Heart Sci J 2022; 3(1): 48-52

Contents list available at www.heartscience.ub.ac.id

Heart Science Journal

Journal Homepage : www.heartscience.ub.ac.id

Case Report

Premature Coronary Artery Disease in Young Male Patient with Strong Family History

Dea Arie Kurniawan[1*], Mohammad Saifur Rohman[2], Anna Fuji Rahimah[2], Budi Satrijo[2]

[1] *Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*
[2] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*

ARTICLE INFO

Keywords:
Premature Coronary Artery Disease,;
Young Male;
Risk Factor

ABSTRACT

Background : Premature coronary artery disease (CAD) occurs in those under the age of 45. According to recent studies, PCAD affects 4-10% of the population. PCAD is linked to negative patient outcomes and has a greater impact on quality of life. The easiest way to describe complex interactions between two risk factors is to look at their family history.
Case : A 37-year-old man was admitted to Saiful Anwar Hospital to have his anginal discomfort evaluated further. The patient has been suffering from recurrent chest pain for the past five months, yet it is still eased by rest. Wellens Type B, which is specific for significant stenosis of the left anterior descending (LAD) artery, was found on the electrocardiogram. A 46 mm drug-eluting stent (DES) was implanted from the proximal to distal LAD. After a day of observation, the patient was discharged.
Discussion : With consideration of atherosclerotic diseases in this patient, we decided to give rivaroxaban as an anticoagulant combined with aspilet and statin high dose. But due to lack of source in our hospital, and patient also denied for further management, treatment for the patient cannot be optimal, so the patient discharge with unresolved limb ischemia.
Conclusion : Approach to a patient with PCAD comprises managing traditional risk factors and careful investigation of Family History. Individuals with a positive family history of PCAD should be treated more cautiously.

1. Introduction

Cardiovascular disease (CVD) is the most common cause of mortality worldwide, with Asia accounting for half of all CVD cases. Although coronary artery disease (CAD) mortality has declined globally, it is still relatively high in several developing countries.[1] In Indonesia, CAD and stroke are estimated to cause more than 470.000 deaths annually.[2]

According to current studies, between 4% and 10% of CAD patients are under 45 years old. Premature coronary artery disease (PCAD) is described as a form of coronary artery disease that develops in women and men under the age of 55 and 45, respectively. The cut-off value for each study, however, varies, ranging from 45 to 65 years old.[3,4] National Cardiac Center Harapan Kita (NCCHK) in 2008 reported the incidence of acute myocardial infarction approximately 1300 cases/per year. Currently, 10% of acute myocardial infarction (MI) cases occur before 40 years old, with all patients having a family history and history of smoking.

Because of the interconnections between hereditary and environmental risk factors, CAD is a complicated illness, and the best tool for assessing the interplay of these shared risk factors is currently family history. Angina, myocardial infarction, angioplasty, or coronary artery bypass surgery in a sibling, uncle or aunt, parent, or grandparent was considered a positive family history (excluding cousins, relatives by marriage, and half-relatives).[6,7] The percentage of patients who have a positive family history ranges from 14% to 69%. The incidence of CAD among siblings of a young patient with MI is 10 times higher, and around half of young patients with MI had single-vessel coronary disease.[8] Nevertheless, there is the utility of family history in terms of the CAD predictive model.

2. Case Illustration

A 37-year-old male with a body mass index (BMI) of 22.[9] kg/m2 was admitted for evaluation of frequent episodes of chest pain, which began five months before admission. It was described as a heavy-like sensation radiating to the back in less than 10 minutes. It occurred while doing heavy activity like running and was relieved by

*Corresponding author at: Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.
E-mail address: dea.arie.kurniawan@gmail.com (D.A. Kurniawan).

https://doi.org/10.21776/ub.hsj.2022.003.01.8
Received 9 August 2021; Received in revised form 30 November 2021; Accepted 15 December 2021
Available online 1 January 2022

