



Prevalence of cutaneous markers in coronary artery disease cases



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ABSTRACT

Background: Coronary artery disease (CAD) that can cause high mortality may be diagnosed by cutaneous markers such as earlobe crease. Aside from the earlobe crease, other cutaneous markers are suspected of helping detect the existence of CAD. Therefore, it is necessary to investigate the prevalence of cutaneous markers in patients with CAD submitted to coronary angiography.

Method: A cross-sectional study was conducted involving 115 patients who had undergone coronary angiography at Hasan Sadikin Hospital from November 2019 to February 2020 to confirm the existence of CAD.

Result: These patients were examined for the presence of seven cutaneous markers. As a result, a preauricular crease was found in 77% of cases, 67.8% corneal arcus, 47% achocordon, and 45.2% cases of earlobe crease.

Conclusion: Preauricular crease was numerous in CAD cases and may be investigated in relationship with CAD.

Keywords: coronary artery disease, cutaneous marker, preauricular crease, sudden death.

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INTRODUCTION

Coronary artery disease (CAD) is known as the leading cause of death globally. CAD is caused by atherosclerosis in which the artery hardens and narrows as a consequence of build-up plaque.¹ In Indonesia, 15 out of 1000 people have coronary artery disease.² Early diagnosis is necessary to reduce the necessity of invasive treatment. It is also required to diagnose the disease using non-invasive markers, such as earlobe crease, xanthelasma, preauricular crease, etc.

The prevalence of CAD in Indonesia in 2013 was 883,447 cases, and the highest number was found in West Java (160,812 cases).³ Data regarding death due to CAD do not exist. However, the mortality rate is suspected to be high. Early diagnosis needs to be carried out before specific symptoms of cardiac diseases, such as chest pain, dyspnoea, or fainting, appear. Early diagnosis can help family or intimate friends understand symptoms related to CAD that need to be observed and sudden death due to CAD can be prevented. In death investigation, the existence of the above markers may also

help in determining the possible cause of death, without having to do autopsy on the deceased.

Investigated signs related to CAD are xanthelasma/xanthoma, corneal arcus (CA), earlobe crease (ELC), etc. A study investigated that ELC was found in 75% of all CAD cases.⁴ Another study also concluded that 78% of patients who were diagnosed as having CAD had ELC.⁵ In addition, it was concluded that ELC could become marker of premature CAD and it could help identify the existence of CAD in the absence of risk factors.⁶ Some other cutaneous markers, aside from ELC, such as xanthelasma, preauricular crease (PAC), acanthosis nigricans (AN), and alopecia, are also suspected to have related to coronary artery disease. Xanthelasma is yellow plaques that was found near the inner canthus of the upper eyelid; acanthosis nigricans are hyperpigmentation and hyperkeratosis of the skin, usually found in the skin folds; and alopecia is premature balding of the hair.⁷ Preauricular crease is a crease that appears as one or more vertical grooves in the skin close to the tragus, also known as

the anterior tragal crease.⁸ Therefore, we investigated the prevalence of ELC and other cutaneous markers in patients with CAD submitted to coronary angiography.

METHODS

A cross-sectional study was conducted involving 115 patients who had undergone coronary angiography at Hasan Sadikin Hospital from November 2019 to February 2020. This study used total sampling to select the research subjects. Data analysis used quantitative primary data from physical examination. All patients that were examined had already been diagnosed as having CAD. They had more than 50% stenosis in their coronary arteries at the examination. All patients gave written informed consent. They were examined for the existence of ELC, CA, xanthelasma, AN, alopecia, PAC and acrochordon.

RESULTS

A total of 115 patients (98 males and 17 females) were enrolled in this study. The ages ranged from 37 to 84 years old, and

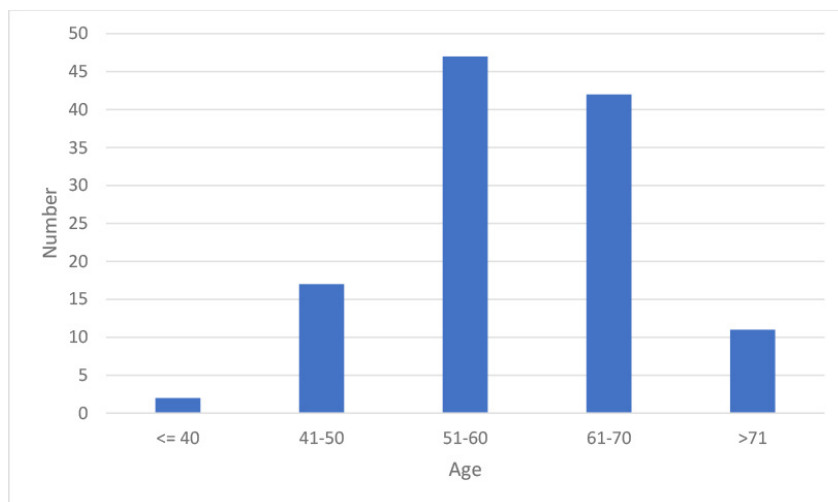


Figure 1. Age of patients who participated in the study.

