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Case report

Optimal medical therapy in a patient with a large area of ischemia

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Abstract **Background.** Although percutaneous coronary intervention (PCI) is the gold standard in the treatment of acute myocardial infarction with ST elevation, its role in the treatment of patients with chronic coronary syndrome versus optimal medicament therapy (OMT) is not clearly defined.
Case report. We present a diabetic patient with typical chest pain and large area of ischemia on stress echocardiography and at high risk of adverse cardiac events who was on intensive OMT for 5 years with good control of the symptoms and without adverse cardiac events.
Conclusion. Despite the advances in the invasive treatment of chronic coronary syndrome, the intensive OMT has a key role in treatment of such patients.

Kew words chronic coronary syndrome, optimal medical therapy

Background

Although percutaneous coronary intervention (PCI) is the gold standard in the treatment of acute myocardial infarction with ST elevation, its role in the treatment of patients with chronic coronary syndrome in comparison to optimal medical therapy (OMT, which implies a lifestyle modifications and medication administration) is not clearly defined. No study has shown clearly an advantage of PCI over OMT in terms of reducing the incidence of cardiac death and non-fatal myocardial infarction (IM), although PCI has shown better symptom control in these patients (1-4). In the 2019 European Cardiac Society Guidelines for Chronic Coronary Syndrome, myocardial revascularization in addition to anatomic evaluation of stenosis by coronary angiography require also functional evaluation of stenosis (except for stenoses ≥90%), which can be achieved by invasive or non-invasive functional testing. Only then, in accordance with the comorbidities present, as well as the symptoms, a decision should be made on the further treatment of the patient (5).

Case presentation

We present a 61 year old female patient with typical chest pain who was referred to the cardiologist because of her symptoms. She had no previous cardiac events, no family history of cornary artery disease (CAD), was a non-smoker and she had diabetes type II for 20 years (treated with oral antidiabetic therapy - OAD), hypertension for 27 years and elevated levels of LDL cholesterol, BMI was 28.58 kg/m^2. She was prescribed a following therapy: Acetyl-salicylic acid 1 x 100 mg, Nebivolol 1 x 5mg, Valsartan 1 x 160 mg, Valsartan/Hydrochlorothiazide 1x 160/25mg, Isosorbide mono-nitrate 20 mg + 20 mg +0, Rosuvastatin 1 x 10 mg and previous OAD therapy (Metformin and Gliclazide). Baseline ESC was recorded (Picture 1.) with normal sinus rhythm, resting heart rate of 82 beat /min and ST depression of 0.5mm i the leads D2 and biphasic T in AVL.
Patient was referred to the echocardiography and stress echocardiography. The echocardiography showed normal dimension of left ventricle (EDV 51mm, ESV 33mm), borderline thickness of interventricular septum and posterior wall (11mm), preserved global systolic function (EF 67%), without segmental wall motion abnormalities and with preserved diastolic function. The stress echocardiography (SEHO) test on treadmill was performed according to the Bruce protocol and stopped at the third minute of first stage because of ischemic ECG changes and chest pain after achieving target heart rate. During the test and recovery period ST depression of 1mm in the leads D2, D3, aVF and V4-V6 and elevation of ST segment in the lead aVR were recorded (Picture 2.).
Echocardiography has shown worsening of the wall motion of medial and distal segment of inferior septum, distal segment of anterior septum and whole posterior and inferior wall (Picture 3.). Duke score was -6, MET 5 and heart rate recovery 23 beats/min. Based on the results of the test patient was advised to perform the coronary angiography but she refused, and decide to stay on OMT.

Amlodipine 1x5mg, clopidogrel 1x75mg, trimetazdine 2x35mg were added to current therapy. Nebivolol was switched with high dose of Bisoprolol 5mg+0+2.5mg.

