Guidelines

Czech Society of Cardiology guidelines for the diagnosis and treatment of chronic heart failure 2011


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Abstract

Guidelines of Czech Society of Cardiology are released in accordance with ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Guidelines summarise and evaluate all currently available knowledge about a particular issue, and whenever it is possible they are based on EBM—Evidence Based Medicine.

Two classifications of level of evidence and the strength of recommendation are used as seen below.

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Abbreviations: A, late diastolic mitral inflow velocity; Aa, mitral annulus movement velocity during atrial contraction; ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; ASA, acetylsalicyc acid; BMI, body mass index; BNP, B-type natriuretic peptide; CHF, congestive (or chronic) heart failure; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; CRT-P, cardiac resynchronization therapy (biventricular pacemaker); CRT–D, cardiac resynchronization therapy (biventricular pacemaker+implantable cardioverter-defibrillator); CT, computed tomography; CTX, heart transplantation; DT, deceleration time of early diastolic mitral flow; E, early diastolic mitral inflow velocity; Ea, mitral annulus movement velocity in early diastole; EBM, evidence based medicine; ECG, electrocardiogram; EF, ejection fraction; EDV, end-diastolic volume; ESC, European Society of Cardiology; ESV, end-systolic volume; GF, glomerular filtration; HF, heart failure; HFPEF, heart failure with preserved ejection fraction; ICD, implantable cardioverter-defibrillator; IVRT, isovolumic relaxation time; LBBB, left bundle branch block; LV, left ventricle; LVAD, left ventricular assist device; NSAIDs, non-steroidal antiinflamatory drugs; NT-proBNP, N-terminal fragment of pro-B-type natriuretic peptide; PAD, peripheral artery disease; PDE5, phosphodiesterase 5 inhibitor; RV, right ventricle; SM, semipermeable membrane; SR, sinus rhythm; 2-D, two-dimensional; 3-D, three-dimensional

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The prevalence of chronic heart failure in European countries is about 1–2% with a significant increase in elderly population. Based on the results of EUROHEART survey the prevalence in Eastern Europe is 1.3%. Improved treatment of acute stages (especially acute myocardial infarction) leads to the higher number of patients with chronic heart failure. Chronic heart failure has bad prognosis, diagnostics and treatment are demanding not only in medical but also economical way.
2. Definition and clinical classification

Completely and fully accepted definition of heart failure is not available. Most used definition highlight one or several features of this complex syndrome such as haemodynamics and evidence about neurohumoral activation. The term of chronic heart failure is thereby a description for many symptoms and signs which are caused by failed heart function. Chronic heart failure is a syndrome of heart impairment which leads to the decreasing minute cardiac output and disability to cover metabolic demands of tissues even the filling of the ventricles is not affected. Symptoms of heart failure can be present even without decrease of cardiac output during an inappropriate increase of end diastolic ventricular pressure (Tables 1 and 2).

Symptoms, signs and objectively proven heart dysfunction must be present to make a diagnosis of chronic heart failure (Table 3).

Heart dysfunction may be divided into

- **Systolic**, when contractility of heart is affected which leads into decreased ejection fraction and lower cardiac output.
- **Diastolic**, when the fulfilment of heart ventricles is affected, most often because of the loss of compliance and worst expandability of heart ventricle. Isolated affection of diastolic function is called heart failure with preserved ejection fraction (HFPEF).

Generally, heart failure can be classified into

- **Acute**—first presentation, acute or slow onset.
- **Transient**—recurrent or episodic.
- **Chronic**—persistent, stable, worsening, or decompensated.

The term **asymptomatic ventricular dysfunction** is described as a presence of decreased systolic/diastolic ventricular function and the patient is asymptomatic without any treatment, meanwhile **heart failure stage NYHA I** means when the patient is treated and asymptomatic.

3. Aetiology, epidemiology and prognosis

3.1. Aetiology

Many cardiovascular diseases lead into ventricular myocardial dysfunction, which is the proper cause of heart failure. This dysfunction may be systolic or/and diastolic. Coronary heart disease, especially the status after the myocardial infarction is by far the most common cause of myocardial disease, being the initiating cause in about 70% of patients with HF. Valve disease accounts for 10% and cardiomyopathies, usually dilated cardiomyopathy, for another 10% [1,2]. Other causes are less common. Aetiology of heart failure with preserved ejection fraction (HFPEF) is different. Most common cause is hypertension, especially in elderly population, when the diastolic dysfunction is worsened by myocardial fibrosis. Diabetes mellitus play also an important role in aetiology of HFPEF.

Heart failure is a syndrome and should never be presented as a final diagnosis. Aetiological diagnosis should always be specified because it may have a crucial impact on choice of optimal treatment.

