

# Heart failure in patients with hypertrophic obstructive cardiomyopathy

Pham Nhat Minh<sup>1,2</sup>✉, Nguyen Thi Nhung<sup>1</sup>, Nguyen Ngoc Quang<sup>1,2</sup>, Pham Manh Hung<sup>1,2</sup>

<sup>1</sup>Hanoi Medical University

<sup>2</sup>Vietnam National Heart Institute, Bach Mai Hospital

► **Correspondence to**

Dr. Pham Nhat Minh  
Hanoi Medical University  
Vietnam National Heart Institute,  
Bach Mai Hospital

► Received: 29 October 2023  
Accepted: 25 November 2023  
Published online: 30 November 2023

**To cite:** Pham NM, Nguyen TN, Nguyen NQ, et al. *J Vietnam Cardiol* 2023;**107E**:80-85

**ABSTRACT**

Hypertrophic cardiomyopathy is a hereditary cardiac disease, diverse in clinical manifestations, cardiac structure and natural progression. Patients with disease are associate with a broad range of clinical presentations, from patients who are asymptomatic, accidentally discovered during routine examination, to patients with chest pain, dyspnea, syncope, and even sudden death. We are presenting the clinical case of a young male patient with hypertrophic cardiomyopathy with rather large left ventricular wall thickness about 37mm who was hospitalized with severe dyspnea accompanied by tachycardia episodes and hypotension. The patient underwent electrical cardioversion, Doppler echocardiography, stress Doppler echocardiography with treadmill, cardiac MRI, basic blood tests, coronary CT angiography and ventriculography. The results showed the patient had a very high NT-proBNP level of 16,271 pg/mL; echocardiography showed asymmetric left ventricular hypertrophy, a maximum resting LVOT gradient of 28 mmHg, increasing to 64 mmHg at peak stress, preserved left ventricular systolic function and grade III left ventricular diastolic dysfunction;

greatly increased left ventricular mass of 199.6 g/m<sup>2</sup>, and delayed contrast enhancement involving the subendocardium of both ventricles and transecting the left ventricular free wall on cardiac MRI. We also discuss various treatment option for this young man.

**Keywords:** Hypertrophic cardiomyopathy (HCM), HOCM, heart failure.

**INTRODUCTION**

Hypertrophic cardiomyopathy is the most common hereditary cardiovascular disease, with an estimated prevalence of 0.2 - 0.5% of the general population, and is one of the leading causes of sudden cardiac death, especially (primarily) in patients under 35 years of age. HCM is characterized by disorganized arrangement of cardiac muscle cells, interstitial fibrosis and asymmetric or concentric left ventricular hypertrophy that cannot be explained solely by volume or pressure overload<sup>1-4</sup>. Hypertrophic cardiomyopathy encompasses a wide range of clinical manifestations from asymptomatic, with the disease discovered accidentally during routine examination, ECG abnormalities, or from family screening after a diagnosis

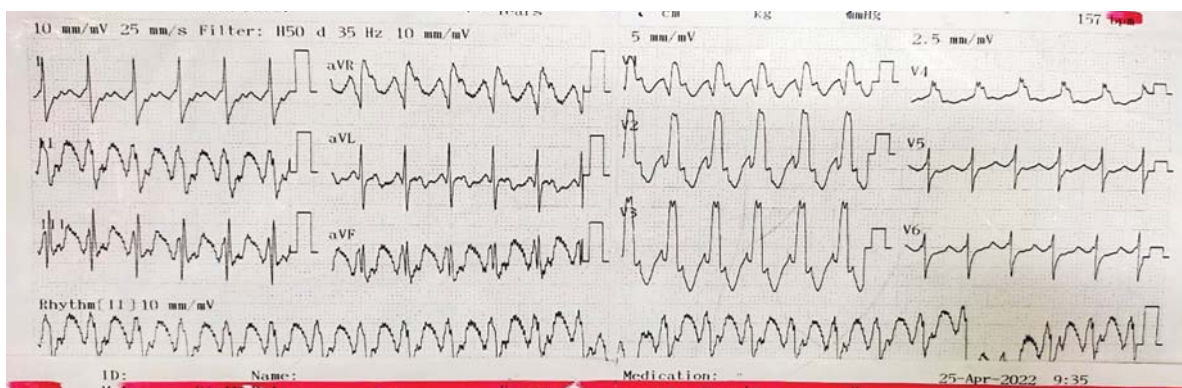
in a first-degree relative; to symptoms such as dyspnea, chest pain and syncope, and even sudden death may be the first presentation. Fatigue and dyspnea occur due to diastolic dysfunction and decreased cardiac output. Maron's 1997 study showed that most patients with HCM have some degree of heart failure according to the NYHA classification, with class I in about 34% to 43% of the cases, class II in 25%, class III in 40%, and 3% with class IV.<sup>5</sup> Palpitations, chest tightness, syncope can occur due to atrial arrhythmias, ventricular arrhythmias or mechanical obstruction in patients with increased left ventricular outflow tract gradient<sup>5</sup>.

