Health Sciences & Disease
The Journal of Medicine and Biomedical Sciences
EISSN: 2309-6535 ISSN: 1684-278

Case Report

Coronary Computed Tomography Angiography for The Diagnosis of Ischemic Heart Disease in a Diabetic Patient: A Case Report and Literature Review

Angiographie Coronarienne par Tomodensitométrie pour le Diagnostic de la Cardiopathie Ischémique chez un Patient Diabétique : À Propos d'un Cas et Revue de la Littérature

Sall F [1] , Meneas GC[2], Akatchi R[1], N'Guessan I[2], Binate A[2] , Kpi Y[1], Adoubi KA[1].

Affiliations

1- Cardiology Department, Alassane Ouattara University, Ivory Coast.
2- Thoracic and Cardiovascular Surgery Department, Alassane Ouattara University, Ivory Coast
Correspondence: Sall Fatouma , Alassane Ouattara University, Ivory Coast
Tel : +225 0748326080; e-mail: fatousall45@yahoo.fr

Article history
Submitted: 11 November 2024
Revisions requested: 7 December 2024
Accepted: 24 December 2024
Published: 27 December 2024

Keywords: coronary artery, CT angiography, heart ischemia, diabetes.

Mots clés : artère coronaire, angiographie par tomodensitométrie, ischémie cardiaque, diabète

ABSTRACT

The search for ischemic heart disease is essential in diabetic patients because of the potential risk of silent myocardial ischemia. Coronary computed tomography angiography (CCTA), readily available, less expensive and less invasive, remains a safe means of detecting coronary lesions. We describe the clinical case of a 67-year-old patient with a 26 year-history of hypertension and a 10 year-history of type 2 diabetes presenting a very high cardiovascular risk (ASCVD risk score = 41.6%), admitted for atypical chest discomfort resistant to usual gastric dressings and traditional analgesics. The electrocardiogram performed was non-specific. A CCTA was performed by prospective acquisition with ECG synchronization in spontaneous contrast then after injection It have revealed a coronary calcium score estimated at 852 AU and a significant tri-vessel coronary stenosis. Pending coronary revascularization, the patient remains stable under medical treatment based on fixed triple antihypertensive therapy, a beta-blocker, a statin and a dual antiplatelet agent.

RESUME

La recherche d'une cardiopathie ischémique est essentielle chez les patients diabétiques en raison du risque potentiel d'ischémie myocardique silencieuse. L'angiographie coronaire par tomodensitométrie (ACT), facilement disponible, moins coûteuse et moins invasive, reste un moyen sûr de détecter les lésions coronaires. Nous décrivons le cas clinique d'un patient de 67 ans, hypertendu depuis 26 ans et diabétique de type 2 depuis 10 ans, présentant un risque cardiovasculaire très élevé (score de risque ASCVD = 41,6 %), admis pour une gêne thoracique atypique résistant aux pansements gastriques habituels et aux analgésiques traditionnels. L'électrocardiogramme réalisé était non spécifique. Une ACT a été réalisée par acquisition prospective avec synchronisation ECG en contraste spontané puis après injection Elle a révélé un score calcique coronaire estimé à 852 UA et une sténose coronaire tri-vaisseaux significative. Dans l'attente d'une revascularisation coronaire, le patient reste stable sous traitement médical basé sur une triple thérapie antihypertensive fixe, un bêta-bloquant, une statine et un double antiagrégant plaquettaire.