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Figure 1. Baseline ECG

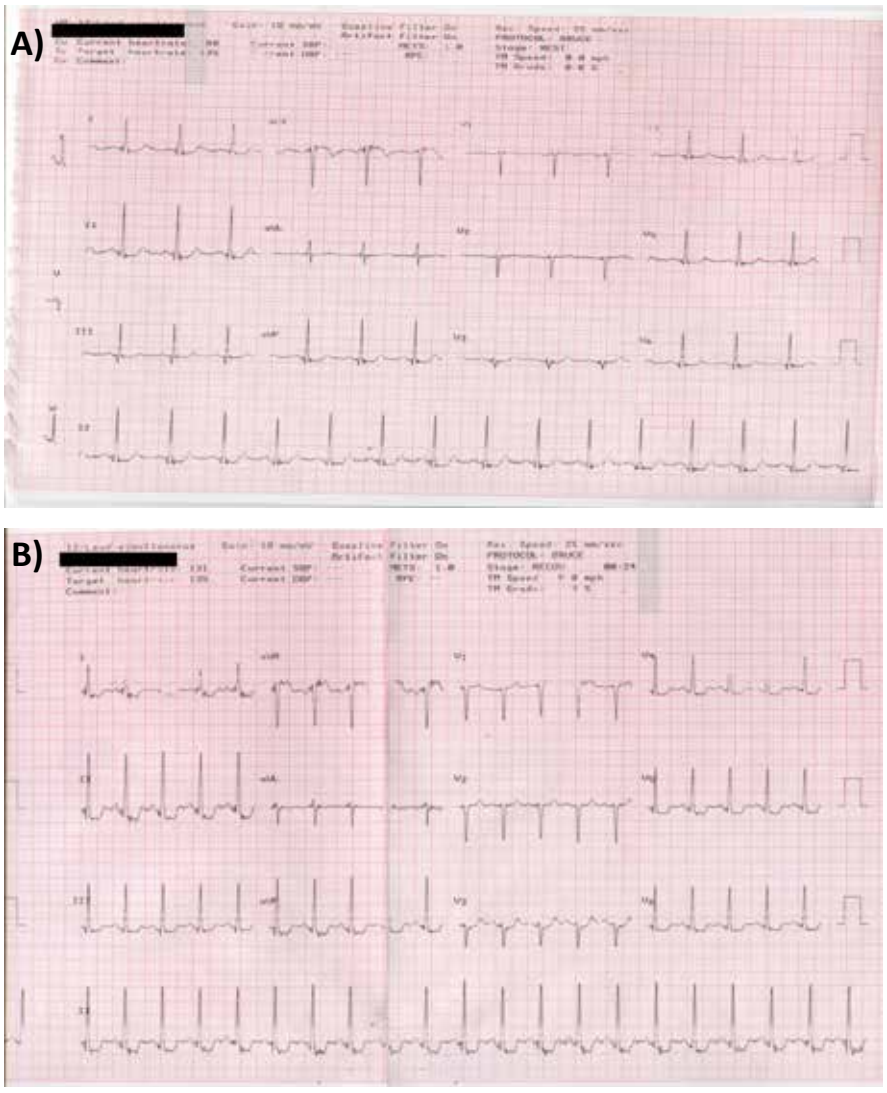

Figure 2. A) resting ECG during SEHO, B) ECG at maximum stress

The next patient visit was scheduled in 6 months. At follow up visit patient stated that she feel much better, that her anginal episodes are rare, and that she endure the effort much better and without a chest pain. The blood sample was drawn and the results showed high level of LDL cholesterol of 3.1 mmol/L and high HbA1c of 9.8%. We increased the dosage of Rosuvastatin to 20mg and sent the patient to the endocrinologist who added the insulin in the therapy. On the next visit in 6 months patient is still satisfied with control of the symptoms and the LDL cholesterol was 1.8mmol/l and HbA1c 6.9%. Patient had regular controls every 6 months without worsening of the clinical status, no new ECG changes and without adverse cardiac events. Amlodipine was increased to 1x10mg. The pharmacological dobutamine stress test was performed four years after initial test, and showed the same ECG result, and at echocardiography wall motion abnormality of inferior and posterior wall was present.
Coronary angiography (13.01.2020.) showed LM without stenosis, stenosis of proximal LAD 70%, middle LAD 90-99%, ostial D1 70-90%, proximal Cx 70-90%, proximal OM1 70-90%, proximal RCA 90-99%, middle RCA 100%. Patient was referred to the CABG operation.

