

The main risk factors associated to CAD could be divided into modifiable (obesity, smoking, diabetes mellitus, hypertension and dyslipidemia) and non-modifiable (age, male sex and family history). The stratification of coronary risk in the population in general depends on verifying these elements and clinical findings, so that an effective intervention in the modifiable factors alters the risk of a primary or secondary coronary event.²

Historically, several dermatologic findings were described as CAD indicators, such as androgenetic alopecia, auricular hairiness, thoracic hairiness and the presence of diagonal earlobe crease (ELC), or Frank's sign (Figure 1).^{3,4} However, the literature contains few controlled studies assessing these associations. These dermatologic findings have not yet been systematically investigated in the Brazilian population.

Moreover, there is a high frequency of preauricular crease (PAC) in coronary patients, but its prevalence has never been assessed in controlled studies.

This study evaluates the presence of dermatologic findings in patients submitted to coronary angiography.



FIGURE 1: Diagonal earlobe crease (ELC) and preauricular crease (PAC)

PATIENTS

A case-control study was conducted involving 110 male adults who had been submitted to coronary angiography at the *Hospital Universitário*, from January 2004 to September 2005.

The research included patients that presented less than 50% obstruction in all coronary arteries at exam (control); later, patients presenting the ratio of 2.5:1 were also included.

Patient epidemiologic data were obtained using a standardized form, and the coronary risk factors taken into account were age, hypertension, dyslipidemia, smoking, diabetes mellitus, family history of coronary disease and body mass index.

Patients were considered as hypertensive when the blood pressure on the day of the exam was over 140x90mmHg or when on antihypertensive drugs; dyslipidemic, when total cholesterol level was above 260mg/dl or when using lipid-reducing agents; smoker, those who smoked regularly for more than five consecutive years; diabetic, those presenting two fasting glucose values above 126mg/dl or in treatment for diabetes; positive family history, those whose first degree relatives suffered from CAD. The body mass index was calculated using the current weight in kilograms divided by the square of height in meters.

The prevalence of diagonal crease (bilaterally), preauricular crease (bilaterally), androgenetic alopecia and thoracic hairiness was measured in cases and controls. The results were adjusted for coronary risk factors using the stepwise logistic regression.

The minimal sample size was calculated based on the prevalence of diagonal earlobe crease found in another controlled study conducted on western populations.⁵ The ratios between the groups were compared using Fisher's exact test, and continuous data were compared by Student's *t* test. The data were input in MS Excel 2003™, and analyzed using the Bioestat 2.0 software. The *p* value < 5% was considered significant

RESULTS

Out of 110 patients, evaluated from January 2004 to September 2005, 80 were cases and 30 controls. The main epidemiologic data collected are listed in table 1, demonstrating that the mean age of patients assessed was over 50 years and the mean body mass index was above normal.

The bilateral presence of ELC and PAC was positively associated to CAD even after adjusting for other coronary risk variables (Table 2). The presence of both creases represented sensitivity of 56.3% and a positive predictive value of 90% (*p*<0.

TABLE 1: Epidemiological characteristics of patients

	Cases %	Controls %	Total %	p*
N	80	30	110	
Age (years) (mean ± SD)	60.2±11.6	53.7±11.5	58.4±12.2	<0.05 (teste T)
BMI** (mean ± SD)	26.4±4.4	28.7±5.0	27.0±4.7	<0.05 (teste T)
Hypertension	59 (73.8)	21 (70)	80 (72.7)	>0.1 (Fisher)
Diabetes mellitus	22 (27.5)	7 (23.3)	29 (26.4)	>0.1 (Fisher)
Smoking	59 (73.8)	19 (63.3)	78 (70.1)	>0.1 (Fisher)
Family history	38 (47.5)	16 (53.3)	54 (49.1)	>0.1 (Fisher)
Dyslipidemia	45 (56.3)	10 (33.3)	55 (50)	<0.05 (Fisher)

*univariate analysis **BMI = body mass index

05 – Fisher)

Androgenetic alopecia was present in 62.5% of cases and in 50.0% of controls, however, alopecia in any of its different patterns (frontal, temporal, vertex and diffuse) did not demonstrate statistical association with CAD ($p > 0.1$ - multiple logistic regression).

The presence of thoracic hairiness or its clinical patterns (sternum, areola or both) did not associate with CAD ($p > 0.1$ - multiple logistic regression).

Both ELC and PAC presented higher prevalence with aging (Graphs 1 and 2), although they were more frequent in the case group than in the controls at different ages.

DISCUSSION

This study verified that PAC and ELC showed positive association with CAD in men, regardless of the other coronary risk factors.

