

IMPORTANCE OF CLASSIC CARDIOVASCULAR RISK FACTORS AND INFLAMMATORY MARKERS IN ST-ELEVATION ACUTE MYOCARDIAL INFARCTION

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Abstract

Acute myocardial infarction represents one of the most frequent and serious pathologies in the field of cardiology and is associated with a very high mortality, especially in elderly patients with multiple comorbidities. The diagnosis of acute myocardial infarction is established by the presence of symptoms, ischemic changes on the electrocardiogram and the increase of biomarkers of myocardial necrosis.

We will extensively study the presence of classic cardiovascular risk factors and their importance in ST-elevation acute myocardial infarction. As a rule, patients who have suffered a myocardial infarction have one or more associated risk factors, these can be modifiable risk factors (hypertension, diabetes, dyslipidemia, obesity, smoking, alcohol, sedentary lifestyle, psychosocial factors) and unmodifiable risk (age, sex, heredity).

Inflammation plays a role in the initiation, progression and rupture of the atheroma plaque, under the action of stimuli such as smoking, hypertension or obesity. Endothelial cells are activated with the expression of adhesion molecules for leukocytes; this endothelial dysfunction has the following causes: increased LDL-cholesterol, free radicals released by smoking, high blood pressure, diabetes, genetic abnormalities, elevated homocysteine plasma concentrations and infections.

It is demonstrated that inflammation in the body in the presence of acute myocardial infarction STEMI leads to a worse prognosis and an increased risk of mortality in these patients. Patients without inflammatory syndrome showed a more favorable prognosis in both the short and long term.

Keywords: myocardial infarction, inflammatory markers, cholesterol.

Rezumat

Infarctul miocardic acut reprezintă una dintre cele mai frecvente și mai grave patologii din sfera cardiologiei și se asociază cu o mortalitate foarte ridicată, în special la pacienții vârstnici și cu multiple comorbidități. Diagnosticul de infarct miocardic acut se stabilește prin prezența simptomatologiei, a modificărilor ischemice survenite pe electrocardiogramă și a creșterii biomarkerilor de necroză miocardică.



INTERNAL MEDICINE

General Reviews

Vom studia pe larg prezența factorilor de risc cardiovascular clasici și importanța lor în infarctul miocardic acut cu supradenivelare de segment ST. De regulă, pacienții care au suferit un infarct miocardic prezintă unul sau mai mulți factori de risc asociați, aceștia pot fi factori de risc modificabili (hipertensiunea arterială, diabetul zaharat, dislipidemia, obezitatea, fumatul, alcoolul, sedentarismul, factorii psihosociali) și factori de risc nemodificabili (vârstă, sex, ereditatea).

Inflamația are rol în inițierea, progresia și ruptura plăcii de aterom, sub acțiunea stimulilor precum fumatul, hipertensiunea arterială sau obezitatea. Se produce activarea celulelor endoteliale cu exprimarea moleculelor de adeziune pentru leucocite; această disfuncție endotelială are ca și cauze următoarele: LDL-colesterol crescut, radicalii liberi care se eliberează prin fumat, hipertensiunea arterială, diabetul zaharat, anomaliile genetice, concentrații plasmatice crescute ale homocisteinei și infecții.

Este demonstrat faptul că inflamația din organism în prezența infarctului miocardic acut STEMI duce la un prognostic mai prost și la risc mai crescut de mortalitate la acești pacienți. Pacienții fără sindrom inflamator au prezentat un prognostic mai favorabil atât pe termen scurt, cât și pe termen lung.

Cuvinte cheie: infarct miocardic, markeri inflamatori, colesterol.

Establishing the diagnosis of acute myocardial infarction with ST segment elevation

Acute myocardial infarction reveals evidence of myocardial necrosis by increasing Troponin associated with a clinical and paraclinical picture suggestive of myocardial ischemia; the association of ST-segment elevation changes appearing on the EKG path indicates the presence of an acute myocardial infarction with ST-segment elevation.

The typical symptomatology for acute myocardial infarction includes anterior chest pain with a constrictive character, squeezing "like a claw" with radiation in the left shoulder, in the left upper limb on the ulnar border, up to the last 2 fingers, while atypical symptomatology occurs more frequently in diabetic, frail, or elderly patients and includes epigastric pain, or anterior chest pain radiating into mandible, in both arms.

