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## Diastolic heart failure: boundaries of term application

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### ABSTRACT

Important changes regarding the understanding of the pathogenesis of chronic heart failure (CHF) marked the beginning of the millennium, and its first decade was called the decade of diastology. Even though numerous studies convincingly proved that deterioration of the left ventricular (LV) filling pressure often precedes impairment of its systolic function and a number of factors affect (especially at the onset) mainly the diastolic function without changing the conditions of blood ejection, modern classifications and approaches to CHF treatment are primarily based on the results of LV ejection fraction (EF) assessment.

In recent years, diastolic heart failure (DHF) has been often overlooked and replaced by the ambiguous term “CHF with preserved EF”. However, sometimes authors use the term DHF extensively, since CHF based on myocardial insufficiency develops only via two mechanisms (systolic and / or diastolic dysfunction), and excluding one of the mechanisms allows to identify the underlying one. The term DHF can be used in clinical practice and cannot be replaced by the diagnosis of CHF with preserved EF. CHF with preserved EF is a broader concept which includes a full spectrum of cardiovascular diseases, complicated by the development of CHF without depression of the global LV contractility and requiring differentiated approaches to therapy. In addition, the results of repeated studies on LVEF in many patients may require reclassification of this CHF phenotype, which is established following the analysis of the baseline value of global LV contractility. We join M.R. Zile in the appeal to stop discriminating against the term “DHF” and present the boundaries of its correct application.

**Keywords:** left ventricle, systole, diastole, heart failure with preserved ejection fraction, diastolic heart failure, diastology, visualization of the heart

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## Диастолическая сердечная недостаточность: границы применения термина

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### РЕЗЮМЕ

Начало тысячелетия ознаменовалось важными изменениями, касающимися представлений о патогенезе хронической сердечной недостаточности (ХСН), а его первое десятилетие стали именовать декадой диастологии. Однако несмотря на многочисленные работы, в которых было убедительно доказано, что ухудшение наполнения левого желудочка (ЛЖ) нередко предшествует нарушению его систолической функции и целый ряд факторов воздействует (особенно в дебюте) преимущественно на диастолическую функцию сердца, не изменяя условия выброса крови, современные классификации и подходы к терапии ХСН в первую очередь основаны на результатах оценки значения фракции выброса (ФВ) ЛЖ.

В последние годы о диастолической сердечной недостаточности (ДСН) нередко незаслуженно забывают, подменяя неравнозначным термином «ХСН с сохраненной ФВ». Вместе с тем иногда приходится сталкиваться с расширенным применением термина ДСН авторами, исходящими из того, что ХСН, в основе которой лежит миокардиальная недостаточность, развивается только по двум механизмам (систолическая и (или) диастолическая дисфункция) и простое исключение первого может без оговорок рассматриваться в качестве подтверждения второго. Термин ДСН имеет право на применение в клинической практике и не может быть заменен диагностическим заключением «ХСН с сохраненной ФВ», так как последняя является более широким понятием, охватывающим весь спектр заболеваний сердечно-сосудистой системы, осложняющихся развитием ХСН без депрессии глобальной контрактильной функции ЛЖ и требующих применения дифференцированных подходов к терапии. К тому же результаты повторных исследований значения ФВ ЛЖ у многих пациентов могут потребовать реклассификации этого фенотипа ХСН, установленного на основании анализа исходной величины обсуждаемого индикатора глобальной сократимости ЛЖ. Авторы лекции присоединяются к известному призыву M.R. Zile прекратить дискриминацию термина ДСН и представляют границы его корректного применения.

**Ключевые слова:** левый желудочек, систола, диастола, сердечная недостаточность с сохраненной фракцией выброса, диастолическая сердечная недостаточность, диастология, визуализация сердца

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## INTRODUCTION

Chronic heart failure (CHF) and the conceptual interpretation of its pathogenesis have been studied for a long time. However, despite the fact that leading cardiologists of Old and New Worlds repeatedly attempted to give a detailed definition of CHF, not a single definition was generally accepted. In our opinion, attention should be paid to the laconic and at the same time meaningful definition of the experts from the American College of Cardiology and the American Heart Association, which essentially has not changed much since 2001: “a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood” [1].

