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Case report

How should we obtain a precise estimate of cardiovascular risk in asymptomatic adults?

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Abstract **Background.** A precise estimate of cardiovascular (CV) risk in asymptomatic individuals is a key factor in the primary prevention of CV disease.
Case report. In this report describe an asymptomatic individual presenting for CV status assessment. After the CV risk assessment using the SCORE risk charts and Framingham score, additional tests were performed, which provided better insight and reclassification of risk in this individual. Carotid Doppler sonography revealed plaques in the carotid arteries. Non-invasive assessment of coronary flow reserve (stress echocardiography test) demonstrated that a considerable area of the left ventricle is suffering ischemia when stressed. This was an indication for coronarography, which showed severe three-vessel coronary disease, that was later successfully treated by surgical revascularization. A year after the surgery a control stress echocardiography was performed, showing a satisfactory coronary flow reserve.
Conclusion. A precise estimate of CV risk in asymptomatic individuals opens the road leading to early diagnosis, adequate therapy, and prevention of CV disease.

Kew words cardiovascular risk, prevention cardiovascular disease, carotid disease

Background

Discovery of the atherosclerotic disease in its early stages is essential in preventive cardiology. The guidelines for the prevention of cardiovascular (CV) diseases of the European and American associations of cardiology stress out the importance of CV risk assessment. The charts from which CV risk can be calculated are based on a mathematical model containing modifiable risk factors. The European Society of Cardiology has developed the SCORE (Systematic Coronary Risk Estimation)[1] system, which utilizes charts containing the variables of age, gender, smoking, systolic blood pressure value and total serum cholesterol value. The result obtained from these charts determines the total CV risk, *i.e*. the risk of dying from CV disease in the next ten years for persons aged 40-65 years. These charts are specifically adjusted for countries with low and those with high CV risk. According to the American guidelines for CV disease prevention[2], the risk is estimated based on the Framingham score[2,3]. Using the most recent version, a ten-year risk of CV event can be calculated for persons aged 30-75 years. The variables included in this score are gender, age, total serum cholesterol value, HDL-cholesterol, systolic blood pressure values, smoking habits, diabetes mellitus and hypertension treatment. In recent years, however, both guidelines suggest the need for additional methods for CV risk reclassification, and especially so in individuals for which low or intermediate risk scores are obtained initially. According to these guidelines, and also the most recent lipid guidelines, the most important is calcium score (coronary artery calcium - CAC - which is determined using the electron beam or multislice CT imaging) and the detection of carotid atherosclerotic plaques by carotid artery scanning[1,2]. Further below, we will describe how one of these methods proved valuable in the detection of severe atherosclerotic disease of the carotid arteries in an asymptomatic individual.

Case presentation

A male patient, 65 years old, presented for an examination in order to assess one's health because of the forthcoming business engagements. He denied having any heart-related symptoms and stated that he had been healthy; except for occasional propranolol, he did not take any heart medications. Regarding other modifiable risk factors, he stated that he had had elevated blood lipids but he had not taken any cholesterol-lowering medications. He was not a smoker, and his blood pressure was normal before that presentation. His office blood pressure measured at that first examination was 110/65 on the left, and 105/63 on his right arm, with heart frequency (HF) of 78/min. On auscultation, a regular heart rhythm was heard, without any additional tones and without noises at auscultatory points. A systolic ejection-type noise was heard in the carotid on the right. Electrocardiography demonstrated sinus rhythm, pathological left heart axis, and corrected QT interval was 423 ms (Fig. 1). According to the SCORE chart for European countries with high CV risk, the total CV risk was 7% (SCORE table

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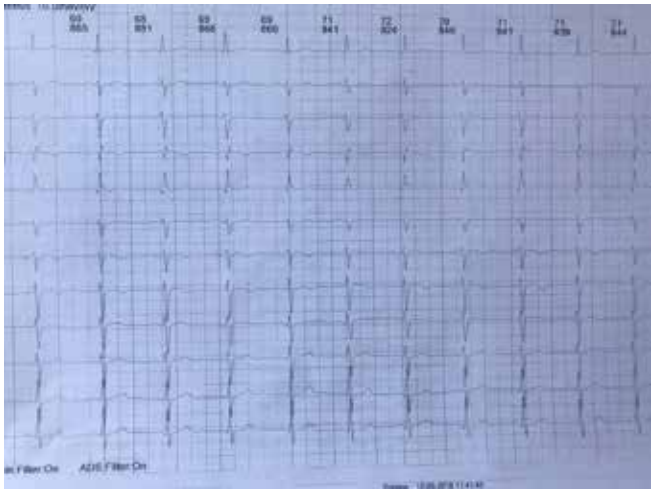