INTRODUCTION

Insulin-resistant diabetes mellitus (T2DM) and coronary artery disease are two very complex pathological entities closely linked to the phenomenon of atherosclerosis **[1-8].** Worldwide, coronary artery disease remains the most widespread cardiovascular disease **[9-11]**. It represents the main cause of cardiovascular morbidity and mortality, especially in diabetics **[2, 12-16].** According to the literature, T2DM multiplies by 2 the risk of developing coronary artery disease **[12]** and approximately ¾ of T2DM patients die from these conditions **[6, 17]**. Its often-silent nature in cases of diabetes makes the diagnosis erroneous for a long time and requires systematic screening in diabetics at very high

cardiovascular risk **[9].** There are several means of cardiovascular exploration including functional or anatomical imaging, in particular CCTA, which is well established as a non-invasive exploration technique and is recommended for the evaluation or search for stable coronary diseases **[1, 18,19].**

CASE PRESENTATION

A 67-year-old patient, with a 26 year-history of hypertension and a 10 year-history of type 2 diabetes, presenting a very high cardiovascular risk with a predictive score for cardiovascular events over 10 years (ASCVD risk score) of 41.6%, was seen in consultation for chest discomfort. Including spontaneous chest pain, in the form of light tingling, without irradiation, sedation factors, or aggravation and without digestive disorders, fever, or other accompanying signs. The electrocardiogram performed was in sinus rhythm at 60 beats per minute with an incomplete right bundle branch block such as right ventricular hypertrophy without repolarization disorder. The pre-test probability of coronary artery disease according to the clinical model based on age, sex, symptoms and cardiovascular risk factors was estimated at 44%. A Coronary computed tomography angiography (CCTA) was performed by prospective acquisition with ECG synchronization in spontaneous contrast and then after injection. In spontaneous contrast, the coronary calcium score or coronary disease diffusion score (Agatson score) on all coronaries was estimated at 852 AU.

On Coronary computed tomography angiography (CCTA), at the level of the common trunk, a proximal plaque responsible for a stenosis of approximately 20% was highlighted (CAD-RADS 1) (Figure 1A).

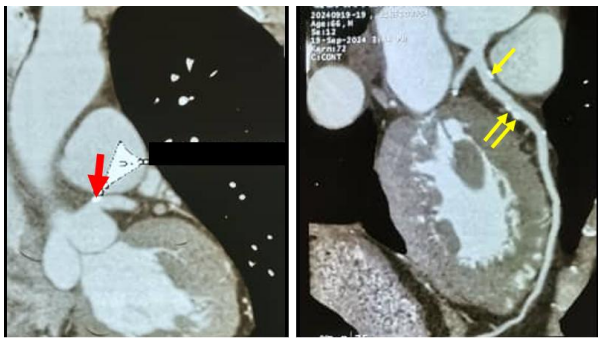

Figure 1: Results of coronary computed tomography angiography (CCTA) highlighting: A: The presence of a proximal plaque responsible for a stenosis of approximately 20% (CAD-RADS 1) **(red arrow)** on the common trunk. **B:** The presence of numerous proximal plaques with stenoses of approximately 50 to 69% (CAD-RADS 3) without intra-myocardial bridge **(yellow arrows)** on the left anterior descending artery (LAD).

On the left anterior descending artery (LAD), numerous proximal plaques with stenoses of approximately 50 to 69% (CAD-RADS 3) were objectified without intramyocardial bridge (Figure 1B). The circumflex (Figure 2A), was permeable with minimal plaques. At the level of the right coronary (Figure 2B), numerous calcifications with stenoses of approximately 50 to >70% (CAD-RADS 3, 4). We conclude to a tri-vessel atheromatous lesion in a type 2 diabetic patient with a coronary calcium score of 852 AU, classifying this patient at the 96th percentile, reflecting a significant calcified atheromatous calcium burden and thus a very high cardiovascular risk. The patient is awaiting coronary revascularization and remains stable under medical treatment based on a fixed triple antihypertensive therapy, a beta-blocker, a statin and a dual antiplatelet agent.