There are two points of great importance in the presented definition. Firstly, the authors, as well as the experts from the European Society of Cardiology [2], rightly consider CHF not as an independent nosological form of disease, but as a syndrome, which prompts the doctor to identify the underlying cause of heart failure in every clinical case, which is fundamental for the correct formulation of the diagnostic conclusion and the choice of therapy [3, 4]. Secondly, the definition clearly states the key mechanisms of myocardial insufficiency: ventricular inotropic and lusitropic dysfunction. At the same time, the conjunction “or” actually confirms recognition of the existence of diastolic heart failure (DHF).

DHF has been known for a long time. Thinking and doubting researchers have a clear understanding that the so-called diastolic markers sometimes reflect the functional state of the myocardium and its reserve more accurately than systolic ones. It can be used more reliably than other hemodynamic parameters to assess the clinical status of a patient with CHF, the effectiveness of therapy, and the disease prognosis [5–13].

Important changes regarding the understanding of the pathogenesis of CHF marked the beginning of the millennium, and its first decade was called the decade of diastology [8, 14]. Even though numerous studies proved convincingly that the deterioration of the left ventricular (LV) filling pressure often precedes impairment of its systolic function and a number of factors affect (especially in the debut) mainly the diastolic function of the heart without changing the conditions of blood ejection [12, 15–20], modern classifications and approaches to CHF therapy are primarily based on the results of assessing the value of LV ejection fraction (EF) [1, 2, 21].

In recent years, DHF has been undeservedly forgotten and replaced by unequal terms based on determining the value of LVEF (for example, “CHF with preserved LVEF”) [1, 2, 22–24]. At the same time, authors extensively use the term DHF since CHF based on myocardial insufficiency develops only through two mechanisms (systolic and / or diastolic dysfunction), and excluding one of them makes it possible to identify the underlying mechanism [22, 25–28].

The aim of this lecture is to consider views on the boundaries of the correct application of the term “diastolic heart failure”.

## LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC DYSFUNCTION

LV systolic (from Greek *systolé* – contraction) dysfunction, which underlies classical systolic heart failure, is characterized by depression of its contractility. Traditionally, CHF is associated with depressed global LV systolic function, an indicator of which is a decrease in the LV ejection fraction (EF) [1, 2, 21, 29].

In general, the lower the EF value (the proportion of LV volume that is ejected into the aorta in the absence of abnormal blood flow into the systole), the worse the quality of life and the disease prognosis [1, 2, 21, 22]. However, the severity of clinical manifestations of heart failure in patients with LV systolic dysfunction does not always depend only on the value of EF. Patients with very low EF may have no symptoms or signs of heart failure, while patients with preserved LVEF can sometimes be severely decompensated [1, 22]. The discrepancy between the severity of clinical manifestations of heart failure and the level of depression of global LV contractility noted by many authors can be partly explained by the presence of valvular pathology, pericardial damage, changes in loading conditions (preload and afterload), rhythm and conduction disorders, or primary pathology of the right ventricle. Manifestation of CHF largely depends on the presence and type of LV diastolic dysfunction, as well as the effectiveness of hemodynamic and neurohumoral compensatory and adaptive mechanisms [16, 21, 30].

It should be remembered that the development of CHF is primarily associated with weakening of the pumping function of heart and the normal value of LVEF (systolic function). The exact calculation of LVEF largely depends on the choice of the imaging technique and the method of its calculation, as well as

on the skills of the operator; it is not a reliable indicator of intact cardiac output (LV pumping function). For instance, LVEF does not always correctly reflect the severity of global systolic dysfunction in primary and secondary valvular regurgitation, which is found in patients with CHF. In such cases, relative safety of EF can be combined with depression of LV pumping function (reverse blood flow leads to a decrease in stroke volume) and does not fully exclude systolic dysfunction, the signs of which can be detected using more informative methods and imaging techniques, in particular magnetic resonance imaging and two- and three-dimensional speckle tracking method [21, 31–36].