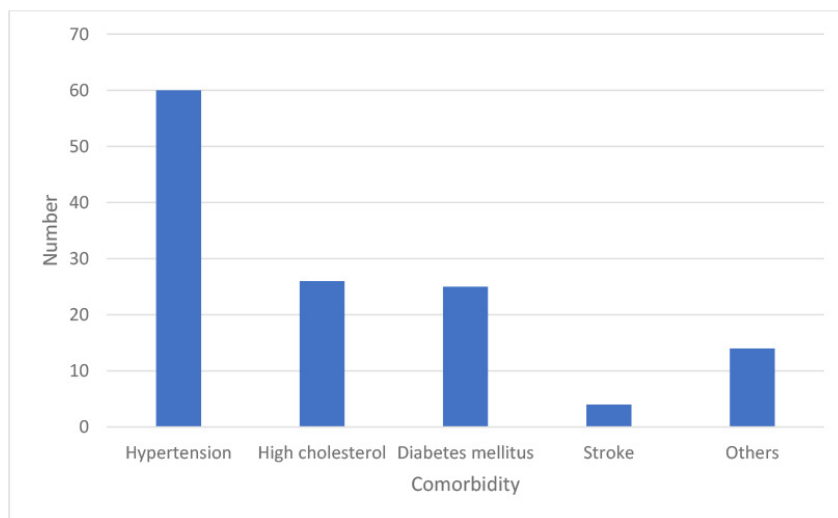


Figure 2. Comorbidities that patients had aside from CAD. Others included obesity, cardiomyopathy, kidney injury, vein thrombosis, leukemia, thyroid, and uric acid.

most of them were in the range of 51 to 60 (Figure 1).

All patients had coronary artery disease which was diagnosed using angiography. Three patients had <70% stenosis and the other 112 patients had >70% stenosis. Fewer than 50% (49 persons) had a family history of coronary artery disease. Most patients had comorbidity, including hypertension, high cholesterol, diabetes mellitus, stroke, and other diseases (Figure 2). Hypertension was the comorbidity found with the highest number in patients with CAD (60 patients), followed by high cholesterol and diabetes mellitus (26 and 25 patients).

There were seven cutaneous markers examined and PAC had the highest number found in patients with CAD (77.4%) (Figure 3). Corneal arcus had the second-highest number and was found in 76 patients (67.8%). ELC, which is considered the clinical sign to indicate CAD, was only found in 52 patients (45.2%). This number was similar to acrochordon, which was found in 54 patients (47%). In addition, 40% of them were found to have a combination of PAC and ELC. The remaining 30% were found to have a combination of PAC, ELC and CA.

There are two types of ELC found in

CAD patients, i.e., bilateral and unilateral, which means it is found in both earlobes or only one earlobe. From all patients with ELC (52 patients), bilateral ELC was found in 35 patients and unilateral ELC was found in 17 patients (Figure 4).

DISCUSSION

Four decades have passed after Frank did his study to investigate the association between ELC and cardiovascular disease.⁹ So far, many studies were carried out to investigate the relationship between ELC and CAD.^{10,11} However, aside from ELC, other cutaneous markers are suspected to be related to cardiovascular diseases, such as preauricular crease (also known as anterior tragal crease), corneal arcus, xanthelasma, etc.⁷ Compared to ELC, fewer studies were investigating the association between those markers and cardiovascular disease, such as CAD. For example, so far, three studies were investigating the association between PAC and CAD, and the first was reported by Miot et al.¹² in 2006.