The increased prevalence of ELC according to age group made many authors consider it only as a confounding variable, considering that CAD is also more frequent as age advances. However, the multivariate analysis showed ELC as an isolated factor for CAD.^{4,5}

The choice of only male patients was based on the attempt of reducing the possibility of detect-

ing creases caused by using earrings, a habit not declared by any patient included in this study. Likewise, considering only bilateral creases and those affecting the total whole extension of the lobe aimed to reduce detection of creases developed by postural vices, especially by sleeping positions.

Other studies that did not take these variables into account found higher prevalence of these variables among the patients.^{4,5,7-9}

The pathophysiological link between ELC and CAD has not been explained yet.

One study evaluated cadavers and found the association between ELC and CAD, and, histologically, there were atherosclerotic changes in earlobes of patients with ELC. These findings suggest simultaneous atherosclerotic involvement in two terminal circulations (heart and earlobe extremity), with no collateral artery supply, would be the pathophysiological basis of the crease.¹⁰

Another suggestion is that the general loss of elastin and elastic fibers, verified in biopsy samples from the ears of individuals affected, reflects the occurrence of the microvascular disease in the coronaries.¹⁰

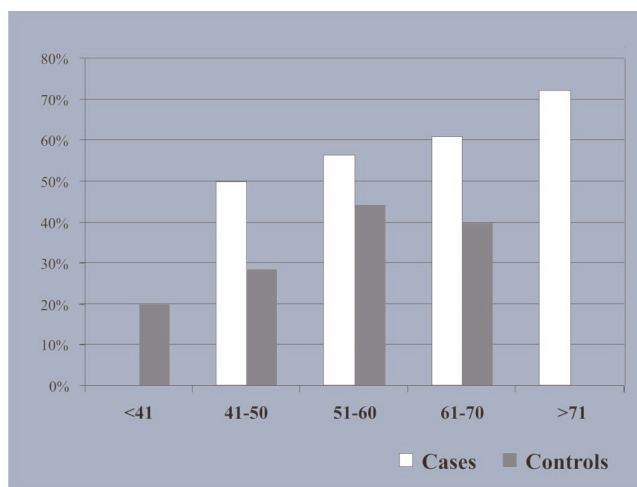
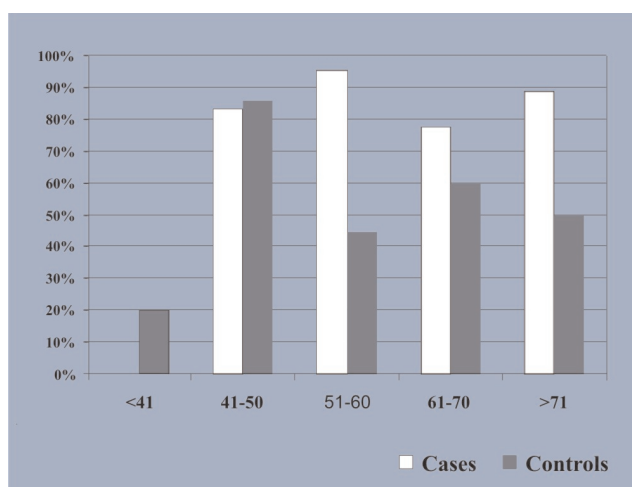
The significance of ELC among patients with coronary disease was not confirmed by certain meticulous prospective studies;^{11,12} nevertheless, a

TABLE 2: Prevalence of dermatological changes in patients

	Cases %	Controls %	Total %	OR (95% CI)*	p**
ELC	48 60	9 30	57 51.8	3.1 (1.2 a 8.3)	<0.05
PAC	70 87.5	16 53.3	86 78.2	5.5 (1.9 a 16.3)	<0.05
ELC+PAC	45 56.3	5 16.7	50 45.5	5.3 (1.8 a 16.0)	<0.05
Alopecia	50 62.5	15 50	65 59.1	1.7 (0.7 a 4.3)	>0.1
Thoracic hairiness	62 77.5	26 86.7	88 80	0.6 (0.2 a 2.2)	>0.1

* OR (95% CI) = Odds Ratio (95% confidence interval)

** multivariate analysis (multiple logistic regression)

GRAPH 1: Prevalence of ELC per age**GRAPH 2: Prevalence of PAC per age**

meta-analysis showed that finding the crease can provide useful information, but racial and gender variations, as well as different age groups can result in wrong evaluations of its value.^{13,14}

The 2.5:1 ratio between cases and controls was determined to reduce the possibility of random error, considering the difficulty of having adult patients with normal exams in an observational study such as this one.

