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Case report

Effective therapeutic strategies for diabetic cardiomyopathy

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Abstract We present a case of 72-years old patients with long standing heart failure with reduced ejection fraction, diabates mellitus with chornic renal failure and previous CRT implantation, in whom inita-tion of new treatment with empaglifozine and sacubitril valsartin in addition to beta-blockers and diuretics significantly improved hic clinical condirion and laboratory status.

Kew words heart failure, diabates mellitus, empaglifozine, sacubitril valsartan

Introduction

Dysregulated glucose and lipid metabolism in diabetes mellitus typ 2 (T2DM) induce several pathophysiological pathways resulting in increased oxydative stress and activation of inflammatory pathways which lead to pathological cardiac remodeling, systolic and diastolic dysfunction in diabetic cardiomyopathy. We present a case with T2DM and heart failure with reduced ejection fraction (HFrEF).

Case presentation

The 72 year old male patient with long-lasting insulin-dependent T2DM, chronic kidney disease and heart failure with reduced ejection fraction (HFrEF) was admited to our hospital due to dyspnea and orthopnea exagereting in the last weeks. Implantable cardiac resynchronization therapy (CRT-D) was implanted in 2013, with no actiovation of ICD in the following years. Patient was on stable medical therapy with amiodaron, diuretics, beta blocker and insulin with no ACE inhibitor due to bad tolerated hypotension. Low dose of sodium-glucose cotransporter 2 inhibitor (SGLT2i) empagliflozin was started in 2019 by HbA1c of 13% and creatinine clearance ClCr 47.2ml/min. Now, at hospital readmission, patient had symptoms and signs of HF, NYHA class III, with low arterial blood pressure (100/60mmHg) and atrial fibrillation on ECG. Laboratory tests showed eleveted natriuretic peptides (NTproBNP) of 2019 pg/ml, reduced renal function by ClCr of 48ml/min, not regulated diabetes with HbA1c 9% and LDL 3.4mmol/l. Due to chronic amiodaron treatment, we checked thyroid function and found severe hypothyroidism: TSH 52 (RV 0.55-4.78 μIU/ml) and FT4 1.39 (RV 11.5-22.7pmol/L). Transthoracic echocardiography revealed left ventricular (LV) ejection fraction of 21%, measured from biplane

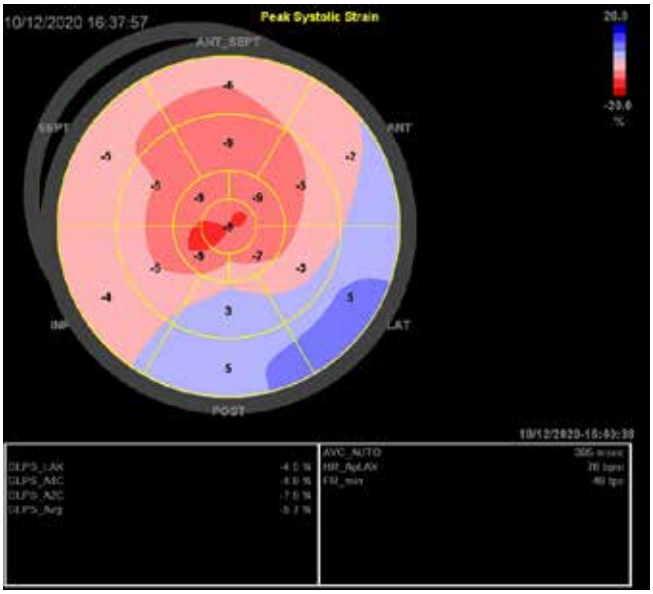

Figure 1. Two dimensional speckle tracking left ventricular global longitudinal strain (GLS)

images, with remodeling, left atrial enlargement and moderate mitral regurgitation. LV diastolic dysfunction was restrictive filling pattern, with the ratio (E/e') of the peak velocity of mitral inflow (E) and the average of septal and lateral mitral annular early diastolic peak velocities (e') of 14. Based on tricuspid regurgitation, pulmonary artery systolic pressure was estimated to 35mmHg. Left ventricular global longitudinal systolic strain (GLS) was severely reduced: -5.7%, with PSD 124ms. Invasive coronary angiography reveled absence of obstructive epicardial coronary disease. Medical therapy was recomended with thyroid hormone therapy, beta blocker, diuretics, rivaroxaban, insulin and empagliflozin. Three months later, patient feels better, NYHA class II/III, hormonal status was TSH 2.68μIU/ml, FT4 23.5pmol/L, NT-