3.2. Epidemiology

In developed countries including the Czech Republic cardiovascular and coronary events mortality is decreasing for the last 20–30 years. Contrary to this positive fact the overall prevalence of HF is increasing because of the ageing of the population, the success in treatment of acute coronary events, and improved pharmacological treatment and whole treatment management. The prevalence of HF is about 2% and rises sharply at 75 years of age, so the prevalence in 70- to
80-year-old people is between 10% and 20%. The prevalence of asymptomatic ventricular dysfunction is similar, about 2% [3]. That means that more than 200,000 patients suffer from heart failure and the similar amount of patients has asymptomatic ventricular dysfunction in the Czech Republic.

3.3. Prognosis

The outlook is, in general, gloomy, although it has improving tendencies. Overall 50% of patients are dead at 4 years and more than 50% of patients with severe heart failure (NYHA IV) are dead at 1 year [4,5]. Forty percent of patients admitted to hospital with HF are dead or readmitted within 1 year.

4. Pathophysiology

Low cardiac output leads to the insufficient fulfillment of arterial bloodstream. This situation is registered by peripheral receptors. Signals from chemo- and mechanoreceptors leads to the activation of sympathoadrenal system, renin-angiotensin-aldosterone system and nonsosmotic releasing of vasopressin and cytokines. These changes in neurovegetative system lead into vasoconstriction which together with retention of sodium is meant to provide perfusion of vitally important organs. Besides progression of myocardial impairment chronic heart failure leads into changes in lung, liver, kidney and peripheral muscle tissues. Late stages of chronic heart failure are connected with muscle atrophy, cachexia, often cardiac liver cirrhosis, anaemia and coagulation disorders.

4.1. Symptoms and signs of heart failure

The symptoms of HF such as breathlessness, tiredness, fatigue and peripheral oedema leads the physician into suspicion of heart failure, but particularly in the elderly, obese and women may be a problem their correct interpretation.

- **Breathlessness, dyspnoea**, which first occur after exertion, lately in rest. The main cause is the increased diastolic pressure in left ventricle, left atrium and pulmonary capillars which leads into pulmonary venous congestion because of systolic or diastolic left ventricle dysfunction.
- **Cough**, during exertion, mental stress or angriness (be-ware cough in patients treated by ACE-I because of the intolerance of ACE-I).
- **Tiredness and fatigue**—the cause is low cardiac output, peripheral hypoperfusion with an inadequate supply of oxygen and nutrients into muscles and other tissues.
- **Peripheral oedema**, the cause are stasis of blood in venous bloodstream (systemic venous congestion) because of right ventricle dysfunction and activation of renin-angio-
tensin-aldosterone system with retention of sodium and water and decreased renal functions because of lower cardiac output.
- **Chest pain**, because of ischaemic heart disease.

The severity of heart failure is most often classified into four functional classes using the NYHA functional classification (Table 4). American guidelines adjust classification into stages A–D. **Stage A** is defined as high risk for developing heart failure (hypertension, aterosklerotic disease, obesity, etc.) with any identified structural or functional abnormality of myocardium. **Stage B** includes asymptomatic dysfunction of left ventricle and class NYHA I, **Stage C** are asymptomatic patients—NYHA II and III, **Stage D** refractory heart failure (NYHA IV) despite maximal therapy [6].

Dominating symptoms and signs of left heart failure are caused by pulmonary congestion (venous stasis). The symptoms are **dyspnoea after exertion** worsening with progression of HF, **paroxysmal nocturnal dyspnoea** (also called **asthma cardiale**) which occurs after few hours from lie down and impel patient to sit (orthopnoea) which leads to subjective relieve. Pulmonary oedema is the most severe manifestation of acute or acutely decompensated chronic left heart failure [1,2].

Signs of pulmonary congestion are crackles or rales over lungs. Severe forms of chronic heart failure leads to unilateral or more often bilateral pleural effusion. Objective signs of right heart failure are usually caused by venous stasis before right heart ventricle which leads to raised venous pressure. Typical signs includes: **raised jugular venous pressure** [7], **hepatojugular reflux, hepatomegaly** and **peripheral oedema**. Oedema first occurs as bilateral plastic ankle swelling. At the moment of peripheral oedema manifesta-
tion 3–5 l of extracellular fluid is already retained. Sensitive indicator of fluid retention is raise of patient’s

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**Table 4 – Functional classification of heart failure according to New York Heart Association (NYHA). Modified in 1994.**

<table>
<thead>
<tr>
<th>NYHA</th>
<th>ACC/AHA 2005</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Stage B</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpititation, or dyspnoea. Patients can handle ordinary physical activity including walking or running 8 km/h</td>
</tr>
<tr>
<td>Class II</td>
<td>Stage C</td>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpititation, or dyspnoea. Patients can handle less than ordinary activity but ordinary activity results in fatigue or dyspnoea.</td>
</tr>
<tr>
<td>Class III</td>
<td>Stage C</td>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpititation, or dyspnoea. Patients suffer from dyspnoea or fatigue during basic activity such as dressing or washing</td>
</tr>
<tr>
<td>Class IV</td>
<td>Stage D</td>
<td>Unable to carry on any physical activity without discomfort. Dyspnoea or palpitation at rest. Patients are unable of independent life</td>
</tr>
</tbody>
</table>

Note: ACC/AHA 2005 stage A are high risk patients for developing heart failure (hypertension, diabetes mellitus, renal failure, pulmonary disease) without identified structural or functional abnormality.
weight. Fast weight reduction is thereby reliable sign of effective diuretic therapy. Extreme form of peripheral oedema is anasarca which is usually connected with ascites, hydrothorax and eventually hydropericardium [8].