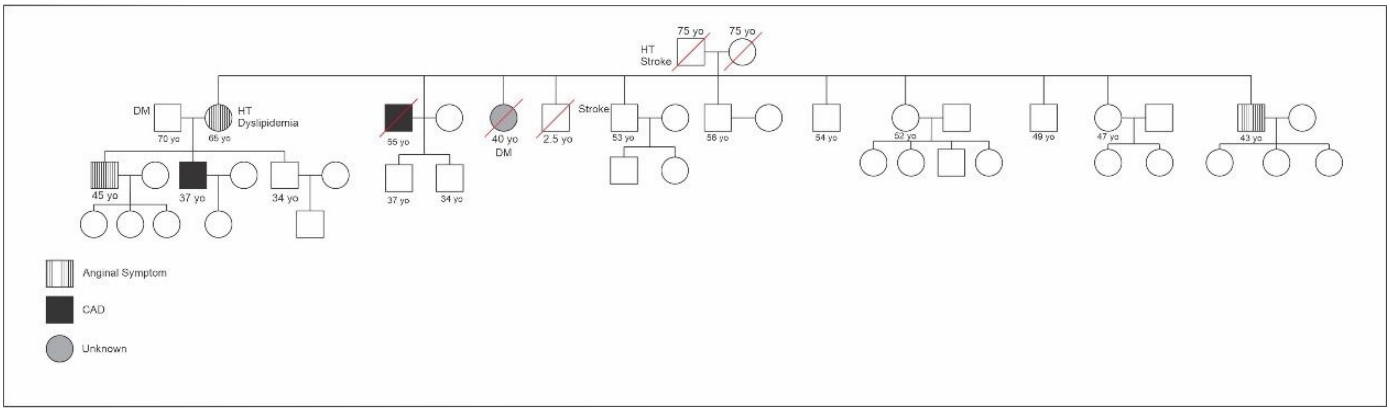


Figure 1. Pathophysiology intracellular calcium overload during ischemia and after reperfusion.12

rest. Chest pain has become more intense and frequent for the last two months. The patient got admitted for a heart attack at a local hospital two months before and hospitalized for three days. After discharge from the hospital, he routinely consumed Bisoprolol 2.5mg once daily, Aspirin 80 mg once daily, clopidogrel 75 mg once daily, atorvastatin 40 mg once daily, ramipril 5 mg once daily, and nitroglycerine 2.5 mg twice daily. The patient had been an active smoker for approximately 25 years with up to 24 cigarettes/day. He had a history of alcoholism for about one year but was completely rehabilitated. Dyslipidemia noticed 2 months ago (Total Cholesterol 212 mg/dL, Triglyceride 304 mg/dL, low-density lipoprotein [LDL] 174 mg/dL, high-density lipoprotein [HDL] 31 mg/dL). The patient had never used recreational drugs before. History of hypertension and diabetes mellitus were denied. There is a strong family history of CAD on his first-degree relatives (figure 1). His mother was known for coronary artery disease and currently consuming dual antiplatelet drugs. She was also known suffering from hypertension and hypercholesterolemia (Total Cholesterol 236 mg/dL, Triglyceride 170 mg/dL, LDL 186 mg/dL, HDL 40 mg/dL). His brother developed similar anginal symptoms, triggered by moderate to heavy activity and relieved by rest.