Figure 2: Results of the coronary computed tomography angiography (CCTA) highlighting:
A: Permeability of the circumflex with minimal plaques. **B:** The presence of numerous calcifications with stenoses of approximately 50 to >70% (CAD-RADS 3.4) **(Arrows)** on the right coronary

DISCUSSION

Major cardiovascular risk factors

Knowledge and early detection of cardiovascular risk factors are useful for screening patients exposed to cardiovascular diseases **[20].** Initiated in 1948 in Massachusetts, United States, the Framingham study identified many major cardiovascular risk factors, including high blood pressure, T2D, obesity, smoking, and dyslipidemia **[21, 22].** Perfect control of these risk factors has slowed the scale and occurrence of cardiovascular diseases **[20, 21, 23, 24].** In developing countries, a century later (21st century) with the epidemiological transition, a similar observation to the phenomena observed in developed countries is made with a surge in non-communicable diseases and a high case fatality rate confirmed by the INTERHEART and INTERSTROKE studies **[20, 25-28].** Among these various major risk factors cited, diabetes mellitus is experiencing exponential growth worldwide and represents a real public health problem [**29-31**]. According to current statistics, 415 million people are affected by this condition, responsible for 1.5 million deaths and an estimated prevalence of more than 50% by 2050 **[2, 9, 32, 33].** Diabetes mellitus is an independent risk factor with a very poor prognosis **[9, 29].** It is a chronic metabolic disease characterized by impaired glucose tolerance with insulin resistance **[9-29].** According to the literature, T2D doubles the risk of death unlike non-diabetic subjects **[29, 34, 35].**

Atherosclerosis and coronary artery disease phenomena

Atherosclerosis is the main entity responsible for coronary artery disease **[10].** This condition is generally observed from the second decade in children **[1, 35-37].** Preclinical lesions evolve into true plaques consisting of a lipid center and a fibrous cap **[1].** This is a phenomenon strongly linked to an inflammatory process inducing activation of proteases of many immune cells leading to plaque instability with rupture [**38-53].** Diabetic coronary atherosclerosis is multifactorial and represents a chronic and complex progressive process [**9, 54**]. According to the literature **[1, 9, 54],** post mortem, a higher plaque load was found in diabetic patients. These plaques consisted of a larger necrotic center and a very pronounced inflammatory phenomenon.

Coronary artery disease screening

Coronary computed tomography angiography (CCTA) is currently a powerful and reliable examination in the diagnosis of coronary stenosis > 50% with a sensitivity of 94–99% and a specificity of 64–83% due to the use of recent systems (64-, 128- or 320-detectors). Its negative predictive value is excellent, 97–99 % **[1,55-62]**. Diagnostic evaluation and monitoring of coronary artery disease use modern noninvasive cardiac imaging, including Coronary computed tomography angiography and cardiac nuclear magnetic resonance**.** Coronary computed tomography angiography identifies coronary atheromatous calcium load by spontaneous contrast with ECG synchronization, identifies plaques at risk and the anatomical structure of coronary vessels using the Agatson score **.** Coronary Artery Calcium (CAC) ≥ 300UA is associated with a 4-fold increased risk of cardiovascular events and an excellent marker of poor prognosis.

Silent myocardial ischemia (SMI)

Silent myocardial ischemia (SMI) is a condition in patients with coronary artery disease (coronary artery stenosis or obstruction) without recognizable and obvious symptoms; which makes its diagnosis and management complex **[63, 64].** The insidious progression of SMI increases cardiovascular morbidity and mortality. SMI is part of chronic coronary syndromes (CCS) when clinically stable **[65]** as illustrated by the present clinical case. In this condition, SMI can remain undetected and cause more serious complications, such as irreversible cardiac damage and heart attacks. Therefore, the management of SMI should focus on the diagnosis of suspected myocardial ischemia.

Pre-test probability and diagnostic tests for obstructive coronary artery disease