Figure 1. Electrocardiogram at the patient's first presentation - 12.05.2018

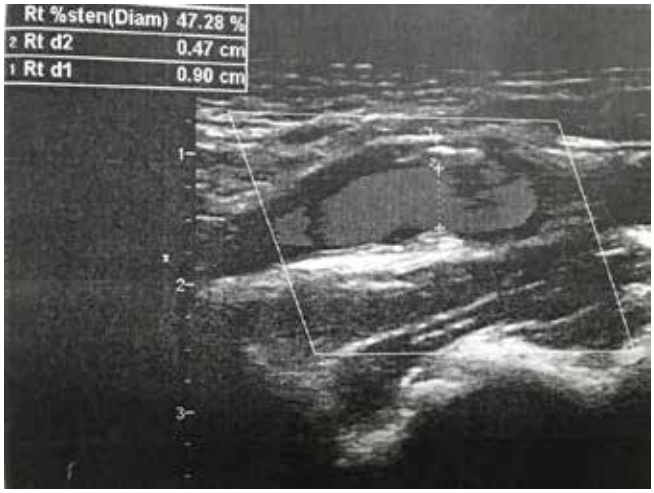

Figure 3. Doppler ultrasound of the carotids - first presentation of the patient

in Fig. 2). Such a value of CV risk categorized this patient into the group with high risk for CV death, mostly due to high cholesterol levels (total cholesterol: 6.95 mmol/l and LDL cholesterol: 4.76 mmol/l) and age (65 years), and his condition required a significant lifestyle modification and medicamentous therapy. According to the European prevention guidelines and the most recent lipid management guidelines (from 2019), a healthy lifestyle and healthy diet were recommended, together with a lipid-lowering drug, rosuvastatin (20 mg a day).

In order to improve the accuracy of risk estimation, we abided by the recommendations for risk reclassification and better CV risk consideration; these were socio-economical status (satisfactory), family history of CV diseases (negative), BMI (25.7 kg/m^2 - at the cut-off between normal and overweight), Doppler of the carotid arteries (sclerotic walls with edge plaques, mixed - predominantly fibrolipomatous with punctiform and dash calcifications (*dot-and-dash*), predominantly in the bulbs and the origins of internal carotid artery (ICA), causing segmental stenosis on the right below 46% and left below 36% (Fig. 3). The ankle-brachial index (ABI) was normal.

The finding of plaques in the carotid arteries of our patient demanded a reclassification of his status into a very

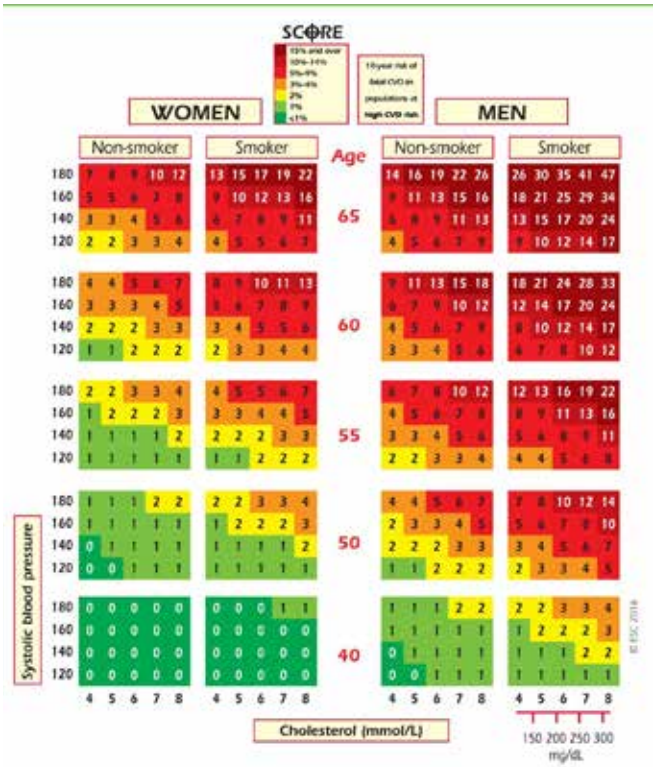

Figure 2. Cardiovascular risk estimated according to the SCORE chart - first presentation

high-risk individual, requiring additional diagnostic examinations directed towards the identification of coronary disease. The method selected was stress echocardiography, a highly specific and sensitive test to detect coronary disease.