We report the case of a patient with hypertrophic cardiomyopathy hospitalized with severe dyspnea, palpitations, chest tightness, accompanied by fainting, diagnosed with: Atrial Fibrillation – Heart Failure – Hypertrophic Obstructive Cardiomyopathy.

## CLINICAL CASE

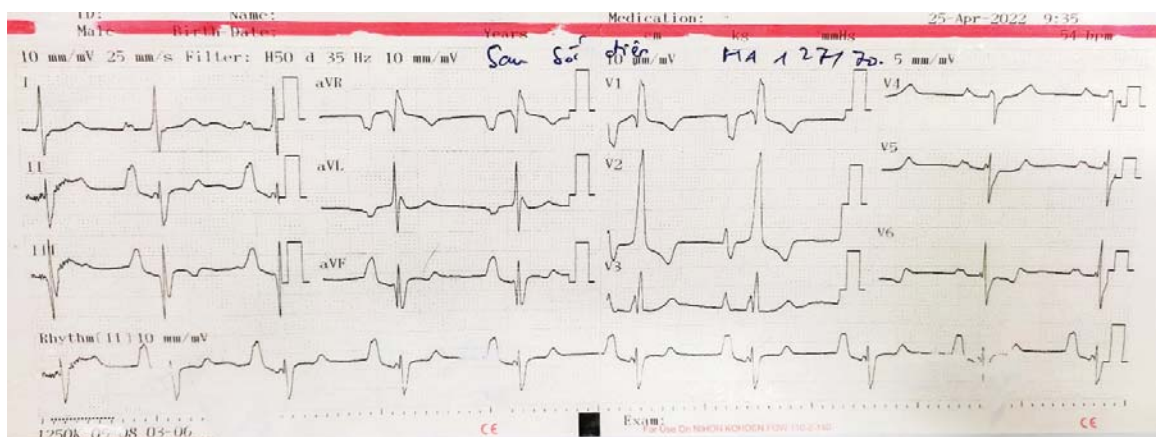
A 19-year-old male patient was diagnosed with hypertrophic cardiomyopathy 12 years ago. He had regular follow-up and was on regular medication with Bisoprolol 2.5mg/day. His father also had obstructive hypertrophic cardiomyopathy and had undergone alcohol septal ablation. The patient was hospitalized for dyspnea, significant fatigue, and palpitations for the past 2 days; no cough or fever. On admission, he had NYHA class III dyspnea, few moist rales (crackles) bilaterally, rapid small pulse of 155 beats/minute, hypotension with BP 80/50 mmHg, cold clammy skin, profuse sweating, 2 cm hepatomegaly, and mild bilateral leg edema.

Admission ECG: atrial flutter with 2:1 AV block, ventricular rate 157 beats/minute, complete right bundle branch block.



**Figure 1.** The patient's admission electrocardiogram

The patient underwent emergency electrical cardioversion. After cardioversion, the ECG showed sinus rhythm, rate of 54 beats/minute, persistent complete right bundle branch block, bifascicular block with second degree AV block.



**Figure 2.** The patient's electrocardiogram after electrical cardioversion

The patient's blood test results showed a very high NT-proBNP level (16,271 pg/mL).