This study showed that the prevalence of PAC (77.4%) was higher than other cutaneous markers. This result was consistent with other studies that confirmed the positive association with CAD with similar result.^{13,14} PAC was also very frequently seen among patients with CAD.⁸ Compared to PAC, ELC (45.2%) had a lower prevalence in association with CAD. This result was also similar to another study in which prevalence of ELC was 51.8% and a review which showed that the prevalence of ELC was less than 70%.^{13,15} However, in another study ELC was found in 98.69% of the cases, but PAC was found lower in prevalence than ELC.¹⁶ In a systematic review about ELC as a marker of CAD, at least 38 studies showed a correlation between ELC and CAD with a prevalence above 70%, while 14 other studies showed no correlation between ELC and CAD with a prevalence below 50%.¹⁷

Aside from PAC and ELC, in this study, CA was also found in 78 patients (67.8%). CA is a gray-white lipid deposition on the periphery of the cornea. CA was recognised as associated with atherosclerosis in 1852 by Rudolf Virchow.¹⁸ In one study the prevalence of CA was 86.93%, much

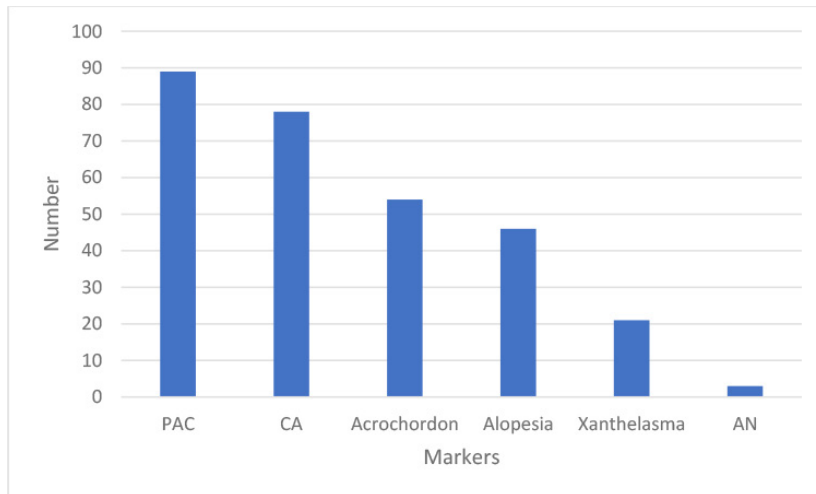


Figure 3. Cutaneous markers found in patients diagnosed as having CAD. Note: AN= acanthosis nigricans; CA= corneal arcus ; PAC= preauricular crease.

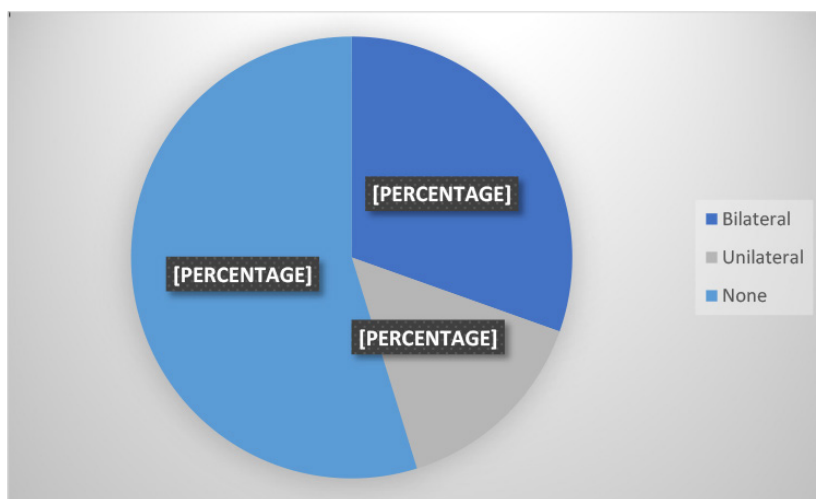


Figure 4. Numbers of earlobe crease found in CAD patients and when there was earlobe crease, whether it was found in both ears or in one ear.

higher than the prevalence found in this study.¹⁶ It was also reported that there was a significant correlation between CA and cardiovascular disease.¹⁹ However, in another study, a lower prevalence of CA in CAD patients (38%) was reported, but the presence of CA at the age of less than 60 years indicated a high risk of multivessel coronary atherosclerosis.²⁰

Another cutaneous marker found in patients with CAD was acrochordon. The number of cases found with acrochordon was 54 patients (46.96%). Acrochordon is also known as fibroepithelial polyps, skin tags, papilloma, soft fibromas,

cutaneous papilloma, cutaneous tags, fibroma pendulums, fibroma molluscum. Acrochordon is benign skin neoplasm and often associated with obesity. It is usually a small polyp and is limited to the axilla, groin, face, neck, intertriginous region, and eyelids.²¹ A study showed similar results that acrochordon was not associated with coronary artery disease.¹⁶ On the other hand, another study concluded that there was a relationship between acrochordon and an atherogenic lipid profile and this is strongly associated with atherosclerosis and cardiovascular disease.⁷

