Folia Cardiologica 2022
vol. 17, no. 5, pages 303–306
DOI: 10.5603/FC.a2022.0044

ISSN 2353–7752
e-ISSN 2353–7760

Initiation of treatment with sacubitril/valsartan during outpatient cardiac rehabilitation program in an octogenarian with heart failure

Piotr Koprowicz[1], Jakub Włodarczyk[1], Małgorzata Kurpesa[2], Jarosław D. Kasprzak[2], Tomasz Rechciński[2]

[1]Student Research Society at the 1st Clinic of Cardiology of the Chair of Cardiology of the Medical University of Lodz, Łódź, Poland
[2]1st Clinic of Cardiology of the Chair of Cardiology of the Medical University of Lodz, Łódź, Poland

Abstract

We present the case of including sacubitril/valsartan in an octogenarian patient with congestive heart failure as a part of the outpatient cardiac rehabilitation program. The case shows that apart from hospital use, it is worth considering including this drug during an outpatient cardiac rehabilitation program, because in such conditions the patient is in frequent contact with the treatment center, so his health status may be assessed almost every day.

Key words: sacubitril, valsartan, ARNI, heart failure, cardiac rehabilitation

Folia Cardiologica 2022; 17, 5: 303–306

Introduction

Sacubitril/valsartan (Entresto™) is the only angiotensin receptor neprilysin inhibitor (ARNI) drug available. Sacubitril is a neprilysin inhibitor that increases the amount of natriuretic peptides in the body, resulting in, among other things:

- increased diuresis and urinary sodium excretion;
- blockade of renin and aldosterone release, reduction of sympathetic nervous system activity;
- vasodilatation, inhibition of pathological myocardial remodeling.

The second component, valsartan, dilates blood vessels and inhibits adverse signaling pathways (inflammation, fibrosis, apoptosis) by blocking the receptor for angiotensin II. To date, sacubitril/valsartan has been indicated for patients who tolerate angiotensin-converting enzyme inhibitor (ACEI)/angiotensin-receptor blocker (ARB) well, with a left ventricular ejection fraction ≤ 35% and present with symptoms of New York Heart Association (NYHA) class II–III severity, despite administration of ACEI/ARB and a beta-blocker as well as aldosterone antagonist at optimal doses. However, according to the latest recommendations of the American College of Cardiology (ACC) [1], it can be used from the beginning of the therapy as a first-line drug.

Case report

We present a case of an 86-year-old patient with chronic heart failure with reduced ejection fraction (HFrEF) in NYHA class II, after hospitalization for exacerbation of heart failure symptoms, admitted to a cardiac rehabilitation day center for rehabilitation. At discharge from the hospital, the patient was prescribed the following medications: acetylsalicylic acid 75 mg, atorvastatin 20 mg, perindopril 2.5 mg, pantoprazole 20 mg, bisoprolol 5 mg, eplerenone 25 mg, amiodarone 200 mg, trimethazine 35 mg, rivaroxaban 15 mg, and nitroglycerin 0.4 mg — for angina pain.

Address for correspondence: Piotr Koprowicz, Studenckie Koło Naukowe przy Klinice Kardiologii Katedry Kardiologii Uniwersytetu Medycznego w Łodzi, Wojewódzki Specjalistyczny Szpital im. dr. Wł. Biegańskiego, ul. Kniaziewicza 1/5, 91–347 Łódź, Poland, phone +48 42 251 62 16, e-mail: piotr.koprowicz@gmail.com

The patient had undergone (stated how many years before the inclusion of sacubitril/valsartan) non-ST-elevation myocardial infarction (NSTEMI) (8 years), coronary artery bypass grafting (8 years), cryoablation for atrial flutter (8 years), and developed post-amiodarone hypothyroidism after the inclusion of amiodarone — substitution of L-tyroxin 50 micrograms was started (1 year) [2]. Echocardiography performed on admission showed enlargement of the heart, segmental left ventricular wall motion abnormalities with an ejection fraction (EF) of 30% (Table 1). Based on the initial electrocardiographic stress test performed on a treadmill according to the Bruce protocol (Table 2), the patient was qualified for exercise rehabilitation in the form of:

- endurance and interval training on a cycle ergometer;
- breathing and general fitness exercises;
- upper and lower limb resistance exercises on a workout station, stepper and elliptical trainer;
- marching.