**Table 1.** Paraclinical test indices

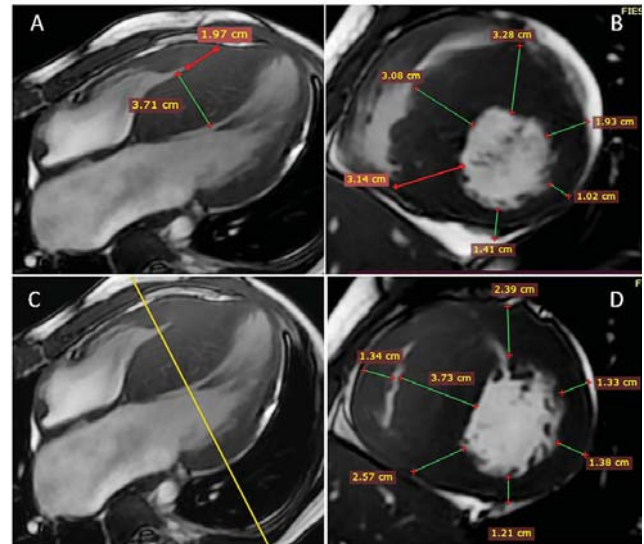
Test Index	Result	Reference Range
Red blood cell count (T/L)	5.55	4.5 – 5.9
Hemoglobin (g/L)	169	135 – 175
White blood cell count (G/L)	8.41	4 – 10
NT-proBNP (pg/mL)	<b>16271</b>	< 125
Troponin T-hs (ng/L)	<b>86.59</b>	=< 14
AST (GOT) (U/L)	<b>166</b>	5 – 34
ALT (GPT) (U/L)	<b>320</b>	0 – 55
Urea (mmol/L)	7.2	3.2 – 7.4
Creatinine (umol/L)	107	63.6 – 110.5
FT4 (pmol/L)	16.12	12 – 22
TSH (uU/mL)	3.370	0.27 – 4.2

Echocardiography showed thickening of left ventricular wall with interventricular septum thickness of 30mm during end-diastolic, end-diastolic left ventricular posterior wall of 20mm; right ventricular free wall thickness was 10.7mm. Moderate mitral and mild tricuspid regurgitation. SAM sign presented. Maximum left ventricular outflow tract gradient was 28 mmHg at rest, 64 mmHg on peak stress. Left ventricular systolic function was preserved (Biplane EF 68%), diastolic function, however, was impaired (Grade III diastolic dysfunction). Minimal pericardial effusion.

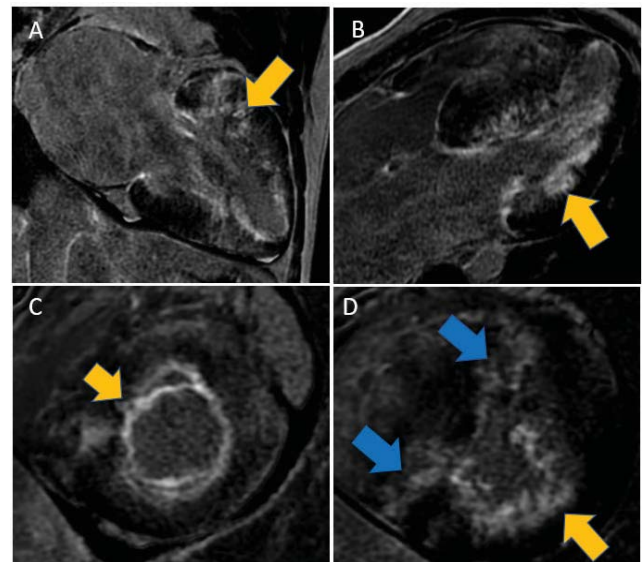
Abdominal ultrasound showed hepatomegaly with heterogeneous liver parenchyma, no focal lesions. Right pleural effusion thickness of 9 mm, ascites up to 18 mm in the deepest area.

Cardiac MRI confirmed asymmetric left ventricular hypertrophy, with greatly increased left ventricular mass (199.6 g/m<sup>2</sup>). Subendocardial perfusion defect involving the apex, mid and base of left ventricle. Delayed gadolinium enhancement showing fibrosis involving the subendocardium of both ventricles and transecting the anterior-septal left ventricular free wall. Left ventricular chamber not dilated, left ventricular systolic function preserved with EF

70%. Massively dilated left atrium. Moderate mitral regurgitation. Increased T2 mapping (50.5 ms) and ECV (48%) values.