The ACC/AHA chest pain guidelines emphasized the importance of a focused history to detect cardiac chest pain and the need to perform the Coronary Artery Disease Probability Pretest to determine whether additional diagnostic testing is appropriate for the patient **[66].** The 2019 European Society of Cardiology (ESC) guidelines for the diagnosis and management of chronic coronary syndrome introduced the clinical model of the risk-factor-weighted obstructive coronary artery disease probability pretest (RF-CL) that includes sex, age, angina symptoms, and number of risk factors **[59].** At the end of this pretest, patients are classified as having a very low probability (≤5%) of obstructive coronary artery disease and do not require further diagnostic testing unless symptoms persist and noncardiac causes have been excluded. In patients with low probability (>5% –15%) of obstructive coronary artery disease, the benefit of diagnostic testing is uncertain but may be performed if symptoms are limiting and require clarification. Patients with moderate (>15%–50%), high (>50%–85%), and very high (>85%) probability of obstructive coronary artery disease are encouraged to undergo further diagnostic testing **[67].** The diagnostic test that is increasingly adopted as first-line to detect segmental myocardial ischemia is coronary computed tomography angiography (CCTA) **[68, 69]** because it has shown similar performance to noninvasive stress tests **[70–72].** Classical invasive coronary angiography (coronary angiography) has become a functional test **[73]** and allows hemodynamic assessment **[74]** of coronary artery disease. In addition, positron emission tomography (PET) **[75]** and magnetic resonance imaging (MRI) **[76]** are of increasing interest as they are non-invasive means that allow precise assessment of coronary microcirculation in a quantitative manner.

CONCLUSION

Coronary computed tomography angiography is a reliable method of exploring coronary artery disease with good diagnostic accuracy in detecting significant coronary stenoses in diabetics. The calculation of the coronary *artery calcification (*CAC) score, with low radiation, allows quantifying the atheromatous coronary calcium load and therefore assessing subclinical atherosclerosis, and is involved in estimating the cardiovascular risk of patients. It also has an excellent negative predictive value (CAC < 100 UA) in screening for silent myocardial ischemia in diabetics.

REFERENCES

1. Dweck MR, Williams MC, Moss AJ, Newby DE, Fayad ZA. Computed Tomography and Cardiac Magnetic Resonance in Ischemic Heart Disease. J Am Coll Cardiol. 2016;68:2201-16.

2. Kennedy MW, Fabris E, Suryapranata H, Kedhi E. Is ischemia the only factor predicting cardiovascular outcomes in all diabetes mellitus patients? Cardiovasc Diabetol. 2017;16:51.

3. Karagiannidis E, Moysidis DV, Papazoglou AS, Panteris E, Deda O, Stalikas N, Sofidis G, Kartas A, Bekiaridou A, Giannakoulas G, Gika H, Theodoridis G, Sianos G. Prognostic significance of metabolomic biomarkers in patients with diabetes mellitus and coronary artery disease. Cardiovasc Diabetol. 2022;21:70.

4. Einarson TR, Acs A, Ludwig C, et al. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientifc evidence from across the world in 2007–2017. Cardiovasc Diabetol 2018;17: 83.

5. Aronson D, Edelman ER. Coronary artery disease and diabetes mellitus. Cardiol Clin 2014; 32:439–55.

6. Naito R, Miyauchi K. Coronary artery disease and type 2 diabetes mellitus. Int Heart J. 2017;58:475–80 .

7. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA 2002; 287: 2570–2581.