Table 1. Selected echocardiographic parameters before and after cardiac rehabilitation

Parameter	Before rehabilitation		After rehabilitation (01.2020)
Dimensions of heart chambers	Left ventricle [mm]	48/58	48/60
	Left atrium [mm]	52	52
	Aorta [mm]	40	40
	Right ventricle [mm]	32	32
	Interventricular septum [mm]	13/12	13/12
	Posterior wall [mm]	12/11	12/11
	Pulmonary trunk [mm]	25	25
	Mass index [g/m^2]	179	173
	Left ventricular muscle mass [g]	336	335
Mitral valve	Valvular stenosis, 5 mm vena contracta, no systolic pulmonary venous flow regurgitation		Valvular stenosis, 5 mm vena contracta, no systolic pulmonary venous flow regurgitation
	V_{max} [m/s]	1.1	1.1
	E/A	2.5	2.6
	E/E'	20	20
	Regurgitation	Trace	—
Aortic valve	Minor marginal valvular fibrosis without the restriction of mobility		Minor marginal valvular fibrosis without the restriction of mobility
	V_{max} [m/s]	1.2	1.2
	Regurgitation	Trace	Trace
Tricuspid valve	No organic lesions		No organic lesions
	V_{max} [m/s]	0.6	0.6
	Regurgitation	I	I
	sPAP [mm Hg]	35	35
Pulmonary valve	No organic lesions		No organic lesions
	V_{max} [m/s]	0.9	0.9
	Regurgitation	Trace	Trace
	AccT [ms]	74	74
	Diastolic function	Restrictive profile	Restrictive profile
Pericardium	Normal		Normal
Contractility	Akinesis of the posterior wall, inferior wall, 1/2 basal septum; hypokinesis of 1/2 apical lateral wall and septum		Akinesis of the posterior wall, inferior wall, 1/2 basal septum; hypokinesis of 1/2 apical lateral wall and septum
	Ejection fraction [%]	30	30
	TAPSE [mm]	14	14

AccT — acceleration time; sPAP — systolic pulmonary arterial pressure; TAPSE — tricuspid annulus peak systolic excursion

Table 2. Results of selected tests before and after cardiac rehabilitation

Parameter	Before rehabilitation	After rehabilitation
eGFR CKD-EPI [ml/min/1.73 m^2]	41.56	37.31
NT-proBNP [pg/ml]	4159	3314
Stress test		
Duration	3 min 53 s	5 min 36 s
Metabolic equivalent [METs]	6.7	7.0
Peak heart rate	108	103
Percentage of maximum heart rate	84	80
Reason for interruption	Fatigue — 13 according to Borg rating. Obtained heart rate limit	Fatigue — 12 according to Borg rating. Obtained heart rate limit
Changes in the analyzed leads	RBBB + LAH	RBBB + LAH
Retrosternal pain	Absent	Absent
Test result	Clinically negative	Clinically negative

CKD-EPI — Chronic Kidney Disease Epidemiology Collaboration; eGFR — estimated glomerular filtration rate; LAH — left anterior hemiblock; NT-proBNP — N-terminal pro-B-type natriuretic peptide; RBBB — right bundle branch block

Outpatient rehabilitation lasted for 2–4 hours a day Monday through Friday for 24 sessions. In addition, the patient participated in an educational program on risk factors for cardiovascular disease, classes with a psychologist on stress management, and relaxation therapy. During the rehabilitation program, a decision was made to optimize HFrEF treatment and after discontinuing perindopril, sacubitril/valsartan was implemented, and rehabilitation was continued. The entire rehabilitation cycle was completed without complications, and the final stress test (Table 2) showed improvement in physical performance indices. This was not the patient's first participation in a cardiac rehabilitation program — the improvement or lack of change in exercise capacity expressed by metabolic equivalent (MET) in subsequent years is shown in Figure 1. It is noteworthy that the patient's physical capacity decreased over the years, and the penultimate cycle of improvement treatment (2017) failed to improve physical capacity parameters. In contrast, it improved after the last rehabilitation, during which sacubitril/valsartan therapy was included.

Discussion

Sacubitril/valsartan is a drug that was included in 2016 by the European Society of Cardiology in its guidelines for the treatment of patients with heart failure and reduced ejection fraction. Since then, its use and efficacy have been documented through numerous randomized clinical trials [3, 4] that demonstrated that taking sacubitril/valsartan — compared to ACEI/ARB therapy of patients with reduced ejection fraction — was associated with a lower risk of death (12–20%) and patient hospitalization (14–16%). Moreover, studies [5] show a positive effect of ARNI on cardiac parameters — functional improvement as determined by NYHA scale and reduction of mitral regurgitation severity. Including sacubitril/valsartan significantly reduces N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, allows for lower doses of diuretics, and increases left ventricular ejection fraction.

However, the available literature lacks data showing the effect of ARNI on the effectiveness of cardiac rehabilitation. The case we discussed highlights the safety and efficacy of the drug in terms of improving physical performance. It is also noteworthy that positive treatment effects can be obtained in patients significantly older than the mean of patients included in the PARADIGM-HF study (63.8 ± 11.3 years) [6], which was the case in our report. According to the available data, a significant decrease in NT-proBNP was observed in this patient [5]. Analyzing the results of the similar PARAGON-HF trial also demonstrated the positive impact of ARNI therapy in patients with preserved ejection fraction and specific clinical profiles (ejection fraction < 57% and female gender) in whom evidence-based heart failure therapy is not available [7].