Patients with heart failure usually suffers from tachycardia as a sign of sympathoadrenal activation. III. and IV. heart sound or their summation can be found in patients with heart failure because of reduction of myocardial compliance. This auscultation finding is called gallop rhythm and is mostly heard at the heart apex. Gallop rhythm is a sign important for prognosis and treatment of heart failure. Pulsus alternans, alternating big and small amplitude of pulse wave, is usual sign of severe heart failure. Lateral and inferior displacement of the apex beat indicates enlargement of the heart, lateral displacement with forceful impulse indicates left ventricle hypertrophy, palpable pulsation of precordium indicates right ventricle hypertrophy. Accentuated II. heart sound above pulmonary valve indicates pulmonary hypertension [9].

The symptoms and signs of HF as breathlessness, tiredness, tachycardia, and auscultation of cracles caused by pulmonary congestion may lead the physician to think about the possibility of heart failure. Unfortunately these signs and symptoms have low specificity and sensitivity which leads into undiagnosed early stages of heart failure or into wrong diagnosis of heart failure. False positive diagnosis is usually caused by patients obesity, unrecognised myocardial ischaemia, chronic obstructive lung disease or anaemia. Dyspnoea as a leading sign of left heart failure is moderately sensitive (66%) and has a low specificity (52%). Very useful for the diagnosis is positive response to the treatment such as remission of dyspnoe after treatment with diuretics [10].

Signs and symptoms of chronic heart failure are summarised in Table 5.

Diagnosis of heart failure based on signs and symptoms is highly unreliable. Objective prove of systolic and/or diastolic heart function impairment is necessary to increase reliability of diagnosis. Several methods are available for this purpose such as Doppler echocardiography, nuclear medicine methods and heart catheterization allowing evaluate systolic and diastolic heart function.

### 4.2. Laboratory tests

A routine diagnostic evaluation of patients with suspected HF includes a complete blood count, serum electrolytes, serum creatinine, glucose, liver function tests, and urinalysis. Increased haematocrit among patients with dyspnoea shows more likely pulmonary cause of this symptom. Anaemia on the contrary is often found in patients with severe heart failure mostly because of insufficient production of erythropoietin caused by renal impairment. Large clinical trials shows little decrease of haematocrit caused by renin-angiotensin-aldosterone blockers therapy. Increased values of serum urea and creatinine most likely signify renal origin of peripheral oedema (except the patients with terminal heart insufficiency). Nevertheless a differential diagnosis of this laboratory status includes also prerenal causes and catabolism during heart failure. Urinalysis can reveal proteinuria and glycosuria and thereby expose renal impairment or diabetes mellitus which can further complicate heart failure.

Treatment with diuretics affect kalaemia, hyponatraemia is an indicator of bad prognosis. Increased liver function tests are caused by hypoperfusion of livers.

In patients with atrial fibrillation with fast ventricle response thyrotoxicosis and pulmonary embolism has to be excluded. The prove of hypothyroidism can explain one of the causes of heart failure. Abnormalities in partial pressure of blood gases including higher arteriovenous difference of oxygen saturation can be found in patients with severe heart failure.

Plasma concentrations of natriuretic peptides, especially B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP), can be useful biomarkers in the diagnosis of HF [11]. Values which excludes heart failure in patients not treated for heart failure are BNP < 100 pg/ml and NT-proBNP < 400 pg/ml. In patients treated for heart failure normal values of BNP or NT-proBNP does not exclude heart failure.

