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Case report

# Acute coronary syndrome associated with occlusion of the main trunk of the left coronary artery in patients with a previously negative exercise stress test

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**Abstract**

**Objective.** A case report of a patient with acute coronary syndrome with occlusion of the left main coronary artery with a typical clinical picture and a negative exercise stres test result.

**Case report.** A 44-year-old patient is presented to our service as STEMI with elevation in the inferior leads and ST depression in the precordial leads. After intrahospital cardiac arrest and resuscitation, primary PCI of left main coronary artery is performed, after which hemodynamic stabilization occurs. Retrospective review of medical history reveals that he was evaluated three years before the acute event due to occasional chest pain. The pretest probability for coronary heart disease was 38%, so in accordance with the then valid ESC guidelines for stable coronary heart disease, a stress ECG test was performed, which was assessed as negative for significant coronary heart disease. All analyzed test parameters indicated a low risk of adverse cardiovascular events: functional capacity, ST segment denivelation, chronotropic competence, blood pressure variations, Duke treadmill score. With a postest probability of 9%, the patient was not further evaluated for coronary heart disease and was asymptomatic for the next three years and did not respond to follow-up examinations. If he presented himself after 2019 according to the newer ESC guidelines for chronic coronary syndromes, the patient would be indicated to perform a functional imaging test or CT coronary angiography at the time of the initial clinical evaluation.

**Conclusion**. The diagnostic algorithm for patients with chest pain is based on a pretest probability that determines further diagnostic workup. Patients with a negative exercise test and a typical clinical presentation should be referred for further diagnostic imaging test because of the risk that a small number of them may have significant and even critical coronary stenosis.

**Kew words** pretest probability, coronary artery disease, CAD, ECG stress test, cardiovascular adverse events

## Introduction

Chest pain is a common problem in everyday clinical practice. Of all visits to a general practitioner in the UK, 1% are due to chest pain. The importance of this cardinal clinical symptom is evidenced by the fact that mortality was doubled in the year after the presentation of a patient with chest pain[1]. Since the introduction of invasive coronary angiography (ICA) into routine clinical practice, it has become the gold standard for the diagnosis of coronary artery disease (CAD)[2] and in the United States alone about 1.1 million procedures[3] are performed each year. However, due to the wide availability of the method, there is an expansion of indications for referral of patients to ICA and only 41% of patients have obstructive CAD[4]. Therefore, there is a need to use non-invasive methods to assess the likelihood of CAD. This is achieved by determining the pretest probability (PTP) for the CAD. One of the oldest in use is the Diamond and Forrester method, which uses the patient's age, gender and chest pain typicality for coronary heart disease[5] in the pretest probability assessment. More recently, the European Society of Cardiology (ESC) has used a modified version of this model[6].

## Case presentation

A 41-years old patient presented to outpatient clinic for atypical chest pain. He had positive family history, was a smoker and had dyslipidemia with total cholesterol 6.1 mmol/L and an LDL fraction of 4.3 mmol/L. The patient was referred to a stress electrocardiographic test that was performed on an ergobycycle in December 2016 using the Bruce protocol. The PTP for CAD was 34%. The test was interrupted at 2th minute of V level at 223W workload and 10.9 MET due to patient fatigue, no anginal discomfort, no ST segment denivelation, and heart

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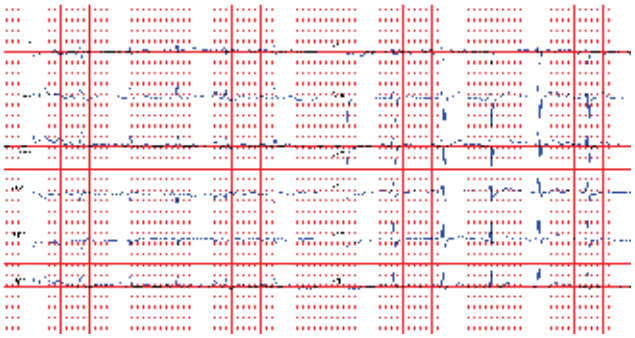

**Figure 1.** ECG at the beginning of the stres test

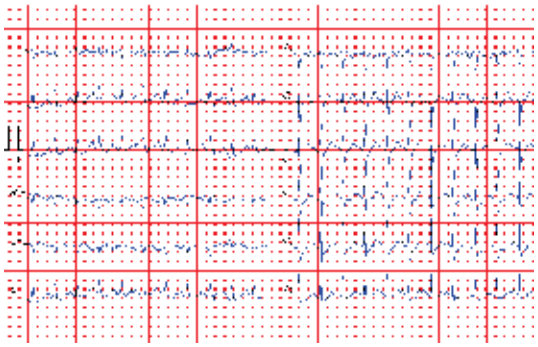

**Figure 2.** ECG in peak workload of 220W

rhythm disturbances. A heart rate of 179/min (91% of maximum predicted), a BP of 190/100 mmHg, and a double product of 34010 were achieved (Figures 1 and 2). The test was rated as negative for significant CAD with a calculated post-test probability of 9%.