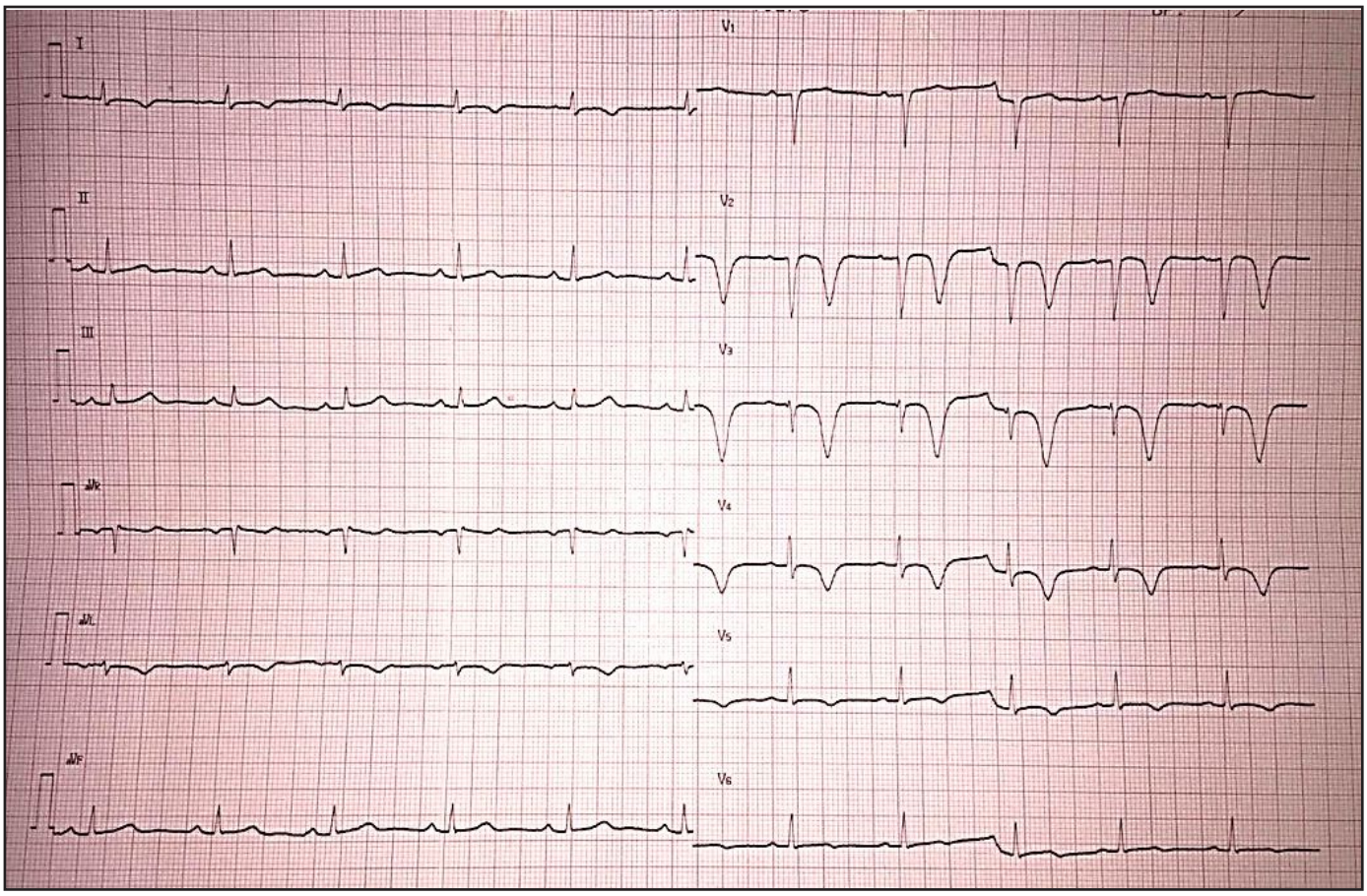