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th>Cardiac</th>
<th>Systemic</th>
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<tbody>
<tr>
<td><strong>Signs</strong></td>
<td>Cracles</td>
<td>Tachycardia</td>
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<tr>
<td></td>
<td>Pleural effusion</td>
<td>III. or IV. heart sound</td>
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<td></td>
<td>Tachypnoea</td>
<td>Cardiac dilatation</td>
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<td></td>
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<td>Left ventricle hypertrophy</td>
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<tr>
<td></td>
<td></td>
<td>Irregular periferal pulsation</td>
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<tr>
<td><strong>Symptoms</strong></td>
<td>Dyspnoea</td>
<td>Palpitations</td>
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<tr>
<td></td>
<td>Ortopnoea</td>
<td>Stenocardia</td>
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<td>Caught</td>
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<td>Astma kardiale</td>
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pulmonary oedema is a sign of acute left heart failure or severe
can be found even on upper lung fields. Next level of pulmonary
increasing pulmonary vessel pressure pulmonary vessels filling
vessels filling in healthy person can be seen on chest X-ray made
blood vessels filling is changed (stage 1). Shadows of pulmonary
shadow can be changed. Cardiothoracic ratio (ratio of cardiac
size enlargement can be found and also the contour of heart
always, not even if systolic heart failure is present. Cardiac
Cardiomegaly can be often found in chronic HF, but not
4.4. Chest X-ray
Cardiomegaly can be often found in chronic HF, but not always, not even if systolic heart failure is present. Cardiac size enlargement can be found and also the contour of heart shadow can be changed. Cardiothoracic ratio (ratio of cardiac shadow width to the width of thorax) is used to assess cardiac size. Values over 0.5 are considered to be pathological.
Patients without pulmonary hypertension tend to have non-
enlarged pulmonary blood vessels without pulmonary congestion (stage 0) [13]. Pulmonary hypertension first manifests itself as enlarged hilar vessels, lately the distribution of pulmonary blood vessels filling is changed (stage 1). Shadows of pulmonary vessels filling in healthy person can be seen on chest X-ray made in upright position just in low and middle lung fields. With increasing pulmonary vessel pressure pulmonary vessels filling can be found even on upper lung fields. Next level of pulmonary congestion is interstitial pulmonary oedema (stage 2). Alveolar pulmonary oedema is a sign of acute left heart failure or severe worsening of chronic HF (stage 3). Oedema can be unilateral or bilateral.

4.5. Echocardiography
Echocardiography is one of the basic imaging techniques in confirming the diagnosis of chronic heart failure, since it allows evaluating and quantifying the dysfunction of left and right ventricle.
The basic parameter for diagnosis of left ventricle (LV) systolic failure is ejection fraction (EF). For left ventricular dysfunction is considered to decrease in EF below 50%, a significant systolic dysfunction is defined by the values of LVEF below 40%. An important additional data, in particular to assess the prognosis of heart failure, are also end-diastolic and end-systolic dimension and volume (EDV, ESV) of LV. All of these parameters, as well as the assessment of LV wall movement, can be obtained from one-dimensional (M-mode) and two-dimensional (2-D) transthoracic echocardiography, recently the three-dimensional (3-D) echocardiography has begun in use.
Pulsed Doppler echocardiography of transmittal filling of LV can obtain the following basic clinically useful parameters. They are early diastolic mitral inflow velocity (E), late diastolic mitral inflow velocity (A) and deceleration time of early diastolic mitral flow (DT) [14]. With parallel recording of transaortic and early diastolic mitral flow velocity an isovolumic relaxation time (IVRT) can be measured. The greatest expansion in the assessment of diastolic LV function and LV filling pressure estimation was achieved by tissue Doppler echocardiography, using the measurement of mitral annulus movement velocity in early diastole (Ea) and during atrial contraction (Aa) [15]. These parameters are less influenced by preload and afterload in comparison with parameters measuring the filling velocities of LV. Measuring analogous parameters of tricuspidal annulus can noninvasively evaluate and quantify the function of right ventricle. It is very useful to combine the measurement of Ea and Aa movement of mitral annulus by tissue Doppler echocardiography with the evaluation of E and A by pulsed Doppler echocardiography of transmittal LV filling. Combination of E and Ea measurements can nearly accurately noninvasively estimate the increased LV filling pressure. Naghue et al. [14] showed good correlation between the ratio E/Ea and pulmonary capillary wedge pressure ($r = 0.87$). The ratio E/Ea < 8 is a sign of normal mean diastolic left ventricle filling.
pressure, the ratio $E/E_a > 15$ indicates increased mean diastolic pressure [16].

Table 6 shows normal normal range of most commonly used echocardiographic parameters of diastolic function of left ventricle at different age categories [17] (Fig. 2).

### 4.6. Selective coronary angiography, left and right cardiac catheterization

In patients with chronic heart failure, coronary angiography is used mainly for explaining the cause of heart failure and to assess prognosis. Dyspnoea of cardiac aetiology or left ventricle dysfunction are clear indications for coronary angiography. Also severe valvular heart disease is an indication for coronary angiography. CT angiography shows promising for the future, especially in patients where we expect a negative finding on the coronary vessels. If noninvasive methods fail for evaluating the cause of left ventricular dysfunction, it is possible to perform left-heart catheterization with assessment of systolic and diastolic parameters of left ventricular function or right-heart catheterization with measurement of pulmonary capillary wedge pressure, which indirectly inform us about the left ventricle inflow pressure [18]. During the cardiac catheterization (and also independently of it) endomyocardial biopsy can be performed when heart failure due to infiltrative or storage disease is suspected.

### 4.7. Magnetic resonance imaging

Magnetic resonance imaging represents a great prospect for quantitative assessment of myocardial viability and function of left and right ventricle. Increased accumulation of gadolinium after intravenous administration in nonviable part of myocardium (positive late enhancement) indicates a presence of irreversible myocardial damage (connective tissue transformation, scar). Nuclear magnetic resonance imaging can highly accurately determine standard (e.g. EF) as well as new parameters of myocardial function (e.g. analysis of...
myocardial deformation–strain). Magnetic resonance is also indicated when myocardial lesion due to infiltrative or storage diseases is suspected.