Of all the serum biomarkers, the most specific for revealing myocardial necrosis are troponins

C and I (these are contractile proteins found only in cardiac myocytes). An elevated value being defined as exceeding the 99th percentile of the normal reference population. The serum level of these biomarkers increases 3-6 hours after the onset of an acute myocardial infarction and reaches a maximum value at 12-24 hours, then returns to normal in 5-14 days, but they are not necessarily well correlated with the extent of myocardial damage. The most useful has been shown to be serum creatine phosphokinase (CPK), especially the MB isoenzyme of creatine kinase. Both CPK and CK-MB rise 3-6 hours after an acute myocardial infarction, peak at 12-24 hours, and return to normal after 3 days. Myocardial necrosis enzymes can also be elevated in pericarditis, myocarditis, heart failure, skeletal muscle damage, acute and chronic renal failure, etc. In the first 24-48 hours, serial determinations of serum biomarkers will be performed.

The electrocardiogram is the most important investigation in a patient with suspected acute myocardial infarction and is performed within the first 10 minutes of the first medical contact, with dynamic repetition. ST-segment elevation must be present in at least two concordant leads ≥ 2.5 mm in men under 40 and ≥ 2 mm in men over 40, ≥ 1.5 mm in women in leads V2-V3 and ≥ 1 mm in the other leads, occurring in the absence of left ventricular hypertrophy or left bundle branch block. Right (V3R-V5R) and posterior (V7-V9) leads are performed in patients presenting with acute myocardial infarction STEMI in the lower territory.

Transthoracic echocardiography highlights contraction abnormalities in the ventricular walls, the appearance of parietal kinetic disorders (hypokinesia, akinesia, dyskinesia) that occur during myocardial necrosis. The presence of dyskinesia, akinesia or hypokinesia

in the presence of elevated troponin demonstrates the presence of acute myocardial infarction. Transthoracic ultrasound is useful in identifying complications and allows differential diagnosis. A normal echocardiography has a negative predictive value of over 95% in establishing the diagnosis of acute myocardial infarction STEMI.

Classic cardiovascular risk factors in acute myocardial infarction STEMI

In the sphere of acute myocardial infarction STEMI, there are non-modifiable risk factors (heredity, sex, age) and modifiable risk factors (obesity, diabetes, hypertension, dyslipidemia). In the following we will expose the modifiable risk factors that are present as patients who suffer an acute myocardial infarction.

Arterial hypertension is an increase in systolic and diastolic blood pressure $> 140/90$ mmHg. An inverse J-shaped correlation was found between DBP and 5-year mortality rate, even after controlling for cardiac medication use, in-hospital revascularization, and risk score, and no further benefit was observed when DBP was >90 mmHg.

Atherosclerosis is a progressive disease that affects both large and medium arteries and is characterized by the local accumulation of lipids (cholesterol) in the intima and cellular infiltrate in an extracellular matrix that causes the progressive narrowing of the arterial lumen.

Smoking is the most important risk factor related to the patient's lifestyle. Quitting smoking can prevent the occurrence of cardiovascular diseases in men as well as in women. The greater the number of cigarettes smoked and over a longer period of time, the greater the cardiovascular risk. Patients who smoke at least 20 cigarettes/day have a 2-3 times higher risk of developing heart disease,



INTERNAL MEDICINE

General Reviews

especially acute myocardial infarction. Long-term tobacco use has also been associated with sudden cardiac death, aortic aneurysm, stroke, and peripheral arteriopathy. After about 2-3 years of quitting smoking, the risk is similar to that of non-smokers.

Alcohol - Studies have shown that alcohol increases LDL-cholesterol by 10%. Chronic alcohol consumption can lead to neoplasms, liver damage, mental disorders, cardiomyopathies, arrhythmias, hypertension, stroke.