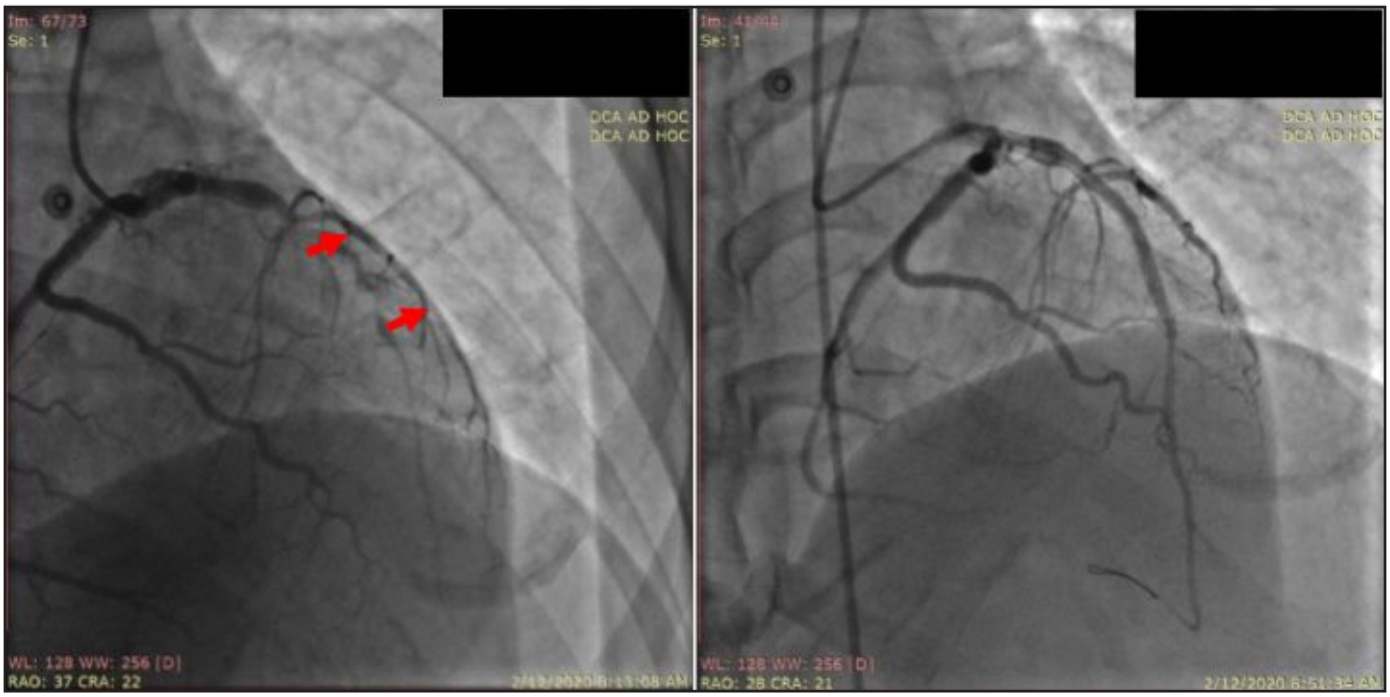