Currently also CT scans begin to be tested for myocardial function and viability evaluation.

4.8. The role of individual methods in diagnosis of chronic HF

Table 7 and Fig. 3 show the diagnostic procedure.

5. Treatment strategy of chronic heart failure

5.1. Prevention

Primary prevention of heart failure represents prevention and strict treatment of all diseases that may lead to ventricular dysfunction. These include treatment of hypertension, arrhythmias, acute forms of ischaemic heart disease with the aim of the earliest recanalization of occluded artery, optimal timing of surgical treatment of valvular heart diseases and prevention of specific myocardial diseases, in which the causality is known and removable (alcohol, cardiotoxic cytostatics, some endocrinopathies).

Secondary prevention of heart failure is meant to prevent the progression of preexisting ventricular dysfunction to manifestation of heart failure and progression of existing heart failure. Tools for primary and secondary prevention are often identical. Progression of heart failure can also be prevented or at least significantly slowed down by medications such as ACE inhibitors, ARBs, betablockers or aldosterone receptors blockers. An essential part of secondary prevention is elimination of all worsening conditions and factors that include myocardial ischaemia, hypertension, arrhythmia, inflammatory diseases, anaemia, hyperthyroidism, metabolic disorders etc.

Class of recommendation I, level of evidence A.

5.2. Objectives and treatment options

The purpose of heart failure treatment is to improve the quality of life, i.e. reduce or completely eliminate symptoms, improve

Table 7 – Summary of diagnostic assessment of CHF.

<table>
<thead>
<tr>
<th>Necessary for diagnosis of CHF</th>
<th>Supports the diagnosis of CHF</th>
<th>Opposes the diagnosis of CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compatible symptoms ++</td>
<td>++ (If absent)</td>
<td>++ (If normal)</td>
</tr>
<tr>
<td>Compatible signs ++</td>
<td>++</td>
<td>++ (If abnormal)</td>
</tr>
<tr>
<td>Response to therapy ++ (If symptoms or dysfunction absent)</td>
<td>++ (If absent)</td>
<td>++ (If normal)</td>
</tr>
<tr>
<td>ECG ++</td>
<td>+</td>
<td>++ (If normal)</td>
</tr>
<tr>
<td>Objective evidence of dysfunction (ECHO and other) ++</td>
<td>+</td>
<td>++ (If normal)</td>
</tr>
<tr>
<td>Chest X-ray ++</td>
<td></td>
<td>++ (If normal)</td>
</tr>
<tr>
<td>BNP, NT-proBNP ++</td>
<td>+</td>
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</tr>
<tr>
<td>BNP, NT-proBNP ++</td>
<td>+</td>
<td>+ (If normal)</td>
</tr>
</tbody>
</table>

Fig. 3 – Algorithm for diagnosis of CHF.
exercise tolerance, reduce mortality and extend the life expectancy [19]. For each patient, the order and importance of these aims can be different. For mildly symptomatic patients it is prior to reduce mortality and slowing the disease progression. For severely symptomatic patients it is more important to release from symptoms and improve the quality of life. Current treatment options, always individualised for each patient, can bring remarkable results (Table 8). Causal therapy of heart failure, such as surgical reconstruction or replacement of damaged heart valves, effective treatment of hypertension, revascularization procedures etc., may be realized only in some patients.

The choice and combination of optimal treatment strategy depends on the underlying disease, severity of CHF, co-morbidities, patient age and number of other factors. Non-pharmacological options such as regimen and diet are an essential part of comprehensive treatment.

### 5.3. Triggering factors, specific causes and co-morbidities

If we find factors causing CHF, which are treatable, it is always necessary to intervene. Their removal sometimes leads to re-compensation. They can be divided into:

1. Volume overload (increased preload): excessive physical or emotional burden, fever, infections (bronchopulmonary, urinary), mitral or aortal valve insufficiency, anaemia, acute abdomen, thyrotoxicosis, drugs that cause sodium and water retention (NSAIDs, corticosteroids), excessive salting, hypervolemia, etc.

2. Pressure overload (increased afterload): hypertension, aortic stenosis, excessive physical burden predominantly isometric, etc.

3. Myocardial damage: missed medication, negative ionotrophic agents (antiarrhythmics, alcohol), NSAIDs, new onset of ischaemia or myocardial infarction, electrolyte, acidobasic or respiratory disturbances, inflammatory myocardial disease, urinary retention, etc.