8. Esper RB, Farkouh ME, Ribeiro EE, et al. SYNTAX score in patients with diabetes undergoing coronary revascularization in the FREEDOM trial. J Am Coll Cardiol. 2018;72:2826–37.
9. Kharbouch, Hanane, et al. "Dépistage de l'ischémie myocardique silencieuse chez le diabétique." *Journal Marocain des Sciences Médicales.*2021 ;23.
10. Shah NR, Pierce JD, Kikano EG, Rahnemai-Azar AA, Gilkeson RC, Gupta A. CT Coronary Angiography Fractional Flow Reserve: New Advances in the Diagnosis and Treatment of Coronary Artery Disease. Curr Probl Diagn Radiol. 2021;50:925-36.
11. Pakkal M, Raj V, Mccann GP. Non-invasive imaging in coronary artery disease including anatomical and functional evaluation of ischaemia and viability assessment. Br J Radiol 2011;84(spec iss 3):S280–95
12. Saraste A, Knuuti J, Bax J. Screening for Coronary Artery Disease in Patients with Diabetes. Curr Cardiol Rep. 2023;251865-71.
13. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375:2215–22.
14. Sattar N, McMurray J, Borén J, Rawshani A, Omerovic E, Berg N, et al. Twenty years of cardiovascular complications and risk factors in patients with type 2 diabetes: a nationwide Swedish cohort study. Circulation. 2023;147:1872–86.
15. Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, Naghavi M, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation. 2015;132:1667–78.
16. Ramsey BC, Fentanes E, Choi AD, Branch KR, Thomas DM. Myocardial Assessment with Cardiac CT: Ischemic Heart Disease and Beyond. Curr Cardiovasc Imaging Rep. 2018;11:16.
17. Hammoud T, Tanguay JF, Bourassa MG. Management of coronary artery disease: therapeutic options in patients with diabetes. J Am Coll Cardiol 2000;36:355-65.
18. Sirajuddin A, Mirmomen SM, Kligerman SJ, Groves DW, Burke AP, Kureshi F, White CS, Arai AE. Ischemic Heart Disease: Noninvasive Imaging Techniques and Findings. Radiographics. 2021;41:990-1021.
19. Jensen RV, Hjortbak MV, Bøtker HE. Ischemic Heart Disease: An Update. Semin Nucl Med. 2020;50:195-207
20. Teo KK, Rafiq T. Cardiovascular Risk Factors and Prevention: A Perspective From Developing Countries. Can J Cardiol. 2021;37:733-43.
21. R. Hajar.Framingham contribution to cardiovascular disease
Heart Views, 2016;17,78-81.
22. Mahmood SS, Levy D, Vasan RS, Wang TJ. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. Lancet. 2014;383:999-1008.
23. Li X, Wu C, Lu J, Chen B, Li Y, Yang Y, Hu S, Li J. Cardiovascular risk factors in China: a nationwide population-based cohort study. Lancet Public Health. 2020 ;5:e672-e681. -2. Erratum in: Lancet Public Health. 2021;6:e271
24. Fletcher B, Gulanick M, Lamendola C. Risk factors for type 2 diabetes mellitus. J Cardiovasc Nurs. 2002;16:17-23.
25. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364:937-52.
26. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, Zhang X, Pais P, Agapay S, Lopez-Jaramillo P, Damasceno A, Langhorne P, McQueen MJ, Rosengren A, Dehghan M, Hankey GJ, Dans AL, Elsayed A, Avezum A, Mondo C, Diener HC, Ryglewicz D, Czlonkowska A, Pogosova N, Weimar C, Iqbal R, Diaz R, Yusoff K, Yusufali A, Oguz A, Wang X, Penaherrera E, Lanas F, Ogah OS, Ogunniyi A, Iversen HK, Malaga G, Rumboldt Z, Oveisgharan S, Al Hussain F, Magazi D, Nilanont Y, Ferguson J, Pare G, Yusuf S; INTERSTROKE investigators. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet. 2016;388:761-75.
27. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015.*Lancet.* 2016; 388:1459-544.
28. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part II: variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation. 2001;104:2855-64.
29. Yun JS, Ko SH. Current trends in epidemiology of cardiovascular disease and cardiovascular risk management in type 2 diabetes.Metabolism. 2021 ;123:154838.
30. Lechner K, von Schacky C, McKenzie AL, Worm N, Nixdorff U, Lechner B, Kränkel N, Halle M, Krauss RM, Scherr J. Lifestyle factors and high-risk atherosclerosis: Pathways and mechanisms beyond traditional risk factors. Eur J Prev Cardiol. 2020 ;27:394-406.
31. WHO. WHO/Fact sheets/Detail/Cardiovascular diseases (CVDs). https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (2017, 14 March 2019).
32. Boyle J, Honeycutt A, Narayan K, Hoerger T, Geiss L, Chen H, Thompson T. Projection of diabetes burden through 2050: impact of changing demography and disease prevalence in the U.S. Diabetes Care. 2001;24:1936–40.
33. J.-L. Schlienger, L. Monnier, N. Essekat, A. ElAzrak, F. Raji, D. Rochd. Risk factors and chronic iseases: Diabetes as an example. Médecine des maladies Métaboliques. 2019;13.
34. S.R. Preis, S.J. Hwang, S. Coady, M.J. Pencina, R.B. D'Agostino Sr., P.J. Savage, *et al.*Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005.Circulation. 2009;119 :1728-35.
35. E.W. Gregg, Y.J. Cheng, S. Saydah, C. Cowie, S. Gar field, L. Geiss, *et al.*Trends in death rates among U.S. adults with and without diabetes between 1997 and 2006: findings from the National Health Interview Survey.Diabetes Care. 2012;35:1252-1257
36. Tuzcu EM, Kapadia SR, Tutar E, Ziada KM, Hobbs RE, McCarthy PM, Young JB, Nissen SE. High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: evidence from intravascular ultrasound. *Circulation.* 2001;*103*:2705–10.
37. Libby P. Inflammation in atherosclerosis. *Nature.* 2002;*420*:868–74
38. Hansson, Göran K. "Inflammation, atherosclerosis, and coronary artery disease." *New England journal of medicine.* 2005;352:1685-95.
39. Kovanen, PT, Kaartinen, M, Paavonen, T. Infiltrates of activated mast cells at the site of coronary atheromatous erosion or rupture in myocardial infarction. *Circulation* 1995;92:1084-88
40. Hansson, GK, Holm, J, Jonasson, L. Detection of activated T lymphocytes in the human atherosclerotic plaque. *Am J Pathol* 1989;135:169-75