Figure 2. ECG shows sinus rhythm, normoaxis, poor R wave progression with symmetrical deep T wave inversion on V2-V4 (Wellens Type B).

In the room air, physical examination revealed blood pressure of 110/70 mmHg, regular heart rate of 70 beats per minute, respiratory rate of 18 times per minute, and peripheral oxygen saturation of 98%. On auscultation, there were no murmurs or rales. The results of other physical examinations were similarly within normal norms. Electrocardiograms (ECGs) with 12 leads revealed sinus rhythm, a heart rate of 70 beats per minute, a normal axis, and a deep, symmetrical T wave inversion V2-V4 (Type B Wellens Syndrome) (Figure 2). A chest radiograph was within the normal limit (cardiothoracic ratio [CTR] 45 %). Two-dimensional echocardiography showed slightly dilated left ventricular dimension (left ventricular internal dimension in diastole [LVIDd] 5.87 cm), left ventricular ejection fraction (LVEF) 62%, normal left ventricular diastolic function, and slight hypokinetic at the anterior segment of the mid and apical level.

The right femoral artery was used to perform the diagnostic coronary angiography (DCA). Multiple stenoses were found from the proximal to the distal Left Anterior Descending (LAD) Artery, with critical stenosis of 99% at the mid LAD and 80% at the proximal LAD. There was also 60% stenosis at the obtuse marginal (OM) 4 branch, which was dominated by the Left Circumflex (LCx). We used a Sirolimus Cre8 3.5x46 mm drug-eluting stent (DES) from the proximal to the distal LAD. Thrombolysis in myocardial infarction (TIMI) flow 3 was seen on cineangiography, with no residual stenosis, and the treatment was completed without complications. (Figure 3). The patient was discharged after 1-day observation with therapy Bisoprolol 2.5mg once daily, Aspirin 80 mg once daily, clopidogrel 75 mg once daily, atorvastatin 40 mg once daily, ramipril 10 mg once daily, and nitroglycerine 2.5 mg twice daily.



(A) **(B)**

Figure 3. A. Coronary angiography shows multiple stenosis proximal until distal LAD with critical stenosis 99% at Mid LAD and 80% at proximal LAD (Red arrow). B. Cineangiography shows TIMI Flow 3 after implantation DES.

3. Discussion

Patients with PCAD are more likely to have negative outcomes. At an early age, it carries severe morbidity, psychological impacts, and financial restraints for the individual and his or her family. In patients with PCAD, some traditional risk factors, such as cigarette smoking, dyslipidemia, and family history, are more prominent.[4,9] In terms of PCAD, patients often have multiple risk factors contributing to the disease (i.e., the culmination of genetic and non-genetic factors). Among those conventional risk factors, age, cholesterol, blood pressure, and cigarette smoking were observed to be strong and independent risk factors for PCAD in long-term follow-up. Exposure to conventional risk factors throughout lifespan increases the risk for cardiovascular disease.[10] Mortality rates for patients with no risk factors, one risk factor, or two or more risk factors respectively were 0.7, 2.4, and 5.4% 1000 person-years.[11,12] Several conventional risk factors are present in this case including, smoking approximately 25 years, newly diagnosed dyslipidemia and a strong history of premature CAD, which make a 5.4% increase in mortality risk, according to the report.

In patients with early-onset coronary artery disease, family history is a significant and independent risk factor. Nearly 40% of young CAD patients have a first-degree relative who has developed early atherosclerosis. Despite this, it rarely follows a Mendelian pattern, implying complicated inheritance and a strong reliance on environmental influences.[13] The risk of premature CAD in people with a positive family history ranged from 3.25 for a standard family history of CAD in a first-degree relative to 5.9 for a family history of early CAD in a first-degree relative before the age of 45, and 6.1 for a strong family history of CAD defined as CAD in at least two first-degree relatives.[7]

There is a strong family history of PCAD in our case that his brother also came with anginal symptoms that began at an early age. Besides, we also found that his mother had already been diagnosed with CAD and consumed DAPT, although it came at a late age. In addition to this finding, we found CAD in second-degree family relatives with a similar symptom. Elucidating the association of Family History of premature CAD with subclinical atherosclerosis may have clinical implications because we should consider performing subclinical disease screening on another degree of family relatives. In general, a history of CAD in a first-degree family member is associated with 1.5 to 3-fold increased disease risk. The risk increased more than 10-fold because the patient's brother was affected before the age of 45.[14]

Table 1. List of conventional and newer risk factors in premature coronary artery disease.[12]

Conventional Risk Factor	Newer Risk Factor
Age	Polymorphisms in CETP gene
Sex	Hepatic Lipase Gene
Hypertension	Lipoprotein lipase gene
Diabetes Mellitus	C-Reactive Protein Gene
Dyslipidemia	Apo A1 Gene
Obesity	Apo B Gene
Smoking	H1F1A gene
Family History of PCAD	Factor 5 Leiden
	MTHFR Gene
	Methionine synthase gene
	Cocaine use
	Lipoprotein-a, Fibrinogen, and D-dimer
	Decreased serum Wnt
	Increased gamma-glutamyl transferase
	Raised Vitamin D2 and D3
	Decreased osteocalcin
	Hypothyroidism
	Systemic lupus erythematosus
	Rheumatoid Arthritis
	HIV patients on HAART
	Homocysteinemia
	Kawasaki disease in childhood
	Patent Foramen Ovalle
	Spontaneous coronary artery dissection