Androgenetic alopecia and thoracic hairiness were not associated to CAD in the population tested. These findings confirm the observations of another controlled study, which did not find association of these elements with CAD. However, controversial results can be identified in the literature, especially associating temporal pattern alopecia and CAD.^{4,15} The present study did not identify any alopecia pattern as indicative of CAD.

This was the first study to describe PAC as an isolated factor associated with CAD and highlights the important predictability of CAD when there is an association with PAC and ELC despite its low sensitivity. This could contribute to classifying coronary risk in a non-invasive manner.

Further studies are necessary to evaluate the impact of these findings on mortality due to coronary event, to investigate the association with athe-

rosclerotic disease in other organs (peripheral arteries and central nervous system) and to effectively reduce the risk of coronary event by changing other risk factors.

CONCLUSION

A positive association between ELC and CAD as well as between PAC and CAD was detected. The simultaneous verification of these two creases presented high predictability for CAD. Further studies must be conducted to determine the impact of these changes on cardiac risk assessment. □

ACKNOWLEDGEMENTS

The authors would like to acknowledge those in charge of the Department of Cardiology and the hemodynamics team at the FMB/Unesp, who allowed performing this research with their patients.

REFERENCES

1. Cotton SG, Nixon JH, Carpenter RG, Evans DW. Factors discriminating men with coronary heart disease from healthy controls. *Br Heart J.* 1972; 34:458-64.
2. Tranchesi Junior B, Barbosa V, de Albuquerque CP, Caramelli B, Gebara O, dos Santos Filho RD, et al. Diagonal earlobe crease as a marker of the presence and extent of coronary atherosclerosis. *Am J Cardiol.* 1992; 70:1417-20.
3. Frank ST. Aural sign of coronary artery disease. *N Engl J Med.* 1973; 289: 327-8.
4. Miric D, Fabijanic D, Giunio L, Eterovic D, Culic V, Bozic I, et al. Dermatological indicators of coronary risk: a case-control study. *Int J Cardiol.* 1998; 67:251-5.
5. Evrengül H, Dursunoglu D, Kaftan A, Zoghi M, Tanriverdi H, Zungur M, et al. Bilateral diagonal earlobe crease and coronary artery disease: a significant association. *Dermatology.* 2004; 209:271-5.
6. Ayres M, Ayres Jr M, Ayres DL, dos Santos AS. Bioestat: 2.0 aplicações estatísticas nas áreas das ciências biológicas e médicas. Belém: Sociedade Civil Mamirauá MCT – CNPq; 2000.
7. Motamed M, Pelekoudas N. The predictive value of diagonal ear-lobe crease sign. *Int J Clin Pract.* 1998; 52:305-6.
8. Elliott WJ, Karrison T. Increased all-cause and cardiac morbidity and mortality associated with the diagonal earlobe crease: a prospective cohort study. *Am J Med.* 1991; 91:247-54.
9. Kuon E, Pfahlbusch K, Lang E. The diagonal ear lobe crease for evaluating coronary risk. *Z Kardiol.* 1995; 84:512-9.
10. Kirham N, Murrels T, Melcher DH, Morrison EA. Diagonal earlobe creases and fatal cardiovascular disease: a necropsy study. *Br Heart J.* 1989; 61:361-4.
11. Gibson TC, Ashikaga T. The ear lobe crease sign and coronary artery disease in aortic stenosis. *Clin cardiol.* 1986; 9:388-90.
12. Kenny DG, Gilligan D. Ear lobe crease and coronary artery disease in patients undergoing coronary arteriography. *Cardiology.* 1989; 76:293-8.
13. Elliott WJ, Powell LH. Diagonal earlobe creases and prognosis in patients with suspected coronary artery disease. *Am J Med.* 1996; 100:205-11.
14. Toyosaki N, Tsuchiya M, Hashimoto T, Kawasaki K, Shiina A, Toyooka T, et al. Earlobe crease and coronary heart disease in Japanese. *Heart Vessels.* 1986; 2:161-5.
15. Schnohr P, Lange P, Nyboe J, Appleyard M, Jansen G. Grey hair, baldness and wrinkles in relation to myocardial infarction: the Copenhagen City Heart Study. *Am Heart J.* 1995; 130:1003-10. *Br J Rheumatol.* 1989; 28:281-6.

MAILING ADDRESS:

*Hélio Amante Miot**Departamento de Dermatologia e Radioterapia da FMB/Unesp - Campus Universitário de Rubião Jr.**18618-000 - Botucatu – SP**Tel./Fax: (14) 3882-4922**E-mail: heliomiot@fmb.unesp.br*