Discussion

We presented a female patient with a high risk of adverse cardiac events, with significant comorbidities and with a large area of ischemia on SEHO testing. According to the new ESC guidelines for chronic coronary syndrome, the patient has a high risk for adverse events and should be referred for myocardial revascularization, (5,6). However, due to the patient's refusal to undergo coronary angiography, she received OMT. After administration of the OMT, the patient felt better and had significantly less episodes of chest pain and better tolerated effort Her cholesterol levels and glycemia were in the range recommendend by Guidelines. Also her physical activities were according to perscription. During 4 years of follow up she has no adverse cardiac event. This is in line with the results of previous studies which showed that there

was no difference in the incidence of adverse cardiovascular events between PCI and OMT in patients with stable CAD. One of the larger randomized studies on this topic was a COURAGE (*Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation*) study (n = 2287) that included patients with a positive SEHO test (proven ischemia). Patients with (previous MI, PCI, or CABG) and without previously known CAD were included in the studt which compared PCI + OMT versus OMT alone .The primary endpoint, all-cause death or non-fatal MI, did not differ between the two groups during a mean follow-up of 4.6 years. However, in patients who were invasively treated, freedom from angina was significantly better up to 3 years of follow-up. In a substudy, patients with >10% ischaemia on stress myocardial perfusion scintigraphy had a higher rate of death or MI. More PCI + OMT patients exhibited significant ischaemia reduction (33 vs. 19%; P= 0.0004).[1]

COURAGE II study, a 15-year follow-up of 1,211 patients included in the original study, also showed the same result for survival in these two groups, (PCI +OMT vs OMT, HR 0.95: 95% CI 0,79 to 1.13, p = 0.53).[7]

These results were confirmed with the prospective, multicenter, randomized ISCHEMIA (*International Study of Comparative Health Effectiveness with Medical and Invasive Approaches)* study (n=5179 pts, follow-up period 3.3 years) whose first results were published in November 2019. Similar like the COURAGE study, this study included patients without and with (previous MI, PCI and/or CABG) previously known CAD. The main criteria for inclusion was moderate to severe ischemia on stress imaging testing (≥3 of 16 segments with stress-induced severe hypokinesia or akinesia) after which patients were referred to the blinded CTA to exclude LMCA disease. The trial hypothesis is that cardiac catheterization followed by complete revascularization (based on the functional and anatomical assessment of stenosis) plus OMT is superior to OMT alone, for patients with moderate-severe ischemia on stress imaging. This study also showed no significant difference in the endpoint (all-cause mortality, non-fatal MI, hospitalization for unstable angina, resuscitated cardiac arrest, or heart failure), between two treatments. Further more, routine invasive therapy was associated with harm at 6 months (increase in periprocedural myocardial infarctions) and with benefit at 4 years (reduction in spontaneous myocardial infarction). These results do not apply to patients with current/recent acute coronary syndrome, highly symptomatic patients, left main stenosis, or left ventricular ejection fraction <35%. The effect of the revascularization on the improvement of the symptoms (quality of life) is not yet published.[8]

De Bruyne B. and al. in their study, which compared the FFR-guided PCI + OMT vs OMT alone in patients with stable CAD (n=888) also showed that there was no difference between the groups regarding the overall rate of death and non-fatal MI (7.1% vs 8.6%, p=0.56 respectively). However in this study, the PCI group had significantly lower rate of urgent revascularization triggered by myocardial infarction or ischemic changes on electrocardiography (4.0% vs. 16.3%; hazard ratio, 0.23; 95% CI, 0.14 to 0.38; P<0.001) respectively) and had better improvement of symptoms at 2 year follow up.[3]