At the time of inclusion, the lowest dose of sacubitril/valsartan was used due to the presence of stage G3a renal failure (acc. to Kidney Disease: Improving Global Outcomes [KDIGO]). Dose escalation was abandoned because the patient maintained a trend towards low blood pressure (systolic 100–110 mm Hg) and his estimated glomerular filtration rate (eGFR) remained stable.

Additionally, we present a safe option to include ARNI as part of outpatient cardiac rehabilitation. Inclusion of this group of drugs during cardiac rehabilitation also enables proper optimization of pharmacological treatment with other cardiological drugs (modification of beta-blocker or diuretic dose).

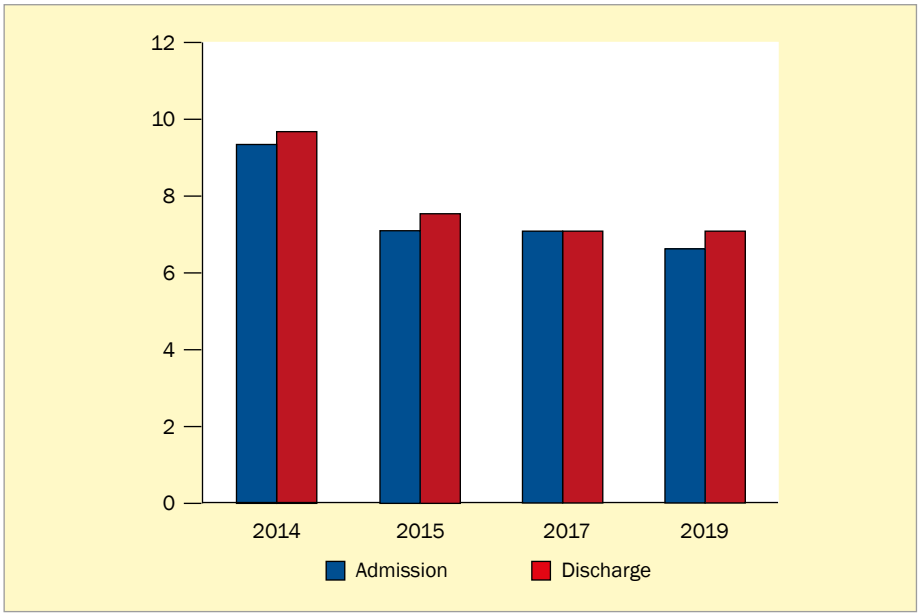

Figure 1. Change in achieved physical fitness in metabolic equivalents (METs) in subsequent years assessed before and after the cardiac rehabilitation program

Conflict of interest

JDK — lecture fees: Novartis. Other authors declare no conflict of interest.

Funding

None.

References

1. Maddox TM, Januzzi JL, Allen LA, et al. Writing Committee. 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021; 77(6): 772–810, doi: 10.1016/j.jacc.2020.11.022, indexed in Pubmed: 33446410.
2. Koprowicz P, Włodarczyk J, Kurpesa M, et al. Amiodaron — tarczyca — arytmia. Taniec na linie endokrynologa i kardiologa. Pacjent z poamiodaronowymi zaburzeniami funkcji tarczycy. Folia Cardiol. 2019; 14(3): 294–297, doi: 10.5603/fc.2019.0062.
3. Tan NY, Sangaralingham LR, Sangaralingham SJ, et al. Comparative effectiveness of sacubitril-valsartan versus ACE/ARB therapy in heart failure with reduced ejection fraction. JACC Heart Fail. 2020; 8(1): 43–54, doi: 10.1016/j.jchf.2019.08.003, indexed in Pubmed: 31838035.
4. Solomon SD, Vaduganathan M, L Claggett B, et al. Sacubitril/valsartan across the spectrum of ejection fraction in heart failure. Circulation. 2020; 141(5): 352–361, doi: 10.1161/CIRCULATIONAHA.119.044586, indexed in Pubmed: 31736342.
5. Romano G, Vitale G, Ajello L, et al. The effects of sacubitril/valsartan on clinical, biochemical and echocardiographic parameters in patients with heart failure with reduced ejection fraction: the „hemodynamic recovery". J Clin Med. 2019; 8(12), doi: 10.3390/jcm8122165, indexed in Pubmed: 31817815.
6. McMurray JJV, Packer M, Desai AS, et al. PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014; 371(11): 993–1004, doi: 10.1056/NEJMoa1409077, indexed in Pubmed: 25176015.
7. Lelonek M. Heart failure with preserved ejection fraction after the PARAGON-HF trial results: current knowledge and future directions. Kardiol Pol. 2020; 78(12): 1199–1205, doi: 10.33963/KP.15639, indexed in Pubmed: 33021355.