Note. PCAD = Premature Coronary Artery Disease; CETP = Cholesteryl Ester Transfer Protein; H1F1A = Hypoxia Inducible Factor 1 Subunit Alpha; MTHFR = Methylenetetrahydrofolate reductase; HIV = human immunodeficiency virus; HAART = Highly active antiretroviral therapy

The Framingham risk score (FRS) is used in current clinical practice guidelines for the primary prevention of CAD; however, a family history of early CAD is not included in this predictive model, which is based on five classical risk factors.[6,15] As a result, the Framingham score may underestimate CAD risk in those with a family history, especially in children and teenagers, when prevention could have a big impact due to the risk of early-onset illness. In the context of secondary prevention, the Korea Acute Myocardial Infarction Registry (KAMIR) Study demonstrates the prognostic significance of family history. MACEs (hazard ratio [HR], 1.41; p = 0.009) and cardiac death (HR, 1.56; p = 0.080) were linked to family history. In female patients and those with a low Framingham risk profile, family history may be an independent prognostic predictor.[16]

Prior to CAD onset patient was a smoker without the concurrent medical disease. Smoking is one of the strongest risk factors for patients with premature CAD. The prevalence of smoking in PCAD was 60% to 90%.[12] Smoking appears to have a multiplicative interaction with the other major risk factors for coronary artery disease, in addition to its status as an independent risk factor. The development of atherosclerotic alterations with narrowing of the arterial lumen, as well as production of a hypercoagulable condition, which increases the risk of acute thrombosis, are the general processes through which smoking causes cardiovascular events.[17]

Dyslipidemia, which is critical in the early stages of CAD, was another risk factor. When compared to matched controls, one study looked at the incidence of lipid abnormalities in early-onset MI patients. A major hallmark of several kinds of genetically determined and/or metabolically induced dyslipidemia is the early development of CAD. Heterozygous family hypercholesterolemia, familial mixed hyperlipidemia, familial dyslipoproteinemia, primary hypolipoproteinemia (low HDL levels), and familial hypertriglyceridemia are among them. Wiesbauer et al.[18] reported that the Familial Combined Hyperlipidemia phenotype was associated with a 24-fold increased adjusted risk for MI (95% CI 7.5–81, P < 0.001). The patient had hypercholesterolemia and hypertriglyceridemia prior to CAD onset, which suggests the probability of familial hypercholesterolemia. Besides, there is a familial history of hypercholesterolemia in his mother. In spite, we still need to establish the diagnosis by checking the apolipoprotein B100 level.

4. Conclusion

PCAD is a multifactorial disease that requires a special clinical approach. A positive family history of coronary artery disease is a strong predictor of PCAD. Patients with this predisposing risk factor should be treated more cautiously, and diagnostic procedures should be considered more frequently when there is a likelihood of PCAD.

5. Declarations

5.1. Ethics Approval and Consent to participate
This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involvement in the study.

5.2. Consent for publication
Not applicable.

5.3. Availability of data and materials
Data used in our study were presented in the main text.

5.4. Competing interests
Not applicable.

5.5. Funding source
Not applicable.

5.6. Authors contributions
Idea/concept: DAK; Design: DAK; Control/supervision: DS, NK, AFR; Data collection/processing: DAK; Extraction/Analysis/interpretation: DAK ; Literature review: DS, NK, AFR; Writing the article: DAK ; Critical review: DS, NS, AFR. Reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

5.7. Acknowledgements
We thank to Brawijaya Cardiovascular Research Center.

References

1. Ohira T, Iso H. Cardiovascular Disease Epidemiology in Asia: An Overview. Circulation Journal. 2013;77(7):1646-52.

2. Hussain MA, Al Mamun A, Peters SA, Woodward M, Huxley RR. The Burden of Cardiovascular Disease Attributable to Major Modifiable Risk Factors in Indonesia. J Epidemiol. 2016;26(10):515-21.