Echocardiography demonstrated that the left ventricle had normal dimensions, normal wall thickness, and preserved regional and global contractile function. Transmitral flow suggested disturbed diastolic relaxation and mitral regurgitation in trace amounts. Mild to moderate (2+) aortic regurgitation was found. The left ventricle was at the normal cut-off. Right heart cavities had normal dimensions and functions. The pericardium had increased signal intensity, without any effusion.

Stress echocardiography was performed on a horizontal ergometer cycle (CardiowiseXrcise), with echocardiographic monitoring. At the maximum reached heartbeat of 151/min and maximum blood pressure of 165/90 mmHg, although there were no subjective complaints except for moderate fatigue, and ST segment depression of -3.32 mm was seen in the V5 lead, -2.37 mm in the V6 lead, and ST elevation in the aVR (Fig. 4). Echocardiographic monitoring, at 45° and under maximal stress, revealed worse kinetics in the basal-medial portion of the lateral wall and basal portion of the inferior wall. This test demonstrated the signs of myocardial ischemia in the inferolateral wall. After the test, the patient was referred for invasive coronarographic testing, which demonstrated three-vessel coronary disease (the main stem stenosed by 60% distally; LAD diffusely changed by 80% in the proximal segment; LCX stenosed ostially by 90%, and distally by 70-80%; RCA stenosed in the medial third by 60%; RCA was the dominant artery). Surgical revascularization of the myocardium was performed on November

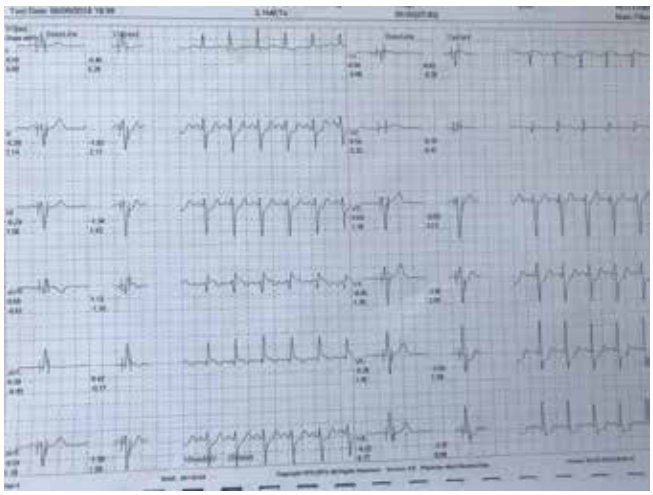

Figure 4. Electrocardiogram at stress echocardiography (physical exercise stress) - 06.09.2018

15, 2018 at the Institute for Cardiovascular Diseases "Dedinje", using the triple aortocoronary bypass approach (RIA - *a. mammariainterna sin.*, OM1 - graft autovenosum, ACDx-PD - graft autovenosum). After the heart surgery, cardiovascular rehabilitation was performed, and a year after the surgery control stress echocardiography testing was done again, which was negative for ischemia at the heart rate of 135/min and BP of 185/90 mmHg.

Discussion

CV risk estimation is one of the key aspects of CV disease prevention. The fundamental idea of the risk estimation is to detect in the simplest way the individuals exposed to high CV risk in order to reduce morbidity and mortality rates that follow CV diseases. This especially relates to asymptomatic individuals who do not have any significant heart-related complaints, but who have numerous modifiable risk factors that can accelerate the process of atherosclerosis and ultimately lead to premature CV events. The European SCORE charts and American Framingham score are the most well-known tools used in CV risk estimation[1,2]. However, although these are widely used and undoubtedly useful, they have shortcomings and limitations. In the European SCORE, the main problem is years of age, which may underestimate the total CV risk in younger patients. That is the reason why relative CV risk charts have been introduced. Another way to improve the accuracy of risk estimation is to perform some additional tests, as soon as possible, after the initial classification into four categories (low, intermediate, high and very high risk) that may reclassify the patient into a higher CV risk category. Thus, the prevention and therapeutic measures could commence as early and as aggressively as possible. These reclassification data or methods are socioeconomic status, family history of CV diseases, BMI or central obesity, coronary artery calcium (CAC) score (determined by way of electron-beam or multislice CT), detection of atherosclerotic plaques in the carotid arteries, and ankle-brachial blood pressure ratio (ankle-brachial index, ABI)[1,2,4].