**Figure 3.** A, B, C, D: Images of cardiomyopathy hypertrophy in multiple sections. C, D, E: Late gadolinium enhancement images of the heart in different slices



**Figure 4.** A, B, C, D: Late gadolinium enhancement images of the heart in different slices (yellow arrows: subendocardial enhancement, blue arrows: transmural enhancement)

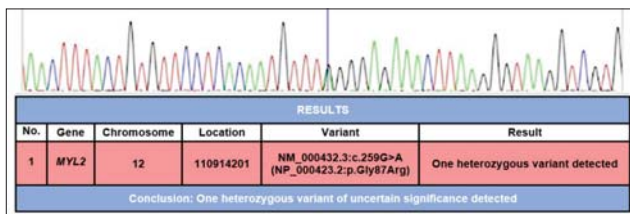
The patient underwent coronary DSA, which showed normal coronary arteries with a small septal branch. Ventriculography showed hypertrophic



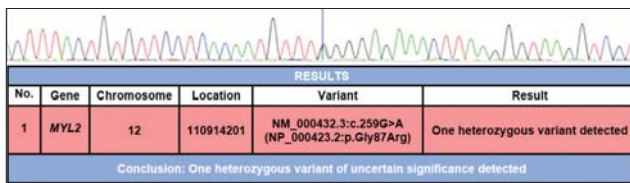
cardiomyopathy. Cardiac chamber pressure measurements: Left ventricular pressure 135/34/72 mmHg at rest, 147/32/73 mmHg on stimulation; LVOT pressure 105/35/63 mmHg; Ao pressure 98/70/87 mmHg.

24-hour Holter monitoring did not show significant ventricular arrhythmias, no AV block of any degree during the entire recording time, rare ventricular ectopy.

We performed genetic testing for the patient and his parents. Results detected a MYL2 gene mutation in both the patient and his father.



**Figure 5.** The patient's genetic test results



**Figure 6.** The patient's father's genetic test results

With the patient's test results, some salient points can be seen: 1) Despite the patient's young age (19 years old), he has very severe left ventricular hypertrophy (maximal wall thickness up to 37 mm) and greatly increased left ventricular mass (199.6 g/m<sup>2</sup>). 2) Clear heart failure manifestations (NYHA class III dyspnea, congestion with hepatomegaly, pericardial effusion, pleural effusion, ascites, elevated NT-proBNP level), although left ventricular systolic function is preserved, there is grade 3 diastolic dysfunction. 3) The patient had dangerous arrhythmias causing syncope, admission ECG showing rapid atrial flutter with ventricular rate of 157 beats/minute. 4) Cardiac MRI showed subendocardial perfusion defects involving the apex, mid and base of the left ventricle, however coronary DSA was normal, consistent with the pathophysiology of HCM

where excessive left ventricular hypertrophy leads to myocardial supply-demand mismatch, additionally the high left ventricular end-diastolic pressure affects subendocardial blood flow 5) Genetic testing results detected a heterozygous variant in the MYL2 gene in both the patient and his father, which is a relatively rare variant in the HCM population (<2%).

The patient was treated with diuretics for congestion. After the condition has improved, he was treated with beta blockers. After 5 days of treatment, the patient's clinical condition improved significantly with resolution of dyspnea and palpitations. 24-hour Holter after 5 days of treatment showed no dangerous ventricular or atrial arrhythmias.

## DISCUSSION

Hypertrophic cardiomyopathy is a condition that we encounter more and more frequently in clinical practice. Diagnosis and treatment have had many advances thanks to developments in echocardiography and imaging modalities like cardiac CT and MRI. Additionally, the genetic factor is an important issue that has been studied extensively in recent years, since hypertrophic cardiomyopathy exhibits **autosomal dominant inheritance** of alleles or non-alleles, with mutations in at least 12 genes encoding sarcomeric proteins. The majority of mutations (>70%) are located in the genes encoding  $\beta$ -myosin heavy chain, troponin T and myosin-binding protein C. We have a very typical clinical case with all the classic symptoms of hypertrophic cardiomyopathy, which here is also characterized by heart failure manifestations in a young patient. Arrhythmic presentations like atrial fibrillation and AV block were also seen in this patient. Echocardiography and cardiac MRI also show typical findings with septal hypertrophy and significant left ventricular outflow tract gradient. Additionally, in this patient genetic testing was done which detected a heterozygous variant in the MYL2 gene in both the patient and his father, a relatively rare variant in the HCM population (<2%).