41. Van der Wal, AC, Becker, AE, van der Loos, CM, Das, PK. Site of intimal rupture or erosion of thrombosed coronary atherosclerotic plaques is characterized by an inflammatory process irrespective of the dominant plaque morphology. *Circulation* 1994;89:36-44
42. Frostegard, J, Ulfgren, AK, Nyberg, P, et al. Cytokine expression in advanced human atherosclerotic plaques: dominance of pro-inflammatory (Th1) and macrophage-stimulating cytokines. *Atherosclerosis* 1999;145:33-43
43. Moreno, PR, Falk, E, Palacios, IF, Newell, JB, Fuster, V, Fallon, JT. Macrophage infiltration in acute coronary syndromes: implications for plaque rupture. *Circulation* 1994;90:775-78.
44. Jones, CB, Sane, DC, Herrington, DM. Matrix metalloproteinases: a review of their structure and role in acute coronary syndrome. *Cardiovasc Res* 2003;59:812-23
45. Liu, J, Sukhova, GK, Sun, JS, Xu, WH, Libby, P, Shi, GP. Lysosomal cysteine proteases in atherosclerosis. *Arterioscler Thromb Vasc Biol* 2004;24:1359-66.
46. Hansson, GK, Hellstrand, M, Rymo, L, Rubbia, L, Gabbiani, G. Interferon-gamma inhibits both proliferation and expression of differentiation-specific alpha-smooth muscle actin in arterial smooth muscle cells. *J Exp Med* 1989;170:1595-608.
47. Amento, EP, Ehsani, N, Palmer, H, Libby, P. Cytokines and growth factors positively and negatively regulate interstitial collagen gene expression in human vascular smooth muscle cells. *Arterioscler Thromb* 1991;11:1223-30.
48. Saren, P, Welgus, HG, Kovanen, PT. TNF-alpha and IL-1beta selectively induce expression of 92-kDa gelatinase by human macrophages. *J Immunol* 1996;157:4159-65.
49. Mach, F, Schonbeck, U, Bonnefoy, JY, Pober, JS, Libby, P. Activation of monocyte/macrophage functions related to acute atheroma complication by ligation of CD40: induction of collagenase, stromelysin, and tissue factor. *Circulation* 1997;96:396-99
50. Momiyama, Yukihiko, et al. "Inflammation, atherosclerosis and coronary artery disease." *Clinical Medicine Insights: Cardiology* .2014; 8: CMC-S39423.
51. Libby, Peter, and Pierre Theroux. "Pathophysiology of coronary artery disease." *Circulation* .2005;111: 3481-88.
52. Onat, A., Dönmez, İ., Karadeniz, Y., Çakır, H., & Kaya, A.). Type-2 diabetes and coronary heart disease: common physiopathology, viewed from autoimmunity. *Expert Review of Cardiovascular Therapy*. 2014;*12*:667–79.
53. Yahagi K, Kolodgie FD, Lutter C, Mori H, Romero ME, Finn AV, Virmani R. Pathology of Human Coronary and Carotid Artery Atherosclerosis and Vascular Calcification in Diabetes Mellitus. Arterioscler Thromb Vasc Biol. 2017;37:191-204.
54. Gitsioudis G., Schüssler A., Nagy E. Combined Assessment of high-sensitivity troponin T and noninvasive coronary plaque composition for the prediction of cardiac outcomes. Radiology. 2015;276:73–81.
55. Barone-Rochette, G. "Comment positionner le score calcique dans le dépistage de la coronaropathie?." *Archives des Maladies du Coeur et des Vaisseaux-Pratique* 2023.319 (2023): 2-7.
56. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol 2008;52:1724–32.
57. Cury RC, Abbara S, Achenbach S, Agatston A, Berman DS, Budoff MJ, et al. Coronary Artery Disease-Reporting and Data System (CAD-RADS): An expert consensus document of SCCT, ACR and NASCI: Endorsed by the ACC. JACC Cardiovasc Imaging 2016;9. 1099-13.
58. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. N Engl J Med 1979;300:1350–8.
59. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Valgimigli M, Achenbach S, Bax JJ; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41:407-77.
60. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol. 1990;15:827-32 **.**
61. McClelland RL, Jorgensen NW, Budoff M, Blaha MJ, Post WS, Kronmal RA, Bild DE, Shea S, Liu K, Watson KE, Folsom AR, Khera A, Ayers C, Mahabadi AA, Lehmann N, Jöckel KH, Moebus S, Carr JJ, Erbel R, Burke GL. 10-Year Coronary Heart Disease Risk Prediction Using Coronary Artery Calcium and Traditional Risk Factors: Derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) With Validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study). J Am Coll Cardiol. 2015;66:1643-53.
62. Blaha MJ, Cainzos-Achirica M, Greenland P, McEvoy JW, Blankstein R, Budoff MJ, Dardari Z, Sibley CT, Burke GL, Kronmal RA, Szklo M, Blumenthal RS, Nasir K. Role of Coronary Artery Calcium Score of Zero and Other Negative Risk Markers for Cardiovascular Disease: The Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2016;133:849-58.
63. Cohn PF, Fox KM, Daly C. Silent myocardial ischemia. Circulation. 2003;108:1263-77.
64. Theofilis P, Antonopoulos AS, Sagris M, Papanikolaou A, Oikonomou E, Tsioufis K, Tousoulis D. Silent Myocardial Ischemia: From Pathophysiology to Diagnosis and Treatment. Biomedicines. 2024;12:259.
65. Berry C, Kramer CM, Kunadian V, Patel TR, Villines T, Kwong RY, Raharjo DE. Great Debate: Computed tomography coronary angiography should be the initial diagnostic test in suspected angina. Eur Heart J. 2023;44:2366-75.
66. Gray AJ, Roobottom C, Smith JE, Goodacre S, Oatey K, O'Brien R, Storey RF, Curzen N, Keating L, Kardos A, Felmeden D, Lee RJ, Thokala P, Lewis SC, Newby DE; RAPID-CTCA Investigators. Early computed tomography coronary angiography in patients with suspected acute coronary syndrome: randomised controlled trial. BMJ. 2021 Sep 29;374:n2106. doi: 10.1136/bmj.n2106. Erratum in: BMJ. 2022;376:o438.
67. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, Banning AP, Budaj A, Buechel RR, Chiariello GA, Chieffo A, Christodorescu RM, Deaton C, Doenst T, Jones HW, Kunadian V, Mehilli J, Milojevic M, Piek JJ, Pugliese F, Rubboli A, Semb AG, Senior R, Ten Berg JM, Van Belle E, Van Craenenbroeck EM, Vidal-Perez R, Winther S; ESC Scientific Document Group. 2024 ESC Guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024;45:3415-3537.
68. Serruys PW, Hara H, Garg S, Kawashima H, Nørgaard BL, Dweck MR, Bax JJ, Knuuti J, Nieman K, Leipsic JA, Mushtaq S, Andreini D, Onuma Y. Coronary Computed Tomographic Angiography for Complete Assessment of