The term “heart failure with preserved (normal) LV systolic function” is usually used to refer to a situation with clinically significant heart failure and the absence of a pronounced decrease in the value of LVEF. However, in view of the above considerations regarding the accuracy of estimating the EF value, most often determined using two-dimensional echocardiography, when LV contractile dysfunction is ruled out, it is better to use the term “heart failure with preserved EF” rather than “heart failure with preserved (normal) LV systolic function” [1, 21].

Again, the classification of CHF phenotypes is based on the results of the LVEF assessment [2]. However, even in a state of relative rest, LVEF does not belong to rigid biological constants and can change in repeated examinations by one operator spontaneously or under the influence of treatment, regardless of the initial CHF phenotype, established by analyzing the

value of this parameter, which obviously requires reclassification of heart failure, based on the changes in the value of the discussed parameter of global LV contractility (Figure) [1, 37].

LV diastolic (from the Greek diastolé – stretching) dysfunction is most often understood as a pathological condition when the ventricle cannot receive blood at low pressure and fill without a compensatory increase in atrial pressure (the average pressure in the pulmonary veins at rest does not normally exceed 12 mm Hg) due to impaired active relaxation of the myocardium and / or deterioration of its wall compliance [5, 38, 39]. The term “diastolic dysfunction” is used to refer to abnormalities in the active and / or passive mechanical properties of the whole ventricle (global diastolic dysfunction) or its segments (local diastolic dysfunction) in the diastole, regardless of whether EF is normal or reduced, and whether there are signs of heart failure [6, 19, 38, 40–42].

Thus, for example, if in a patient with hypertension without symptoms and signs of heart failure, an echocardiographic examination demonstrates normal EF and signs of LV diastolic dysfunction well described in modern guidelines [12, 13, 43–46], then this condition is referred to as asymptomatic diastolic dysfunction. [47, 48]. If such a patient with isolated LV diastolic dysfunction begins to experience shortness of breath, fatigue, and palpitations, a physical examination reveals signs of CHF, and laboratory tests show an elevated level of natriuretic peptides, then we can use the term DHF [6, 38, 40, 49–53].

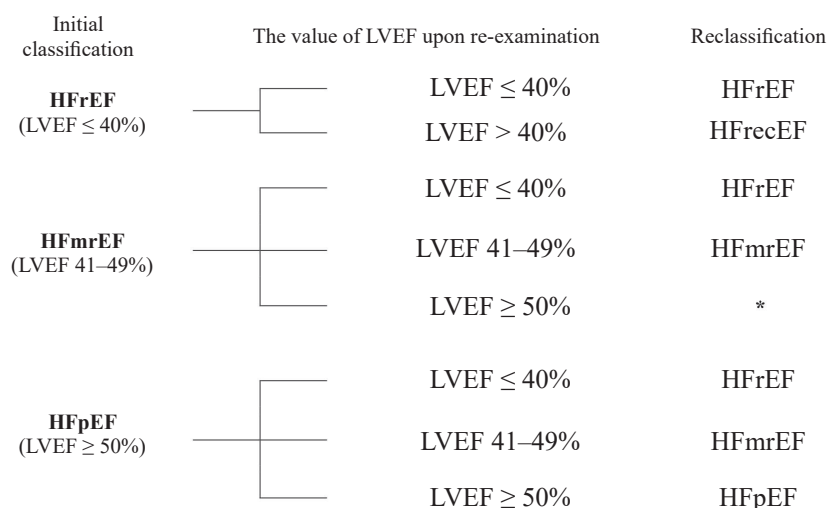


Figure. Classification and reclassification of CHF phenotypes [1]: HFrEF – CHF with reduced ejection fraction; HFmrEF – CHF with mildly reduced ejection fraction; HFrecEF – CHF with recovered ejection fraction; \* – CHF phenotype does not have a generally recognized designation

Thus, it is impossible to fully associate the concept of “diastolic dysfunction” with DHF: DHF always includes diastolic dysfunction, but the presence of the latter does not yet indicate the presence of the former [6, 47, 48]. In other words, the term “diastolic dysfunction” describes disturbances in the biomechanics of the heart in the diastole, while the term “DHF” is used to refer to the syndrome of heart failure in a patient with isolated diastolic dysfunction [40].