In fact, in current conditions in Vietnam and globally, diagnosis is no longer a difficult issue, apart

from some challenges with the high costs of certain tests like cardiac MRI, or genetic testing in patients and related family members<sup>6-8</sup>. However, treatment is not a simple issue. Although there has been progress in treatment of heart failure, specific therapy for HCM has not been truly proven yet, apart from some recent studies on Mavacamten, a gene-targeted drug that can reduce LVOT gradient. The 2020 EXPLORER-HCM trial, a phase 3 clinical trial enrolled 429 patients across 68 cardiovascular centers in 13 countries, showed that Mavacamten (starting at 5mg dose) compared to placebo can improve pVO<sub>2</sub> and NYHA functional class, LVOT gradient as well as heart failure assessment scores like KCCQ-CCS and Hypertrophic Cardiomyopathy Symptom Questionnaire Shortness of Breath score (HCMSQ-SoB), while drug tolerability was similar to placebo<sup>9</sup>. A pooled analysis of 539 patients from 4 major clinical trials with average patient age of 57.9 years and average 29.3 weeks of follow-up showed the Mavacamten group had improved clinically (LogOR=0.65; p=0.01) and more patients had reduced NYHA dyspnea score (LogOR=0.64; p=0.001). Improvements in KCCQ and PVO<sub>2</sub> scores were not clearly significant (p=0.08 and 0.42), meanwhile the Mavacamten group showed a trend of LV EF reduction on echo. Thus, Mavacamten is a new drug with potential for clinical use, however its efficacy still requires more studies to demonstrate<sup>10</sup>. Additionally, the drug is not yet available in the Vietnamese market, so more time is needed to truly have clinical experience in Vietnamese patients.

Heart failure in hypertrophic cardiomyopathy patients, especially those with symptoms or reduced EF, still mainly follows general guidelines for acute and chronic heart failure<sup>11</sup>. This includes medical therapies, ICD/CRT-D implantation and ventricular assist devices as well as heart transplantation... Medical treatment for HFrEF is based on large randomized controlled trials, including ACE inhibitors/ARBs, beta blockers, ARNI, MRAs, SGLT2 inhibitors<sup>11</sup>..., especially in the late stages of HCM when left ventricular function deteriorates. In early stages of disease, when left ventricular systolic function is still compensated

or only mildly or moderately reduced (HFpEF or HFmEF), we can currently still treat according to the 2023 updated European Society of Cardiology guidelines on diagnosis and treatment of chronic heart failure<sup>12</sup>. (Treatment of HCM in early stages when left ventricular systolic function is preserved or only mildly or moderately reduced currently based on recommendations of 2023 updated ESC guidelines on diagnosis and treatment of chronic heart failure). For obstructive HCM patients like the young patient above, in addition to heart failure treatments per guidelines, non-vasodilating beta blockers can be used as first-line to treat and improve heart failure, if beta blockers have little to no effect or poor tolerability, verapamil and diltiazem are alternatives. However, verapamil and diltiazem are contraindicated in hypotension, dyspnea at rest or in children <6 years old, and when the gradient is >100mmHg. For cases with severe symptoms poorly responsive to medical therapy, disopyramide and septal reduction procedures are recommended. Currently, surgical myectomy is preferred over alcohol septal ablation with recommendations from both ESC and ACC<sup>6,7</sup>, especially in young patients who are still surgical candidates. Alcohol septal ablation can also be done based on the Heart Team's decision in experienced centers, or depending on patient and family preferences. In patients with atrial fibrillation/flutter, anticoagulation or DOACs/warfarin should be used regardless of CHADS<sub>2</sub>VAS<sub>2</sub> score<sup>6</sup>. Additionally, ICD implantation should be considered if patients have uncontrolled dangerous ventricular arrhythmias despite medical therapy. If all above treatments fail, heart transplantation should be considered for patients (although still rarely performed in Vietnam).<sup>6</sup>