Three years later, in August 2019, the patient presented with myocardial infarction with ST segment elevation in D2, D3, aVF and deep ST segment depression in leads V1-V4 (Figure 3) with intrahospital cardiac arrest immediately upon admission to the Internal Department of the Zajecar Health Center. The patient was resuscitated for about 40 minutes using advanced life support measures including 8 asynchronous DC shocks and 20 ampules of Adrenaline. After that, he recovered cardiac activity with a frequency of 25 / min and an complete heart block, the patient was placed on mechanical ventilation, and a temporary pacemaker lead was placed. Coronary angiography verifies the occlusion of the distal segment of the left main coronary artery. After placement of coronary wires in the distal segments of LAD and Cx (Figure 4), the lesion was predilatated with a Sprinter Legend 2.5x15mm balloon and then implanted with a Resolute Onyx 4.5x18mm stent in LM-LAD with provisional technique and excellent angiographic result with TIMI3 flow through LAD and Cx arteries (Figure 5). The patient was hemodynamically stable, following intervention. After 24 hours, control coronary angiography conformed patent stent. In the further course of hospitalization, clinical improvement occurs with weaning the patient from mechanical ventilation. Echocardiography registers the left ventricle diameter of 66/43mm, left ventricular ejection fraction of 35-40% with hyoikinesia of distal anterior, septal and lateral walls. The patient was discharged on the 18$^{th}$ hospital day. Four months after the acute event, control coronary angiography was performed with a transradial apprach, showing patent coronary arteries without in-stent restenosis, and intermedaite lesion in medial segment of LAD and mild stenosis in RCA. In further clinical follow-up the patient was asymptomatic, with maximal doses of drugs and LDL cholesterol value of 1.5 mmol/L.

## Discussion

In patients with chest pain, the first step in the diagnostic algorithm is to determine the pretest probablity (PTP). PTP predicts the existence of angiographic stenosis of at least 50% of the diameter of at least one coronary artery. The patient's complaints at the initial presentation were understood as atypical angina with 2 of 3 features of anginal pain and a calculated pretest probability of 38% for CAD according to the ESC guidelines from 2013[7]. Since he had an normal electrocardiographic finding at rest and preserved functional ability, we decided to perform a stress electrocardiographic test. The test was considered negative.

According to the valid ESC guidelines, at the time of testing, the most important predictors of exercise stress test were: functional capacity, test duration, changes in arterial blood pressure and myocardial ischemia according to clinical and electrocardiographic parameters. Functional capacity was shown as the most important prognostic parameter for mortality and adverse cardiovascular events, regardless of gender, age, presence and severity of CAD[8,9,10,11,12,13,14]. It can be expressed in metabolic equivalents (1 MET corresponding to O2 consumption of 3.5ml/kg/ min), workload in watts (W), heart rate at peak load and double product. It has been shown that each achieved MET in the stress test reduces the total mortality and cardiovascular events by 13-15%[15]. Another predictor of adverse events is chronotropic incompetence during the stress test. A study of 1575 healthy men who underwent an ECG stress test and were followed for 7.7 years showed that failure to achieve submaximal HR, the level of HR increase during the test, and the chronotropic index were predictors of overall mortality and incidental coronary heart disease[16]. Interestingly, according to all parameters, the ergometric test of our patient was clearly low risk. Another widely used and validated predictor of adverse CV events is the Duke treadmill score designed by Mark et al[17]. It uses the duration of the test in minutes, the value of the ST segment of denivelation and angina level in the calculation. Low-risk values are 5 and higher, intermediate -11 to 4 and below -11 patients are stratified as high-risk. According to the ESC guidelines, the one-year risk of CV death over 3% was a category of high-risk patients in whom potential revascularization has prognostic significance and they should be referred to ICA[7]. It has been shown that low risk carries only 0.25% of annual CV mortality as opposed to high risk which carries over 5%. Of the patients with calculated low risk, 60% did not have significant obstructive CAD and 16% had single-vessel disease (stenoses over 75% of the diameter were considered angiographically significant). Better test performance was also shown in women and poorer in the elderly[18]. Our patient had a Duke score of