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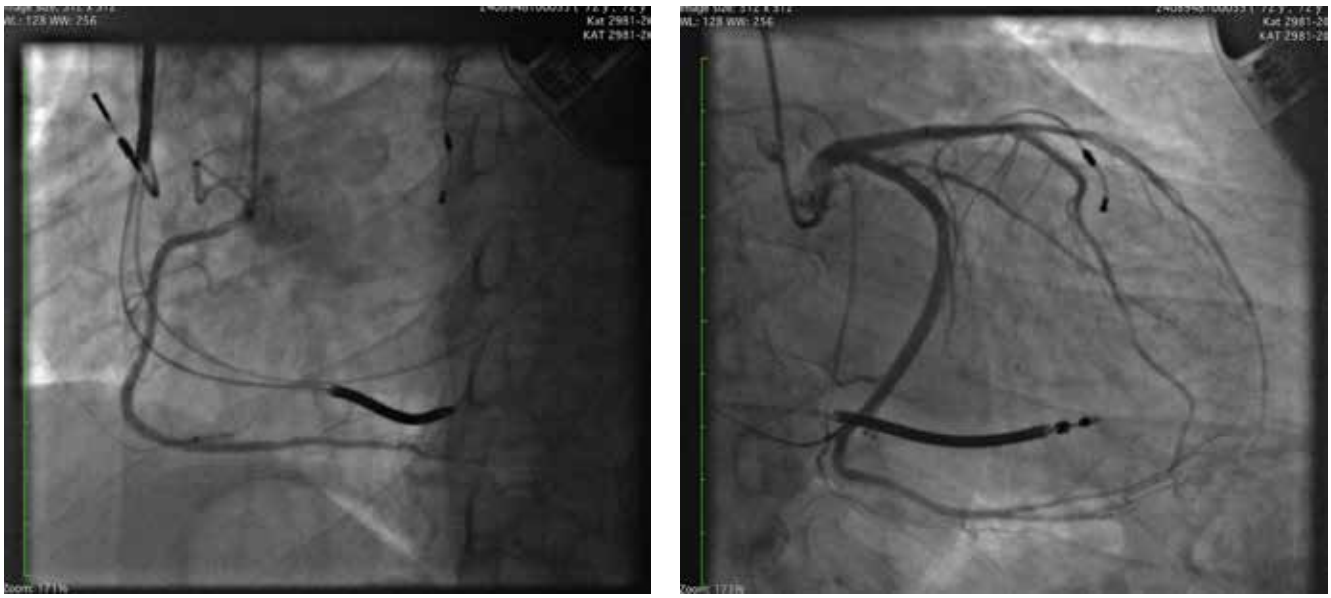

Figure 2. Selective coronarography

proBNP still very high 2946pg/ml and blood pressure was 110/70mmHg. We started sacubitril/valsartan 24/26mg, twice daily. Two months later patient is in NYHA class I/II, NTproBNP of 890 pg/ml, HbA1c 8% and ClCr of 54ml/min.