Obesity is one of the most important cardiovascular risk factors, which leads to the progression of atherosclerosis, insulin resistance and the onset of type 2 diabetes. In recent decades, the prevalence of obesity has increased dramatically, a person is considered overweight if he has an index body mass ≥ 25 kg/m² and obese at a body mass index ≥ 30 kg/m², it was found that the majority of the population is overweight or obese and there is an increase in morbidly obese patients with a body mass index ≥ 40 kg /m². Central obesity is the key element of the metabolic syndrome, which leads to a change in the lipid profile with a decrease in HDL-cholesterol and an increase in LDL-cholesterol and triglycerides, thus leading to the appearance and progression of atherosclerosis. Abdominal circumference reveals abdominal obesity if it is ≥ 102 cm in men and ≥ 88 cm in women.

Diabetes mellitus is a major cardiovascular risk factor. More than 60% of diabetic patients

will suffer from cardiovascular disease at some point compared to the non-diabetic population. Management of diabetic patients recommends lifestyle changes by adopting a healthy, preferably Mediterranean-style diet based on fruits and vegetables and at least 30 minutes of physical activity per day.

Inactivity it is defined as physical activity under 30 minutes per day, at least 3 days per week. Several risk factors for atherosclerosis are influenced by exercise: it lowers blood pressure, lowers triglycerides, increases HDL-cholesterol, improves insulin sensitivity, lowers glycosylated hemoglobin, lowers inflammation, and improves endothelial dysfunction.

Psychosocial factors comprise several external risk factors (work stress, financial problems, adverse events) and potential reactions to stress (exhaustion, depression, sleep difficulties, psychological stress). Patients with depression have a much higher risk of suffering from cardiovascular diseases, including the risk of acute myocardial infarction.

Heredity is demonstrated by the fact that there is an inherited component to atherosclerosis, cardiovascular risk factors include history of major cardiovascular events or sudden cardiovascular death in first-degree male relatives <55 years in men and <65 years in women.

Age represents a major, independent and uninfluenceable risk factor in the occurrence of

cardiovascular diseases, once aging occurs there is an increase in cardiovascular risk factors. A person's life expectancy depends on changing modifiable risk factors, and cardiovascular disease risk can be optimized by correcting or avoiding exposure to risk factors. The female sex is more prone to cardiovascular diseases over 65 years, while men are prone from the age of 55 onwards. Recently, it has been found that in Europe the main cause of death for women over 65 is cardiovascular disease.

Inflammatory markers present in acute myocardial infarction STEMI

Inflammation has a role in the initiation, progression and rupture of the atheroma plaque, under the action of stimuli such as smoking, arterial hypertension or obesity, where the activation of endothelial cells occurs with the expression of adhesion molecules for leukocytes; this endothelial dysfunction has the following causes: increased LDL-cholesterol, free radicals released by smoking, high blood pressure, diabetes, genetic abnormalities, increased homocysteine plasma concentrations and infections. In the following we will study the importance of inflammatory markers in the evolution and prognosis of acute myocardial infarction with ST segment elevation. The increase in inflammatory markers leads to an increased mortality both during hospitalization, but also 1 year after the acute event and to a risk of complications after myocardial infarction.

C- reactive protein (CRP) is the objective marker of inflammation, endothelial dysfunction and infections. Serum levels of C-reactive protein reflect increased production of interleukins and proinflammatory proteins that have prothrombotic properties. The direct relationship between serum levels of C-

reactive protein and the risk of cardiovascular events has been demonstrated. C-reactive protein is a risk factor independent of other lipid and non-lipid risk factors.

Leukocytes and neutrophils - WBC counts were determined in all patients, with 4,000–10,000 cells/ μ L considered normal. WBC counts were higher in patients diagnosed with STEMI than in the general population. Increased white blood cell count has been associated with increased risk of myocardial infarction. Cigarette smoking was strongly associated with a proportional increase in white blood cell count.

Neutrophils will release oxidants and proteases, they can express mediators capable of amplifying cell recruitment. Neutrophils are large rigid cells that adhere to the capillary endothelium preventing capillary reperfusion after coronary ischemia, the mechanism by which neutrophil entrapment in microvessels occurs is multifactorial. Neutrophils produce vasoconstriction and platelet aggregation, such as thromboxane B2 and LTB4.