**Figure 3.** ECG at the admision to the Coronary unit – 30 minutes after the onset of chest pain

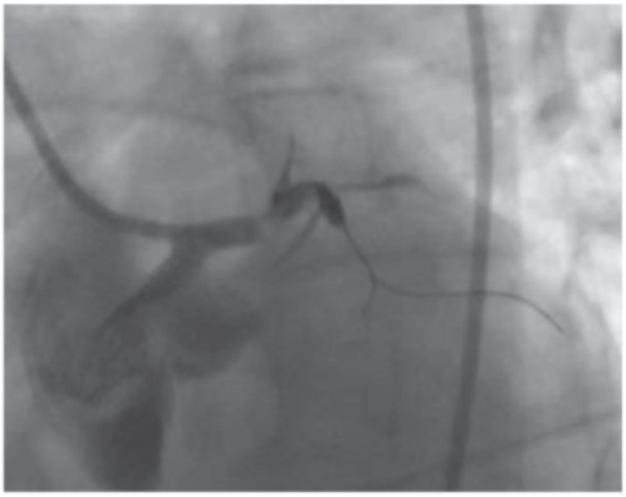

**Figure 4.** Angio after wiring LAD and Cx

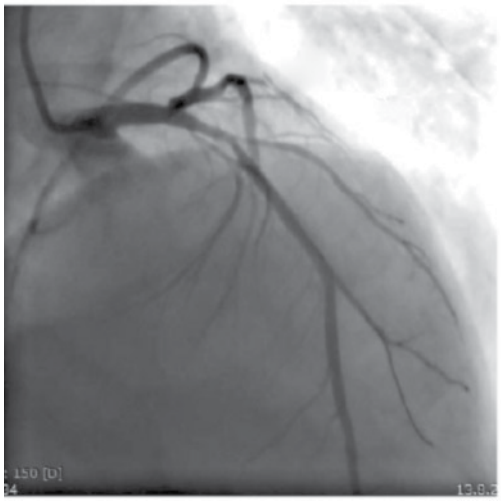

**Figure 5.** Angio after stent implantation in LM-LAD

+13 which stratified him as low risk for CV events with a one-year mortality below 1%. The question was whether something would change in the diagnostic algorithm and stratification of the CV risk of our patient if he was evaluated in the light of the new ESC guidelines for chronic coronary syndromes from 2019[19]. They retained the earlier concept of PTP based on gender, age, and typicality of chest pain with the addition of a PTP assessment for patients presenting with dyspnea only. The values of PTP are noticeably lower because the pooled analysis of three contemporary studies indicated a threefold lower prevalence of CAD than previously considered[20]. It is recommended that non-invasive diagnostic treatment be performed in patients with PTP over 15%, and in case of refractory angina or if PTP is very high invasive diagnostic assesment. Patients with PTP below 5% have a very low risk of adverse CV events so no further diagnostic workup is required. In patients with intermediate PTP 5-15%, additional diagnostics are indicated according to the factors that modify PTP, giving the so - called clinical probability of CAD. Our patient would have a PTP of 10%. According to the factors that modify PTP (hypertension, smoking, positive family history) and the normal finding of the ECG stress test which is a factor in reducing the clinical probability for CAD, he would also be excluded from further diagnostic workup. But if we stratified the patient based on clinical assessment, we should do a non-invasive functional imaging test or CT coronary angiography, which have better sensitivity and specificity in relation to the specificity of 85-90% and sensitivity of 45-50% of the stress ECG test[21,22]. In the case of our particular patient, this would mean referring the patient to a stress cardiocardiography test or stress-rest myocardial perfusion scintigraphy. Would further treatment have a different course? Due to the higher sensitivity, functional imaging would reveal a significant coronary disease and the patient would be referred to ICA. Earlier publications indicate high sensitivity of both stress ECG test and myocardial perfusion imaging in patients with angiographically verified left main stenosis above 50%. In a study of 57 patients with left main stenosis who underwent a stress ECG test according to the Bruce protocol, only 4% of the tests were negative and 9% were non-conclusive. In 91% of patients, the test was stoped before reaching the level IV, the achieved HR was 76 +/- 2% predicted and achieved double product of 20490 +/- 830. Our patient had significantly better test scores compared to the results of this cohort, which calls into question the clinical significance of the putative initially stable atherosclerotic plaque. What distinguishes the patients in this series from ours is the degree of anatomical prevalence of CAD: only 2% had left main lesion as the only one, 32% two vessel and 61% three vessel disease[23]. In a study of 101 patients with angiographically significant left main stenosis without previous infarction or myocardial revascularization who underwent SPECT myocardial perfusion imaging in 13% visually and 15% quantitatively there were no significant perfusion defects larger than 5% of the left ventricular myocardium. 56% of patients visually and 59% by quantitative analysis of scans had a high-risk scan (perfusion defect over 10% of left ventricular myocardium). By including nonperfusion variables, primarily transient ischemic dilatation of the left ventricle, it was obtained that 83% of patients with angiographically significant left main stenosis had a high-risk scan. This method, in the conclusion of the researchers, identifies most patients with angiographi-