There has been considerable research

on the relationship between alopecia and CAD. Alopecia as a risk factor for CAD was first suggested by Cotton et al.²² This study found a prevalence of alopecia of 40% (46 patients). A study also showed a significant relationship between alopecia and CAD. Androgenetic activity in the body was reported to be associated with ischemic heart disease and atherosclerosis.²³⁻²⁵

A total of 21 patients (18.26%) in this study had xanthelasma. This result was different from a study which revealed that patients with xanthelasma had significantly higher serum levels of atherogenic low-density lipoproteins. They also bore a significantly higher risk of atherosclerosis with a thick carotid intima-media.²⁶ Another study found that the prevalence of single-vessel, two-vessel, three-vessel disease and left main artery disease by coronary angiography was more prevalent in patients with xanthelasma.²⁷

The last cutaneous marker we examined in this study was AN. There were only 3 patients (2.61%) who had AN. AN is characterised by hyperpigmentation and hyperkeratosis of the skin, occurring mainly in the folds of the skin, back of the neck, the axilla and / or groin.⁷ In contrast to this study, another study found that AN was associated with CAD with prevalence of 41.18% (OR= 4; p <0.001).¹⁶

CONCLUSION

This study suggests that preauricular crease, diagonal earlobe crease, corneal arcus, acrochordon, alopecia and xanthelasma could be found in patients with coronary artery disease. On the contrary, acanthosis nigricans were found to be rare in patients with coronary artery disease. It is necessary to carry out more study to investigate the relationship between these cutaneous markers with coronary artery disease. The identification of these markers may prevent the severity of the disease.

LIMITATIONS

The sample size in this study was small, that it is not possible to make a definitive conclusion. In addition, the relationship between these markers and cutaneous markers was not investigated.

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None.

CONFLICTS OF INTEREST

There is no conflict of interests.

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ETHICAL CLEARANCE

This study's ethical clearance was approved by Hasan Sadikin Hospital No. LB.02.01/X.6.5/178/2019.