Erythrocyte sedimentation rate (ESR) was analyzed for the effectiveness of erythrocyte sedimentation rate as a potential additional indicator for coronary heart disease, with the aim of enabling faster identification of patients with myocardial infarction so that they can be treated as quickly as possible. It is demonstrated that the erythrocyte sedimentation rate increases in patients with acute myocardial infarction. The determination of VSH is a non-specific test and is one of the oldest methods, the accelerated rate of sedimentation of red blood cells indicates the presence of inflammation in the body. Erythrocyte sedimentation rate is measured at 1 hour and 2 hours, normal values were considered to be <10 mm in the first hour and <20 mm in the second hour.



INTERNAL MEDICINE

General Reviews

Fibrinogen is the central protein of the coagulation system, human gelatinous and fibrous plaques are rich in fibrinogen and its degradation products such as: thrombin, fibrinogen and fibronectin, are involved in cell proliferation. Fibrinogen is also involved in the following mechanisms (platelet aggregation, endothelial cell damage and plasma viscosity), it has a central role in the formation of thrombus, and thrombosis is a major determinant of myocardial ischemia.

Pharmacological treatment of acute myocardial infarction with ST segment elevation

Fibrinolytic treatment has been shown to decrease mortality in the acute phase of acute STEMI and should be administered within the first 3 hours of pain onset. Several types of thrombolytics can be used: Alteplase, Reteplase, Streptokinase or Tenecteplase. This treatment has both relative contraindications (transient stroke in the last 6 months, oral anticoagulant therapy, pregnancy, first week postpartum, systolic blood pressure > 180 mmHg and/or diastolic > 110 mmHg, advanced liver diseases, infective endocarditis, active peptic ulcer, prolonged traumatic resuscitation), as well as absolute contraindications, these being (previous intracranial hemorrhage, stroke of unknown cause, ischemic stroke in the last 6 months, lesions of the central nervous system,

neoplasms, arteriovenous malformations, recent major trauma/surgery/ head injuries in the previous month, gastrointestinal bleeding in the last month, dysfunctions of the bleeding process, aortic dissection, non-compressible punctures in the last 24 hours). The evaluation of the effectiveness of thrombolysis will be performed clinically, biologically, electrocardiographically and sometimes by imaging or coronary angiography.

Antithrombotic therapy has the role of preventing the formation of new thrombi after thrombolysis, but also blocking the existing thrombi, this will be performed with fractionated heparin or unfractionated heparin or with direct anticoagulants in some cases.

Antiplatelet therapy - patients who have suffered an acute myocardial infarction STEMI will require the administration of double antiplatelet therapy for a period of at least one year. For a long time the combination of aspirin with clopidogrel was recommended, but in recent years ticagrelor and prasugrel have replaced clopidogrel. Some patients have developed resistance to clopidogrel, so it is only recommended in cases where the patient is intolerant to prasugrel or ticagrelor. In some cases, the third class of antiplatelet agents can be used, glycoprotein IIb/IIIa receptor inhibitors such as Abciximab, Tirofiban which are administered in intravenous or intracoronary bolus, then in continuous intravenous infusion.

Nitrates will initially be administered sublingually, being useful in relieving coronary spasm and for vasodilatation of the coronary arteries, later it will be possible to administer intravenous infusion with blood pressure and heart rate monitoring.

Beta-blocker medication will be administered intravenously in the acute phase of myocardial infarction with ST-segment elevation in patients who do not present contraindications, without heart failure, with systolic blood pressure > 120 mmHg, the most frequently used is Metoprolol intravenously because it has beneficial effects such as decreased myocardial oxygen consumption.

Lipid-lowering medication is essential to be administered from the first day, the objective being to reduce LDL-cholesterol below 70 mg/dl or to reduce it by 50% of the initial value, these have the role of stabilizing the atheroma plaque.

Angiotensin-converting enzyme inhibitors are administered from the first day a patient has suffered an acute ST-segment elevation myocardial infarction, with the role of increasing survival, reducing mortality, and preventing ventricular remodeling in patients with left ventricular dysfunction.