### Table 8 – Treatment options for heart failure.

<table>
<thead>
<tr>
<th>Self-care and diet recommendations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction in patients with overweight and obese</td>
</tr>
<tr>
<td>Limit salt intake (&lt; 4–5 \text{ g a day})</td>
</tr>
<tr>
<td>Abstinence (restriction) of alcohol</td>
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<tr>
<td>Smoking cessation</td>
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<tr>
<td>Adequate physical exercise (except for acute heart failure)</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Pharmacological treatment:</th>
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<tbody>
<tr>
<td>Angiotensin-converting enzyme inhibitors (ACEIs)</td>
</tr>
<tr>
<td>Angiotensin receptor blockers (ARBs)</td>
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<tr>
<td>Beta-blockers (BB)</td>
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<tr>
<td>Aldosterone antagonists</td>
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<tr>
<td>Diuretics</td>
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<tr>
<td>Digoxin</td>
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<td>Ivalbutamide</td>
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<tr>
<td>Vasodilators anticoagulants, antiplatelet agents</td>
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<tr>
<td>Amiodarone</td>
</tr>
<tr>
<td>Positive ionotropic agents (PDE inhibitors, catecholamines, levosimendane)</td>
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<table>
<thead>
<tr>
<th>Surgery and devices:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical (CABG) or catheter (PCI) revascularization</td>
</tr>
<tr>
<td>Cardiac resynchronization therapy</td>
</tr>
<tr>
<td>Implantable cardioverter-defibrillator</td>
</tr>
<tr>
<td>Left ventricular assist devices</td>
</tr>
<tr>
<td>Elimination methods: ultrafiltration, haemodialysis</td>
</tr>
<tr>
<td>Heart transplantation</td>
</tr>
</tbody>
</table>

Class of recommendation I, level of evidence C.

Patients in NYHA functional classes I–III are free to drive motor vehicles for private purposes, professional drivers must be in NYHA functional class I or II, with EF >40% and without ventricular tachycardia (repeated mandatory testing once a year). In NYHA functional class IV is not allowed to drive motor vehicles.

### 5.4. Self-care management

#### 5.4.1. Everyday activities

Patient education plays a fundamental role for appropriate self-care behaviour management: patient should have an adequate knowledge of his disease and treatment to improve the most the adherence to all procedures. The education and psychological support should be provided to him at every opportunity by healthcare professionals and relatives. The patient should weigh himself on a regular basis, preferably in the morning after emptying. A weight gain of 1 kg from day to day already suggests fluid retention. In case of sudden weight gain of >2 kg in 3 days, well cooperating patient may increase his diuretic dose or contact his doctor. The patient should have an adequate knowledge of his medical treatment including possible side effects. He should also be aware about medication which would be inappropriate. These are mainly:

- NSAIDs (notice over-the-counter drugs as Ibuprofen, Brufen, Voltaren, Diclofenac, Veral) including coxibs are contra-indicated for long term use in severe heart failure;
- some calcium channel blockers (verapamil, diltiazem, short-acting dihydropyridines);
- tricyclic antidepressants;
- corticosteroids;

5.4.2. Diet

It is based on a rational balanced diet with enough nutrients and maintaining an optimal weight. Weight reduction in overweight and obese is necessary.

Intake of salt depends on the severity of disease. Even patients with mild heart failure should have the salt intake less than 5 g per day before diuretics are ordered. Salt shaker removal out of table and avoidance of food that contains large amounts of salt (smoked meat, white bread, canned food, mineral water) could be helpful.

Alcohol is absolutely contraindicated in alcohol-induced cardiomyopathy. Moderate alcohol consumption is allowed for other patients with maximal day limit of 40 g for men and 30 g for women (that is equivalent to 1 beer or 1–2 dl of wine per day).
Smoking is strictly prohibited.

Fluids should not be significantly restricted with an optimal intake of 1.5–2 l per day. Fluid restriction is considered in patients with severe symptoms accompanied by hyponatremia, but always with strict monitoring of fluid balance and serum electrolytes.

Cardiac cachexia: a clinical or subclinical malnutrition is presented in approximately 50% of patients with advanced heart failure. It is an important predictor of worse prognosis. Cardiac cachexia is likely when:

- documented unintentional weight loss of ≥5 kg or ≥7.5% from the previous stable weight without the presence of oedema;
- BMI < 22 kg/m².

The patient with cardiac cachexia should attempt to increase the muscle mass by performing the exercise training regularly. The weight gain by fluid retention is undesirable. **Class of recommendation I, level of evidence C.**

5.4.3. Exercise

The level of physical activity depends on the patient’s current condition. It varies from resting, preferably in a chair for patients in NYHA functional class IV, to regular daily activity excluding the heavy physical strain in patients in NYHA functional classes I–II. Disability pension should be considered for the patients in NYHA III–IV functional classes in relation to individual situation. Regular exercise is recommended for all patients with mild or moderate functional limitations. Exercise training is recommended to stable patients in NYHA I–III functional classes without malignant ventricular arrhythmias or other contraindications. 20–30 min of dynamic exercise up to individual submaximal level (e.g. cycling or fast walking) completed with daily morning exercise 3–5 times a week is crucial. **Class of recommendation I, level of evidence C.**

5.4.4. Travelling

Travelling to very hot and humid destinations is not recommended as well as high altitudes. Long flights in which there is a risk of dehydration, peripheral edemas and deep vein thrombosis, are not recommended. On the contrary, air travel is preferable to long journeys than travelling by bus. **Class of recommendation I, level of evidence C.**

5.4.5. Sexual activity

Sexual activity cannot be dictated. It is important to reassure anxious patients and also their sometimes even more anxious partners. Phosphodiesterase 5 (PDE5) inhibitors (e.g. sildenafil, tadalafil, vardenafil, etc.) are not currently recommended for patients with an advanced heart failure (NYHA III–IV) and they are strictly contraindicated for those using nitrates.