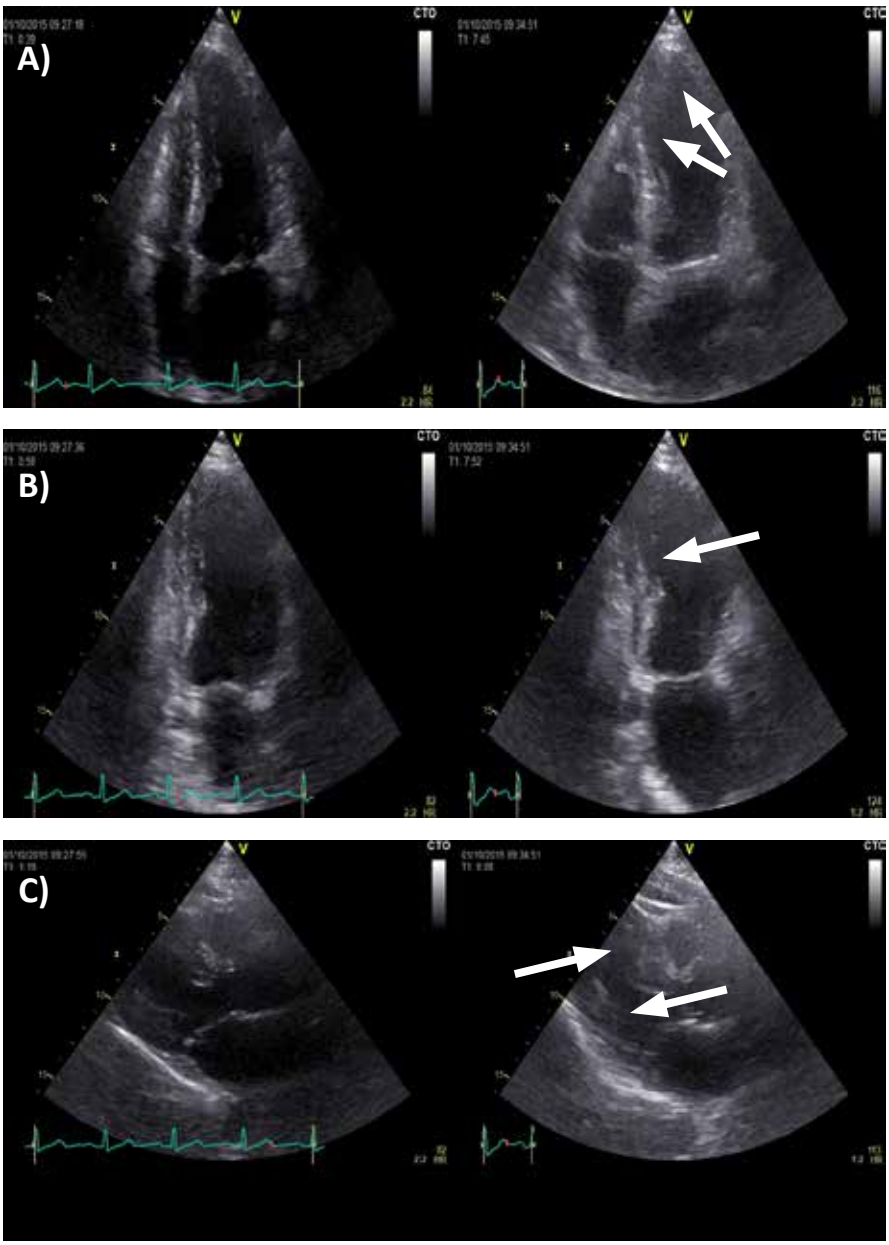

Figure 3. A) 4-chambers view at rest (left side) and on SECHO test (right side) B) 2-chambers view at rest (left side) and on SECHO test (right side) C) Parasternal long axis view at rest (left side) and on SECHO test (right side); arrows showing wall motion abnormalities

Conclusion

Our case report showed successful prevention of adverse cardiac events and improvement of symptoms in the patient with large area of inducible ischaemia and unfavorable risk profile with OMT and optimal risk factor control. This example confirms the existing guidelines on the management of chronic coronary syndrome provided only when intensive OMT is initiated and maintained. Nevertheless, clinical practice should be driven by the objective assessment of the patient's clinical status and in the case of clinical deterioration myocardial revascularization should be performed.

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Sažetak

Uvod. *Iako je perkutana koronarna intervencija (PKI) zlatni standard u lečenju akutnog infarkta miokarda sa ST elevacijom, njegova uloga u lečenju pacijenata sa hroničnim koronarnim sindromom u odnosu na optimalnu medikamentnu terapiju (OMT) nije jasno definisana.*

Prikaz slučaja. *Predtavljamo slučaj bolesnice sa dugogdišnjim dijabetesom, tipičnim anginoznim tegobama i velikom zonom ishemije na stres ehokardiografskom testu koja je u visokom riziku od nastanka neželjenih kardiovaskualrnih događaja. Bolesnica je 5 godina na inzentzivnoj OMT sa dobrom kontrolom simptoma i bez neželjenih događaja.*

Zaključak. *Uprkos napretku u invazivnom lečenju hroničnog koronarnog sindroma, intenzivna OMT ima ključnu ulogu u lečenju takvih pacijenata.*

Ključne reči: *hronični kronarni sindrom, optimalna medikamentna terapija*