cally significant stenosis of the left main coronary artery as high-risk[24]. This method could therefore be of great importance in assessing the functional significance of patients with a potential lesion of the left main coronary artery, especially in patients whose ECG stress test is undiagnostic: resting ECG changes or poor functional capacity of patients. Acute coronary syndrome with dramatically difficult clinical presentation in our patient probably occurred in the field of destabilization of previously angiographically insignificant atherosclerotic plaque. Reviews of patients with a similar clinical scenario have been published - a patient with a negative ECG stress test and achieved functional capacity of 12.1 MET is presented two months after the test as anterior STEMI and two-vessel CAD with occlusion of the proximal LAD[25]. It has been shown that the long-term prognosis of patients with angiographically nonsignificant stenosis of the left main coronary artery is worse than patients with normal findings based on the CONFIRM register of 5166 patients, 18% of whom had insignificant left main disease (diameter stenosis below 50%). Multivariate analysis concluded that nonsignificant left main stenosis was a predictor of cumulative adverse events (death, myocardial infarction, and revascularization) over a 5-year follow-up period in women (HR 1.78, $p<0.005$) but not in men (0.98, $p=0.806$)[26].

## Conclusion

The diagnostic algorithm for patients with chest pain is based on a pretest probability that determines further diagnostic workup. Patients with a negative exercise test and a typical clinical presentation should be referred for further diagnostic imaging test because of the risk that a small number of them may .have significant and even critical coronary stnosis.

## References


1. Ruigómez A., Rodríguez LA., Wallander MA, et al. Chest pain in general practice: incidence, comorbidity and mortality. Fam Pract 2006;23(2):167-74.
2. Rauf A, Denny SJ, Pierres F, et al. Diagnostic yield of invasive coronary angiography in a UK district general hospital. Eur Heart J 2017;38 (suppl 1): ehx501, P897.
3. DeFrances CJ, Lucas CA, Buie VC, et al. 2006 national hospital discharge survey. Natl Health Stat Report 2008:1-20.
4. Patel MR, Peterson ED, Dai D. et al. Low diagnostic yield of elective coronary angiography. N Engl J Med 2010;362:886-95.
5. 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.
6. Genders TS, Steyerberg EW, Alkadhi H, et al. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. Eur Heart J 2011;32(11):1316-30.
7. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013; 34(38):2949-3003.
8. Myers J, Prakash M, Froelicher V, et al. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002;346(11):793-801.
9. Roger VL, Jacobsen SJ, Pellikka PA. et al. Prognostic value of treadmill exercise testing: a population-based study in Olmsted County, Minnesota. Circulation 1998;98(25):2836-41.
10. Miller TD. Exercise treadmill test: estimating cardiovascular prognosis. Cleve Clin J Med 2008;75(6): 424-430.
11. Miller TD. Stress testing: the case for the standard treadmill test. Curr Opin Cardiol 2011;26(5):363-369.
12. DeFina LF, Haskell WL, Willis BL, et al. Physical activity versus cardiorespiratory fitness: two (partly) distinct components of cardiovascular health? Prog Cardiovasc Dis 2015;57(4): 324-329.
13. Hagnäs MJ, Kurl S, Rauramaa R, et al. The value of cardiorespiratory fitness and exercise-induced ST segment depression in predicting death from coronary heart disease. Int J Cardio. 2015; 196:31-33.
14. Laukkanen JA, Mäkikallio TH, Rauramaa R, et al. Cardiorespiratory fitness is related to the risk of sudden cardiac death: a population-based follow-up study. J Am Coll Cardiol 2010; 56(18):1476-83.
15. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA 2009;301(19): 2024-35.
16. Lauer MS, Okin PM, Larson MG. et al. Impaired heart rate response to graded exercise. Prognostic implications of chronotropic incompetence in the Framingham heart study. Circulation 1996;93(8):1520-6.
17. Mark DB, Hlatky MA, Harrell FE Jr, et al. Exercise treadmill score for predicting prognosis in coronary artery disease. Ann Intern Med 1987;106(6):793-800.
18. Sharma K., Kohli P, Gulati M. An update on exercise stress testing. Curr Problem Cardiol 2012; 37(5):177–202.
19. Knuuti J, Wijns W, Saraste A, et al. ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). Eur Heart J. 2020;41(3):407-77.
20. Juarez-Orozco LE, Saraste A, Capodanno D, et al. Impact of a decreasing pre-test probability on the performance of diagnostic tests for coronary artery disease. Eur Heart J Cardiovasc Imaging 2019;20(11):1198-207.
21. Dennis C, Shabetai R, Do D, Froning J. The electrocardiographic exercise test in a population with reduced workup bias: diagnostic performance, computerized interpretation, and multivariable prediction. Veterans Affairs Cooperative Study in Health Services #016 (QUEXTA) Study Group. Quantitative Exercise Testing and Angiography. Ann Intern Med 1998;128(12 Pt 1):965-74.
22. Morise AP, Diamond GA. Comparison of the sensitivity and specificity of exercise electrocardiography in biased and unbiased populations of men and women, Am Heart J 1995,130(4): 741-747.
23. Salem B, Terasawa M, Virendra S, et al. Exercise testing and left main coronary artery disease: experience with 57 patients. Cardiovasc Dis 1978;5(4):384–90.
24. Berman DS, Kang X, Slomka PJ, et al. Underestimation of extent of ischemia by gated SPECT myocardial perfusion imaging in patients with left main coronary artery disease. J Nucl Cardiol 2007;14(4):521-8.
25. Hassan AM. Negative exercise stress test. Does it mean anything? Libyan J Med 2007; 2(2):103–5.
26. Xie JX, Eshtehardi P, Varghese T, et al. Prognostic Significance of Nonobstructive Left Main Coronary Artery Disease in Women Versus Men: Long-Term Outcomes From the CONFIRM (Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter) Registry. Circ Cardiovasc Imaging 2017; 10(8):e006246.