5.4.6. Influenza vaccination

Annual influenza vaccination is extremely underestimated in general population. Influenza is very serious disease that causes large number of deaths, especially for patients with chronic illness. It is mainly recommended for people over 65 years and people with chronic diseases. Data from randomized clinical trials show that annual influenza vaccination leads to reduction in morbidity and mortality in patients with cardiovascular disease. Using live attenuated vaccines with intranasal administration is not recommended yet [20]. **Class of recommendation I, level of evidence C.**

5.5. Pharmacological therapy

5.5.1. Angiotensin-converting enzyme inhibitors (ACEIs)

ACE inhibitors are drugs of first choice in chronic heart failure even when asymptomatic left ventricular dysfunction [1,2]. A meta-analysis of clinical trials showed that the average decline in mortality is 23% and in total mortality and morbidity (measured by number of hospitalisation) even 35%. Differences in demanded effects and side effects are irrelevant [21,22]. Due to individual hypotensive response and possible worsening of renal functions (especially in elderly patients with pre-existing chronic renal insufficiency) the initial dose, so-called testing dose, should be small, with titration until the maximum tolerated. Overview of ACE inhibitors and their recommended dosage in chronic heart failure are listed in Table 9 (we present only ACE inhibitors where the effect was proven in mortality trials) [23–27]. **Class of recommendation I, level of evidence A.**

First finished randomized double-blind trial PEP CHF showed safety, improvement of quality of life and reduction of the number of admissions to hospital [28]. The trial Preserve did not prove the benefit of irbesartan [29]. On the base of these trials we consider ACE inhibitors as a possible treatment for diastolic heart failure (especially when left ventricular hypertrophy presented). **Class of recommendation IIa, level of evidence B.**

ACE inhibitors are well tolerated. Adverse effects are rare, except hypotension and troublesome cough. Those are renal function impairment, often in elderly patients, skin rush, angioneurotic oedema, sensory disturbance, more rarely leucopenia and glomerulopathy with proteinuria. Combination potassium-sparing diuretics therapy (except spironolactone) may be dangerous for a risk of hyperkalemia. Severe renal insufficiency is a contraindication but the exact plasmatic creatinine level and glomerular filtration rate is not

### Table 9 – Recommended daily dosage of ACE inhibitors in chronic heart failure.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>3 × 6.25</td>
<td>3 × 50</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2 × 2.5</td>
<td>2 × 20</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>1 × 2.5</td>
<td>1 × 20</td>
</tr>
<tr>
<td>Perindopril-Erbumine</td>
<td>1 × 2-2.5</td>
<td>1 × 8–10</td>
</tr>
<tr>
<td>Perindopril-Arginine</td>
<td>1 × 2.5</td>
<td>1 × 10</td>
</tr>
<tr>
<td>Ramipril</td>
<td>1 × 2.5</td>
<td>1 × 10</td>
</tr>
<tr>
<td>Trandolapril</td>
<td>1 × 0.5</td>
<td>1 × 4</td>
</tr>
</tbody>
</table>

Note 1: Captopril and enalapril are the oldest ACE inhibitors historically with RCTs made in 80s and 90s of 20th century and today they have been already replaced by modern ACE inhibitors with once a day dosage.
determined. It is recommended to try at least small dose of ACEI while monitoring renal functions (the level of serum creatinine >180 μmol/l is an exclusion criterion in most clinical trials). Other contraindications are hypotension and hypovolemia caused by massive diuretic treatment, absolute contraindication then bilateral renal artery stenosis, history of angioneurotic oedema and pregnancy (for teratogenic effect). Dry troublesome cough appears in 5–10% of patients and it usually leads to discontinuation of ACE inhibitor. The change of product is not usually helpful and the cough disappears rarely after dose reduction. If an ACE inhibitor causes a cough, switch to ARB is indicated.

Table 10 shows the strategy for initiation of ACE inhibitors therapy.

5.5.2. Angiotensin receptor blockers (ARB)

First clinical trials with ARB in patients with chronic heart failure have shown improvement of hemodynamical parameters and improvement in exercise tolerance. Other trials have shown equal effect of ARB on mortality and morbidity as ACE inhibitors. Adding ARB to ACEI did not lead to a further decrease in mortality. In the VALLIANT trial in patients after myocardial infarction, the addition of ARB led to an increase in side effects, but in the CHARM trial it decreased the number of hospitalisations [30].

The current findings about angiotensin receptor blockers in heart failure and after myocardial infarction can be summarised:

- Indications of ARB are the same as indications for ACEI. ARB are recommended in patients intolerant of ACEI.
  