Discussion

The prevalence of diabetes in patients with heart failure is very high, 35-40%, and it is not in direct correlation with the degree of impairment in ejection fraction. Sacubitril/valsartan, as the first in the class of ARNis (angiotensin receptor neprilysin inhibitors) in the treatment of patients with chronic heart failure (HF) with reduced ejection fraction (HFrEF) is associated with improved outcomes compared with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, and has a greater beneficial effect on myocardial reverse remodelling. The landmark trial on the use of sacubitril/valsartan in HFrEF, the PARADIGM-HF, was stopped early due to clear clinical benefit of sacubitril/valsartan, with a significant reduction in the risk of cardiovascular death (including sudden cardiac death), and in HF hospitalisation with the good safety profile[1]. In the post-hoc analysis of patients with mostly type 2 diabetes and HFrEF from the PARADIGM-HF study, the treatment with sacubitril/valsartan was associated with greater reductions in HbA1c concentrations than treatment with enalapril[2,3]. Sacubitril/valsartan blocks both the renin-angiotensin system and inhibits neprilysin resulting in increase in natriuretic peptides concentration, insulin sensitivity and metabolism. Those are main potential mechanisms leading to improvement in glycaemic control.

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) reduce the risk of hospitalization for heart failure in patients regardless of the presence or absence of diabetes. There is growing evidence regarding the effects of these drugs on patients with a wide range of heart failure, including those with markedly reduced left ventricular ejection fraction (HFrEF). EMPA-REG OUTCOME (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients) is the first study to prove the efficacy of empagliflozin in reducing cardiovascular events as well as hospitalization for heart failure in diabetics, regardless of glycemic value[4]. This efficacy of empagliflozin is constant and independent of the degree of cardiovascular risk and previous history of heart failure[5]. The European Society of Cardiology (ESC) and the European Diabetes Association (EASD) 2019 Guidelines for the treatment of diabetes, prediabetes and cardiovascular disease recommend as Class I, level of evidence A, the use of SGLT2i empagliflozin in patients with type 2 diabetes mellitus with proven cardiovascular disease or at high or very high risk for cardiovascular disease with the aim of reducing cardiovascular events and the risk of hospitalization due to heart failure in diabetics[6].

It is still unknown whether ARNi/SGLT2i therapies in patients with HFrEF should be implemented simultaneously or sequentially[7,8].

In conclusion, there are growing evidence that combining ARNi, SGLT2i, MRA and β-blocker therapy will lead to a significantly better prognosis in HFrEF.

References

1. McMurray J, Packer M, Desai A, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014; 371:993–1004.
2. McMurray JJ, Gerstein HC, Holman RR, et al. Heart failure: a cardiovascular outcome in diabetes that can no longer be ignored. Lancet Diabetes Endocrinol 2014;2:843–51.
3. Seferovic JP, Claggett B, Seidelmann SB, et al. Effect of sacubitril/valsartan versus enalapril on glycaemic control in patients with heart failure and diabetes: a post-hoc analysis from the PARADIGM-HF trial. Lancet Diabetes Endocrinol 2017;5:333–40.
4. Zinman B, Wanner C, LachinJM et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117-2128.
5. Packer M, Anker SD, Butler J, et al; EMPEROR-Reduced Trial Investigators. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med 2020;383:1413–24.
6. Cosentino F, Grant P, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed

in collaboration with the EASD: The Task Force for diabetes, prediabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD) . Eur Heart J 2020;41 (2):255–323.
7. Vaduganathan M, Claggett BL, Jhund PS, et al. Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials. Lancet 2020;396:121–128.
8. Greene S, Butler J, Fonarow G. Simultaneous or rapid sequence initiation of quadruple medical therapy for heart failure-optimizing therapy with the need for speed. JAMA Cardiol. Published online March 31, 2021.

Sažetak

Efikasna strategija lečenja kod pacijenta sa dijabetesnom kardiomiopatijom

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Predstavljamo slučaj 72-godišnjeg pacijenta sa hroničnom srčanom slabošću sa smanjenom ejekcionom frakcijom, dijabaeesom, hroničnom bubrežnom slabošću i prethodno implantiranim CRT-om kod kojeg je došlo do značajnog poboljšanja kliničke slike i laboratorijskih nalaza posle iniciranja novee terpije sa empaglifozinom i posebno sakubitril valsartanom.

Ključne reči: srčana slabost, dijabetes melitus, empaglifozin, sakubitril valsartan