In this patient, despite the LVOT gradient not being very high at 64mmHg on echo and 49mmHg on cath, with 30mm septal thickness, and concomitant valvular disease, the severe heart failure symptoms despite medical therapy may warrant consideration of more aggressive approach. According to current ESC and ACC guidelines, the appropriate treatment would likely be surgical myectomy followed by

mitral valve repair. After operation, depending on the clinical condition, additional treatments like ICD implantation or AF ablation may be indicated if ventricular arrhythmias persist. Additionally, thorough counseling of the family and patient regarding the hereditary nature of the disease and potential consequences on future generations is important. New drugs like Mavacamten may also be an option in this case, however the drug is not yet available in Vietnam and there is no experience with use in Vietnamese patients yet.

## CONCLUSION

Hypertrophic cardiomyopathy nowadays is a not uncommon hereditary disease, and can be diagnosed more easily than before with advanced diagnostic tools like echocardiography and cardiac MRI, especially at specialized centers like the Vietnam National Heart Institute. However, treatments are still challenging, with patients presenting increasingly complex genotype-phenotype manifestations like the clinical case above. Although currently in Vietnam there are no specialized treatment guidelines for cardiomyopathies in general or hypertrophic cardiomyopathy specifically, current ESC and ACC guidelines show that a comprehensive approach with a well-trained Heart-team is compulsory to manage complex cardiovascular patients like those with HCM.

## REFERENCES

1. Maron BJ. Clinical Course and Management of Hypertrophic Cardiomyopathy. *N Engl J Med*. Aug 16 2018;379(7):655-668. doi:10.1056/NEJMra1710575
2. Corrado D, Zorzi A. Declining Risk of Sudden Cardiac Death in Young Athletes. *Circulation*. Nov 13 2023;doi:10.1161/CIRCULATIONAHA.123.067243
3. Maron BJ, Maron MS. Hypertrophic cardiomyopathy. *Lancet*. Jan 19 2013;381(9862):242-55. doi:10.1016/S0140-6736(12)60397-3
4. Maron MS, Olivetto I, Betocchi S, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. *N Engl J Med*. Jan 23 2003;348(4):295-303. doi:10.1056/NEJMoa021332
5. Maron BJ. Hypertrophic cardiomyopathy. *Lancet*. Jul 12 1997;350(9071):127-33. doi:10.1016/S0140-6736(97)01282-8
6. Leggit JC, Whitaker D. Diagnosis and Management of Hypertrophic Cardiomyopathy: Updated Guidelines From the ACC/AHA. *Am Fam Physician*. 2022;105(2):207-209.
7. Arbelo E, Protonotarios A, Gimeno JR, et al. [2023 ESC Guidelines for the management of cardiomyopathies]. *G Ital Cardiol (Rome)*. Nov 2023;24(11):1e-127e. Linee guida ESC 2023 per il trattamento delle cardiomiopatie elaborate dalla task force per il trattamento delle cardiomiopatie della Societa Europea di Cardiologia (ESC). doi:10.1714/4127.41209
8. Butzner M, Maron M, Sarocco P, et al. Clinical Diagnosis of Hypertrophic Cardiomyopathy Over Time in the United States (A Population-Based Claims Analysis). *Am J Cardiol*. Nov 15 2021;159:107-112. doi:10.1016/j.amjcard.2021.08.024
9. Olivetto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. Sep 12 2020;396(10253):759-769. doi:10.1016/S0140-6736(20)31792-X
10. Rabiee Rad M, Ghasempour Dabaghi G, Habibi D. Safety and efficacy of mavacamten for treatment of hypertrophic cardiomyopathy: a systematic review and meta-analysis of randomized clinical trials. *Egypt Heart J*. Jan 12 2023;75(1):4. doi:10.1186/s43044-023-00328-7
11. McDonagh TA, Metra M, Adamo M, et al. Corrigendum to: 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. Dec 21 2021;42(48):4901. doi:10.1093/eurheartj/ehab670
12. McDonagh TA, Metra M, Adamo M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. Oct 1 2023;44(37):3627-3639. doi:10.1093/eurheartj/ehad195