3. Rubin JB, Borden WB. Coronary Heart Disease in Young Adults. Current Atherosclerosis Reports. 2012;14(2):140-9.

4. Poorzand H, Tsarouhas K, Hozhabrossadati SA, Khorrampazhouh N, Bondarsahebi Y, Bacopoulou F, et al. Risk factors of Premature Coronary Artery Disease in Iran: A Systematic Review and Meta-analysis. European journal of clinical investigation. 2019;49(7):e13124.

5. Baransyah L, Rohman MS, Suharsono T. Faktor-Faktor yang Berpengaruh terhadap Kejadian Gagal Jantung pada Pasien Infark Miokard Akut di Rumah Sakit dr. Saiful Anwar Malang. Majalah Kesehatan FKUB. 2014;1(4):209-13.

6. Bachmann JM, Willis BL, Ayers CR, Khera A, Berry JD. Association between family history and coronary heart disease death across long-term follow-up in men: the Cooper Center Longitudinal Study. Circulation. 2012;125(25):3092-8.

7. Eaton CB, Bostom AG, Yanek L, Laurino JP, McQuade W, Hume A, et al. Family History and Premature Coronary Heart Disease. The Journal of the American Board of Family Practice. 1996;9(5):312.

8. Ahmadi SH, Abbasi SH, Ugurlucan M, Bina P. Positive family history as the single traditional risk factor for developing extensive very premature coronary artery disease: a case report. J Tehran Heart Cent. 2013;8(1):54-7.

9. Abderrahman HA, Al-Abdallat IM, Idhair AK. Age Threshold for Proper Definition of Premature Coronary Artery Disease in Males. Journal of Forensic Legal Medicine. 2018;58:45-9.

10. Berry JD, Lloyd-Jones DM, Garside DB, Greenland P. Framingham risk score and prediction of coronary heart disease death in young men. Am Heart J. 2007;154(1):80-6.

11. Celik T, Iyisoy A. Premature Coronary Artery Disease in Young Patients: An Uncommon But Growing Entity. International journal of cardiology. 2010;144(1):131-2.

12. Aggarwal A, Srivastava S, Velmurugan M. Newer Perspectives of Coronary Artery Disease in Young. World Journal of Cardiology. 2016;8(12):728.

13. Stitziel NO, MacRae CA. A Clinical Approach to Inherited Premature Coronary Artery Disease. Circulation: Cardiovascular Genetics. 2014;7(4):558-64.

14. Christiansen MK. Early-onset Coronary Artery Disease Clinical and Hereditary Aspects. Dan Med J. 2017;64(9).

15. Nasir K, Budoff M, Wong N, Scheuner M, Herrington D, Arnett D. Family history of premature coronary heart disease and coronary artery calcification - Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2007;116:619-26.

16. Kim C, Chang H-J, Cho I, Sung JM, Choi D, Jeong MH, et al. Impact of family history on the presentation and clinical outcomes of coronary heart disease: data from the Korea Acute Myocardial Infarction Registry. Korean J Intern Med. 2013;28(5):547-56.

17. Aggarwal A, Aggarwal S, Sarkar PG, Sharma V. Predisposing Factors to Premature Coronary Artery Disease in Young (Age ≤ 45 Years) Smokers: A Single Center Retrospective Case Control Study From India. J Cardiovasc Thorac Res. 2014;6(1):15-9.

18. Wiesbauer F, Blessberger H, Azar D, Goliasch G, Wagner O, Gerhold L, et al. Familial-combined hyperlipidaemia in very young myocardial infarction survivors (≤ 40 years of age). European Heart Journal. 2009;30(9):1073-9.