Coronary angiography is the invasive exploration of the coronary arteries, it should be performed as soon as possible in patients with acute myocardial infarction with ST-segment elevation. Percutaneous coronary angioplasty is a class I indication for cases of acute ST-segment elevation myocardial infarction, in cases where transfer to a cardiac catheterization laboratory can be made within 120 minutes at most. The rate of myocardial recovery is inversely proportional to the length of time to revascularization. The right radial approach is recommended and a device called a stent will be inserted into the lumen of the obstructed coronary artery, these stents can

be metallic or pharmacological containing an active substance (everolimus, sirolimus, paclitaxel) and have the role of reducing the rate of intrastent restenosis.

Conclusion

Acute myocardial infarction with ST segment elevation represents one of the main causes of mortality and morbidity in the whole cardiovascular pathology. This pathology continues to be frequent despite advanced treatments and it does not take long to surprise us with its complexity and severity.

Recent studies in patients with ST-elevation acute myocardial infarction demonstrate the particular importance of inflammatory markers that tend to increase and remain elevated in these patients. It is recommended to measure inflammatory markers at admission and at discharge to assess the prognosis of patients. It has been shown that patients with elevated levels of inflammatory markers at admission will have a worse prognosis than those with normal levels of these markers. Therefore, the association between inflammatory markers and cardiovascular risk factors leads to a high risk of complications of infarction, a poor prognosis and an increased risk of death.

In a large proportion, patients with acute myocardial infarction have at least one associated cardiovascular risk factor, the most frequent of which are essential hypertension, type 2 diabetes both insulin-requiring and non-insulin-requiring, mixed dyslipidemia, obesity and chronic smoking. As we note all the cardiovascular risk factors above are modifiable and can be kept under control.

In conclusion, acute myocardial infarction with ST segment elevation is one of the main cardiovascular pathologies with a high mortality, especially if it is not intervened in



INTERNAL MEDICINE

General Reviews

time. Patients who have suffered an acute event, such as myocardial infarction, will require lifelong drug treatment with antiplatelet agents and statin, as well as the adoption of a healthy lifestyle consisting of a vegetarian diet, moderate physical exercise and smoking cessation, if applicable.

References

1. Thygesen K, Alpert JS, Jaffe AS, et al. Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth Universal of Myocardial Infarction (2018). *J Am Coll Cardiol* 2018; pii: S0735-1097(18)36941-9.
2. Carmen Ginghină. *Mic tratat de cardiologie* 2017, Editura Academiei Române: 291-379.
3. Cunha PG, Boutouyrie P, Nilsson PM, et al. Early Vascular Ageing (EVA): Definitions and Clinical Applicability. *Curr Hypertens Rev.* 2017;13(1):8-15.
4. Ibanez B, James S, Agewall S, Antunes MJ, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39(2):119-177.
5. Mahmood SS, Levy D, Vasan RS, et al. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet* 2014;383:999-1008.
6. Damen JA, Hooft L, Schuit E, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. *BMJ* 2016;353:i2416.
7. Ginghină C. *Mic tratat de cardiologie*. București: Editura Academiei Române; 2017:175-187.
8. Williams B, Mancia G, Spiering W, et al. ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J.* 2018;39,3021-3104.
9. Mach F, Baigent C, Catapano A, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modifications to reduce cardiovascular risk. *Eur Heart J.* 2020;41,111-188.
10. Gaita D, Mosteoru S. Metabolically healthy versus unhealthy obesity and risk for diabetes vascular. *Endocrinology&Metabolism.* 2017;6(1):23-26.
11. Cosentino F, Grant PJ C, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes and cardiovascular disease developed in collaboration with EASD. *Eur Heart J.* 2020;41,255-323.
12. Mitchell S, Malanda B, ...Gaita D, et al. A Roadmap on the Prevention of Cardiovascular Disease Among People Living With Diabetes. *Global Heart.* 2019;14: 215-40.
13. Valgimigli M, Bueno H, Byrne RA, et al. 2017 ESC Focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2018;39(3):213-260.
14. Littnerova S, Kala P, Jarkovsky J. GRACE Score among Six Risk Scoring Systems (CADILLAC, PAMI, TIMI, Dynamic TIMI, Zwolle) Demonstrated the Best Predictive Value for Prediction of Long-Term Mortality in Patients with ST-Elevation Myocardial Infarctions. *PLoS One.* 2015 Apr 20;10(4):e0123215.