REFERENCES

- Coronary artery disease: U.S. Department of Health & Human Services; 2020 [updated 19 July 2021]. Available from: https://www.cdc.gov/heartdisease/coronary_ad.htm.
- Data WHO: Lebih dari 17 juta orang di dunia meninggal karena serangan jantung, kenali gejala awalnya. *Tribun Manado*. 2019 18 July 2019.
- Putri RD, Nur'aeni A, Belinda V. Kajian Kebutuhan Belajar Klien dengan Penyakit Jantung Koroner. *Journal of Nursing Care*. 2018;1(1):60. <https://doi.org/10.24198/jnc.v1i1.15771>
- Blodgett G. The presence of a diagonal ear-lobe crease as an indicator of coronary artery disease: College of Nursing, University of Utah; 1983.
- Wang Y, Mao L-H, Jia E-Z, Li Z-Y, Ding X-Q, Ge P-C, et al. Relationship between diagonal earlobe creases and coronary artery disease as determined via angiography. *BMJ open*. 2016;6(2):e008558. <https://doi.org/10.1136/bmjopen-2015-008558>
- Corina I, Zaghoul A, Aakash D, Krishnan AM, Kathir B. Bilateral Earlobe Crease as a Marker of Premature Coronary Artery Disease. *Cureus*. 2018;10(5). <https://doi.org/10.7759/cureus.2616>
- Dwivedi S, Jhamb R. Cutaneous markers of coronary artery disease. *World journal of cardiology*. 2010;2(9):262. <https://doi.org/10.4330/wjc.v2.i9.262>
- Friedlander AH, Couto-Souza PH, Berti-Couto SA. Surgeons Beware: The Preauricular Crease Is an Indicator of Coronary Artery Atherosclerosis as well as an Anatomic Landmark. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*. 2020;S0278-2391(20) 30557-7. <https://doi.org/10.1016/j.joms.2020.05.032>
- Frank ST. Aural sign of coronary-artery disease. *The New England journal of medicine*. 1973;289(6):327. <https://doi.org/10.1056/nejm197308092890622>
- Kirkham N, Murrells T, Melcher D, Morrison E. Diagonal earlobe creases and fatal cardiovascular disease: a necropsy study. *Heart*. 1989;61(4):361-4. <https://doi.org/10.1136/hrt.61.4.361>
- Mishra V, Khanra D, Himanshu K, Jain B, Tripathi S, Aggarwal P, et al. Correlation between earlobe crease and coronary artery disease in Indian population-A multicentre experience. *Journal of Clinical and Preventive Cardiology*. 2020;9(2):67. https://doi.org/10.4103/jcpc.jcpc_10_20
- Agouridis AP. Anterior Tragal Crease: A Marker of Coronary Artery Disease. SAGE Publications Sage CA: Los Angeles, CA; 2020. <https://doi.org/10.1177/0003319720923196>
- Miot HA, Roberto LMdMC, de Siqueira S, de Chiara Cardoso L, Gumieiro JH, Filho MAP, et al. 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. *An Bras Dermatol*. 2006;81(1):29-33. <https://doi.org/10.1590/s0365-05962006000100003>
- Ramos PM, Gumieiro JH, Miot HA. Association between ear creases and peripheral arterial disease. *Clinics*. 2010;65(12):1325-7. <https://doi.org/10.1590/s1807-59322010001200016>
- Lucenteforte E, Romoli M, Zagli G, Gensini GF, Mugelli A, Vannacci A. Ear lobe crease as a marker of coronary artery disease: a meta-analysis. *Int J Cardiol*. 2014;175(1):171-5. <https://doi.org/10.1016/j.ijcard.2014.04.025>
- Sharma RK, Pulimood S, Peter D, George L. Association of the cutaneous markers with coronary artery disease: a case control study. *IJCD*. 2018;1(01):4.
- Agouridis AP, Elisaf MS, Nair DR, Mikhailidis DP. Ear lobe crease: a marker of coronary artery disease? *Archives of Medical Science*. 2015;11(6). <https://doi.org/10.5114/aoms.2015.56340>
- Shetty K, Gonsalves S, Gonagi S. Correlation of corneal arcus and serum lipid profile. *IP International Journal of Aesthetic and Health Rejuvenation*. 2019;2(2):23-5.
- Ang M, Wong W, Park J, Wu R, Lavanya R, Zheng Y, et al. Corneal arcus is a sign of cardiovascular disease, even in low-risk persons. *American Journal of Ophthalmology*. 2011;152(5):864-71. <https://doi.org/10.1016/j.ajo.2011.04.014>
- Hoogerbrugge N, Happee C, van Domburg R, Poldermans D, van den Brand MJ. Corneal arcus: indicator for severity of coronary atherosclerosis? *The Netherlands journal of medicine*. 1999;55(4):184-7. [https://doi.org/10.1016/s0300-2977\(99\)00054-6](https://doi.org/10.1016/s0300-2977(99)00054-6)
- Bajaj A. The Benign Annexure-Acrochordon. *Journal of Medical Oncology and Therapeutics*. 2020;5(2).10.35841/medical-oncology.5.2.22-24
- Vora RV, Kota RKSK, Singhal RR, Anjaneyan G. Clinical profile of androgenic alopecia and its association with cardiovascular risk factors. *Indian journal of dermatology*. 2019;64(1):19. https://doi.org/10.4103/ijd.ijd_526_16
- Pechlivanis S, Heilmann-Heimbach S, Erbel R, Mahabadi AA, Hochfeld LM, Jöckel K-H, et al. Male-pattern baldness and incident coronary heart disease and risk factors in the Heinz Nixdorf recall study. *Plos One*. 2019;14(11):e0225521. <https://doi.org/10.1371/journal.pone.0225521>
- Suastika L, Oktaviono Y, Soemantri D, Sandra F. Purple sweet potato extract and vitamin C increase the proliferation of endothelial progenitor cells from stable coronary artery disease patients. *Bali Medical Journal* 2021; 10(1): 243-248. DOI:10.15562/bmj.v10i1.2261
- Prabawa IPY, Lestari AAW, Muliarta IM, Mardhika PE, Pertiwi GAR, Bhargah A, et al. The Stromal Cell-derived Factor-1/CXCL12 3'A-gene Polymorphism is Related to the Increased Risk of Coronary Artery Disease: A Systematic Review and Meta-analysis. *Open Access Maced J Med Sci*. 2020;8(F):197-202.
- Chang H-C, Sung C-W, Lin M-H. Serum lipids and risk of atherosclerosis in xanthelasma palpebrarum: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2020;82(3):596-605. <https://doi.org/10.1016/j.jaad.2019.08.082>
- Hassanin N, Bakhom SWG, Saraya ME. Coronary angiographic profile in Egyptian patients with xanthelasma palpebrarum. *Kasr Al Ainy Medical Journal*. 2020;26(2):83. https://doi.org/10.4103/kamj.kamj_30_20



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