The existence of primary DHF is traditionally recognized. Wherein, it is believed that systolic dysfunction with unfailing regularity occurs in patients with diastolic dysfunction. The pathology of diastolic relaxation usually precedes systolic dysfunction, which appears later (the impaired filling pressure will sooner or later negatively affect the efficiency of the systole), but it is the appearance of systolic dysfunction, which accompanies diastolic disorders, that often manifests the clinical presentation of heart failure [6, 16].

Many patients with the classic systolic form of CHF also show signs of diastolic dysfunction [6, 16, 30]. Naturally, in this case, they do not talk about DHF. However, taking into account the independent clinical and prognostic value of LV inotropic and lusitropic dysfunction, the diagnostic conclusion should reflect “mixed” heart failure, for example, “CHF with reduced LVEF (38%) and restrictive LV diastolic dysfunction” [4, 42].

## BOUNDARIES OF THE TERM APPLICATION

It is necessary to answer the question that many clinicians ask [26, 27]: is heart failure with preserved EF similar to DHF? Indeed, if LV systolic function is preserved in a patient with manifested CHF, it is logical to assume that LV diastolic dysfunction should underlie the development of such heart failure. However, despite the external validity, such a conclusion may be erroneous and is subject to reasonable criticism [28].

In our opinion, the known technical limitations of the possibility of an accurate non-invasive quantitative assessment of LV diastolic function [54, 55] are not a peremptory reason to completely dismiss the diagnosis of DHF in favor of the broader concept of “heart failure with preserved EF”. To draw reasoned conclusion about DHF in a patient with objective signs of CHF and preserved LV EF, it is necessary to exclude all other cardiac and extra-cardiac causes that can lead to the development of heart failure with

normal systolic function (in particular, cor pulmonale, pulmonary artery stenosis, primary tricuspid regurgitation), on the one hand. It is also necessary to confirm the presence of LV diastolic dysfunction (also in the so-called diastolic stress test), on the other hand [26, 28, 56].

The definition of LV diastolic dysfunction does not include patients with mitral stenosis, in whom impaired LV filling pressure and increased pressure in the left atrium are caused by a mechanical obstruction to blood flow in the left atrioventricular valve [6]. A similar judgment can be made regarding some other diseases, in which heart failure develops due to impaired LV filling pressure caused by external causes (constrictive pericarditis, pericardial effusion) [22, 26]. Since in this pathology relaxation of the LV myocardium is not impaired and / or myocardial stiffness is not increased, after timely correction (for example, valvotomy or effective removal of pericardial effusion), the left ventricle regains the ability to receive blood at low pressure and fill without a compensatory increase in pressure in the left atrium [22].

Thus, it is necessary to distinguish between heart failure that has developed following a primary impairment of active relaxation of the ventricular myocardium and / or deterioration of its wall compliance and heart failure in which disturbances of heart filling pressure, which underly it, are not the result of LV diastolic dysfunction.

## CONCLUSION

The term “diastolic heart failure” can be used in clinical practice and cannot be replaced by an unequal diagnostic conclusion “CHF with preserved LVEF”, since the latter is a broader concept referring to a full spectrum of cardiovascular diseases complicated by the development of CHF without depression of the global LV contractility and requiring the use of differentiated approaches to therapy. In addition, the results of repeated studies on the value of LVEF in many patients may require reclassification of this CHF phenotype, which is established by the analysis of the baseline value of global LV contractility. We join M.R. Zile [26] in the appeal to stop discriminating against the term “diastolic heart failure”. However, it is necessary to clearly understand the boundaries of its correct application.

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