In our patient, the findings of Doppler ultrasound in the carotids was shown to be essential for the use of other

Figure 5. Coronarography finding of the patient – 21. 09. 2018

sensitive and specific methods in CV disease detection, but also for the initiation of intense statin therapy. Population studies have shown a correlation between the severity of atherosclerosis in one artery and the degree of involvement of other arteries[5]. There are two key information that can be obtained by Doppler ultrasound of the carotid arteries: intima-media thickness (IMT) and the presence of the plaque(s). The upper cut-off value for IMT is at present 0.9 mm. The risk of brain stroke and coronary events is related to IMT, but the relationship is not linear. The lack of standardization as to the definition and measurement of IMT, its considerable variability and low intra-individual reproducibility have been limiting the significance of IMT for the time being. A recent meta-analysis has failed to demonstrate any additional value of IMT compared to the Framingham risk score in the prediction of future CV disease, even in intermediate-risk groups[6]. The plaque is usually defined as the presence of a thickening in the artery core at least by 50% larger than the adjacent arterial wall, or as an injury region (IMT ≥ 1.5 mm) bulging into the arterial lumen[7]. Plaques can be characterized by their number, size, irregularity and echodensity (echolucent vs calcified). Plaques are associated with coronary and cerebrovascular events, and echolucent plaques (in contrast to calcified ones) increase the ischemic cerebrovascular event[8]. Numerous studies have stressed that plaque quality assessment (including the surface and thickness of the plaque, instead of IMT measurement) is more valuable in the prediction of CV events[1]. In our patient, IMT in a standard measurement position was 1.2 mm in the common carotid artery, and his plaques were fibrocalcified, leading to 47% stenosis. Such findings required further diagnostic procedures.

Functional non-invasive tests for the diagnosis of ob-

structive CAD are designed to detect myocardial ischemia through ECG changes, wall motion abnormalities by stress CMR perfusion or stress echocardiography[9]. We chose stress echocardiography as a visual method and were able to demonstrate significant wall motion abnormalities. Since five segments of the left ventricle had contractility changes, this definitely indicated that our patient was a high-risk one.

Coronarography confirmed the findings and high-risk patient status (the high-risk criteria were three-vessel disease with proximal stenosis, LM disease, or proximal anterior descending disease)[9]. Our patient fulfilled these criteria: the main stem stenosed distally by 60%; LAD in the proximal segment 80% diffusely changed; LCX ostially stenosed by 90%.

The next question would be how to treat this patient? The indications for revascularization in patients with stable angina or silent ischemia are left main disease with stenosis over 50%; proximal LAD stenosis over 50%; and a large area of ischemia (over 10% of the left ventricle. The decisions for revascularization by percutaneous coronary intervention or coronary artery bypass grafting (CABG) are based on clinical presentation (symptoms present or absent) and prior documentation of ischemia (present or absent).

The superiority of CABG over a strategy of initial medical therapy was established in a meta-analysis of seven RCT[6,8] more than two decades ago, demonstrating a survival benefit of CABG in patients with SCAD and left main (LM) or three-vessel disease, particularly when the proximal LAD coronary artery was involved, and has been confirmed in more recent studies[10].The coronarography finding and the estimation of functional ischemia led our heart team to decide in favor of CABG in our patient. The intervention was performed without any complications, followed by a specialized cardiovascular rehabilitation program. A year after, stress echocardiography demonstrated preserved coronary reserve.

Conclusions

An asymptomatic adult person does not always mean a healthy adult person. A patient was presented in whom a high CV risk was demonstrated already by using the CV risk estimation charts/scores. His further diagnostic management took place in accordance with the current guidelines, involving the methods for CV risk reclassification (in our case, Doppler ultrasound imaging of the carotid arteries). Identifying a patient with vascular disease and even a higher degree of risk, significant areas of ischemia were demonstrated by non-invasive functional testing - stress echocardiography. Coronarographic testing showed that the patient had a multivessel disease with severe three-vessel coronary disease, which was successfully treated by surgical revascularization.

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