Coronary Artery Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2021;78:713-736.

69. Serruys PW, Kotoku N, Nørgaard BL, Garg S, Nieman K, Dweck MR, Bax JJ, Knuuti J, Narula J, Perera D, Taylor CA, Leipsic JA, Nicol ED, Piazza N, Schultz CJ, Kitagawa K, Bruyne B, Collet C, Tanaka K, Mushtaq S, Belmonte M, Dudek D, Zlahoda-Huzior A, Tu S, Wijns W, Sharif F, Budoff MJ, Mey J, Andreini D, Onuma Y. Computed tomographic angiography in coronary artery disease. EuroIntervention. 2023;18:e1307-e1327.

70. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, Cole J, Dolor RJ, Fordyce CB, Huang M, Khan MA, Kosinski AS, Krucoff MW, Malhotra V, Picard MH, Udelson JE, Velazquez EJ, Yow E, Cooper LS, Lee KL; PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372:1291-300.

71. SCOT-HEART Investigators; Newby DE, Adamson PD, Berry C, Boon NA, Dweck MR, Flather M, Forbes J, Hunter A, Lewis S, MacLean S, Mills NL, Norrie J, Roditi G, Shah ASV, Timmis AD, van Beek EJR, Williams MC. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. N Engl J Med. 2018;379:924-933.

72. Mézquita AJV, Biavati F, Falk V, Alkadhi H, Hajhosseiny R, Maurovich-Horvat P, Manka R, Kozerke S, Stuber M, Derlin T, Channon KM, Išgum I, Coenen A, Foellmer B, Dey D, Volleberg RHJA, Meinel FG, Dweck MR, Piek JJ, van de Hoef T, Landmesser U, Guagliumi G, Giannopoulos AA, Botnar RM, Khamis R, Williams MC, Newby DE, Dewey M. Clinical quantitative coronary artery stenosis and coronary atherosclerosis imaging: a Consensus Statement from the Quantitative Cardiovascular Imaging Study Group. Nat Rev Cardiol. 2023;20:696-714.

73. Kunadian V, Chieffo A, Camici PG, Berry C, Escaned J, Maas AHEM, Prescott E, Karam N, Appelman Y, Fraccaro C, Louise Buchanan G, Manzo-Silberman S, Al-Lamee R, Regar E, Lansky A, Abbott JD, Badimon L, Duncker DJ, Mehran R, Capodanno D, Baumbach A. An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. Eur Heart J. 2020;41:3504-20.

74. Ong P, Athanasiadis A, Borgulya G, Vokshi I, Bastiaenen R, Kubik S, Hill S, Schäufele T, Mahrholdt H, Kaski JC, Sechtem U. Clinical usefulness, angiographic characteristics, and safety evaluation of intracoronary acetylcholine provocation testing among 921 consecutive white patients with unobstructed coronary arteries. Circulation. 2014;129:1723-30.

75. Taqueti VR, Hachamovitch R, Murthy VL, Naya M, Foster CR, Hainer J, Dorbala S, Blankstein R, Di Carli MF. Global coronary flow reserve is associated with adverse cardiovascular events independently of luminal angiographic severity and modifies the effect of early revascularization. Circulation. 2015;131:19-27

76. Ong P, Seitz A. Advances in Risk Stratification of Patients With Coronary Microvascular Dysfunction: Usefulness of Stress Perfusion CMR. JACC Cardiovasc Imaging. 2021;14:612-614.