## Sažetak

### *Akutni koronarni sindrom udružen sa okluzijom glavnog stabla leve koronarne arterije kod bolesnika sa prethodno negativnim nalazom stres elektrokardiografskog testa*

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***Cilj rada.*** *Prikaz slučaja bolesnika sa akutnim koronarnim sindromom sa okluzijom glavnog stabla leve koronarne arterije sa tipičnom kliničkom slikom i negativnim nalazom testa fizičkog opterećenja.*

***Prikaz slučaja.*** *Pacijent starosti 44 godine prezentuje se našoj službi kao STEMI sa ST segment elevacijom u inferiornim i ST depresijom u prekordijalnim odvodima. Nakon intrahospitalnog srčanog zastoja i sprovedene reanimacije uradi se primarna PCI glavnog stabla leve koronarne arterije nakon čega dolazi do hemodinamske stabilizacije. Retrospektivnom analizom u medicinsku dokumentaciju saznaje se da je tri godine pre akutnog događaja evaluiran zbog povremenih bolova u grudima. Pretest verovatnoća za KB iznosila je 38% pa je u skladu sa tada važećim ESC smernicama za stabilnu koronarnu bolest urađen stres EKG test koji je ocenjen kao negativan za značajnu koronarnu bolest. Svi analizirani parametri testa ukazivali su na nizak rizik od neželjenih kardiovaskularnih događaja: funkcionalni kapacitet, ST segment denivelacija, hronotropna kompetentnost, varijacije krvnog pritiska, Duke treadmill skor. Sa postest verovatnoćom od 9% pacijent nije dalje evaluiran u pravcu koronarne bolesti i naredne tri godine je bio asimptomatski i nije se javljao na kontrolne preglede. Da se prezentovao nakon 2019. godine po novijim ESC smernicama za hronične koronarne sindrome kod pacijenta bi u trenutku incijalne kliničke evaluacije bilo indikovano uraditi funkcionalni imaging test ili CT koronarnu angiografiju.*

***Zaključak*** *Dijagnostički algoritam za pacijente sa bolom u grudima baziran je na pretest verovatnoći koja opredeljuje dalji dijagnostički tok. Pacijente sa negativnim testom fizičkog opterećenja a tipičnom kliničkom prezentacijom trebalo bi uputiti na dalju dijagnostičku imaging obradu zbog rizika da mali broj njih može imati i značajnu i čak kritičnu koronarnu bolest.*

*Ključne reči: pretest verovatnoća, koronarna bolest, EKG stres test, neželjeni kardiovaskularni događaji*