  **Recommendation I, level of evidence A.**

- We do not have proof that ARB are better than ACEI, therefore they are the drug of choice in heart failure only in case of intolerance of ACEI.

<table>
<thead>
<tr>
<th>Table 10 – Strategy for initiation of ACE inhibitors therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Avoid high doses of diuretics before starting the treatment for a risk of hypovolemia, diuretics should be discontinued for 24 h</td>
</tr>
<tr>
<td>2. The first dose of ACE inhibitor to be taken at bedtime to minimise the possible hypotensive effect. When the therapy is started in the morning, the patient should be monitored for several hours (3–4 h), including blood pressure checks</td>
</tr>
<tr>
<td>3. Always begin with small, so-called test dose and slowly up-titrate to recommended maintenance doses</td>
</tr>
<tr>
<td>4. Renal functions and serum electrolytes should be checked every 3–5 days during the dose up-titration. After the maintenance dose is reached and the patient is stable, the check should be once every 3 months, later once every 6 months. When the renal function is worsening, the treatment usually has to be discontinued</td>
</tr>
<tr>
<td>5. Never simultaneously start the treatment with potassium-sparing diuretics! Reduce the dose or discontinued established potassium-sparing diuretics therapy and continue only in case of persistent hypokalemia</td>
</tr>
<tr>
<td>6. Do not administer NSAIDs, they reduce the effectiveness of ACE inhibitors</td>
</tr>
<tr>
<td>7. Check blood pressure every 1–2 weeks after each dose increase</td>
</tr>
</tbody>
</table>

Table 11 – Recommended daily doses of ARB in chronic heart failure.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan</td>
<td>1 × 4</td>
<td>1 × 16–32</td>
</tr>
<tr>
<td>Losartan</td>
<td>1 × 25</td>
<td>1 × 100</td>
</tr>
<tr>
<td>Valsartan</td>
<td>2 × 40</td>
<td>2 × 160</td>
</tr>
</tbody>
</table>

- The benefits of combined therapy with ACEI and ARB on mortality have not been proven. This combination is appropriate in patients with inadequately controlled hypertension or marked proteinuria. Combination therapy decreases the amount of hospitalisations for heart failure and it requires careful follow-up controls.

**Recommendation I, level of evidence B.**

Recommended starting and target doses of ARB (only those ARB that have mortality trials in heart failure are shown in Table 11).

Similarly as in ACE inhibitors, we start treatment with a dose equal to approximately ¼ of the target dose and we up-titrate the doses in 7–14-days’ intervals.

**Recommendation I, level of evidence A–C.**

The HEAAL trial investigated the efficacy of low and high doses of losartan: 50 mg vs. 100 mg. It proved a decrease in death or hospitalisation for heart failure in the group of patients with the higher dose. Patients in this group observed improvement of symptoms and a lower risk of side effects was found [31].

**Recommendation I, level of evidence B.**

Note:

Direct inhibitors of renin, mainly aliskiren, are currently in phase III. trials. In the clinical trial ALOFT (Aliskiren observation of heart failure treatment) in patients with stable heart failure, aliskiren significantly decreased the plasma renin activity and the levels of brain natriuretic peptide. Mortality trials in patients with chronic heart failure with the acronyms ATMOSPHERE and ASTRONAUT are ongoing.

5.5.3. Betablockers (BB)

Betablockers should be used in all patients with heart failure (NYHA II–IV) when the patient is stabilized, in both ischaemic and nonischaemic aetiology, and decreased LVEF, unless they are contraindicated. Their positive effect on mortality, functional improvement and delay of progression of heart failure was observed without difference in sex, age, functional class or level of LVEF in clinical trials.

**Recommendation I, level of evidence A.**

BB are always indicated after myocardial infarction (unless contraindicated), even in asymptomatic patients with LV dysfunction (NYHA I), in combination with ACEI/ARB, as demonstrated in the CAPRICORN study [32].

**Recommendation I, level of evidence B.**

Due to different clinical effects of betablockers, only those betablockers that have clear positive mortality data from double blind multicentric studies: bisoprolol, carvedilol, metoprolol succinate (ZOK) and nebivolol are recommended.

**Recommendation I, level of evidence A.**
The effect of betablockers on mortality is additive to the effects of ACEI (CARMEN). The two groups of drugs do not compete with each other, instead combined therapy is favourable. The positive effect of betablockers can be explained mainly by decrease of sympatoadrenal activation, decrease in heart rate, an increase in the length of diastole and by their antiarythmic effect [33].

As demonstrated by the CIBIS III trial, heart failure treatment can be started either with a betablocker with the addition of an ACE inhibitor, or the other way around. In mild forms of heart failure with signs of sympathicotonia, it is better to start with a betablocker and after their titration to add ACEI or ARB. On the other hand, in more severe cases of HF it is recommended to stabilise the patient with an ACEI or with diuretics, and start the titration of betablockers afterward. Importantly, combined therapy should be used, unless contraindicated [34].

Recommendations for starting treatment and steps to be followed in case of adverse effects during treatment are shown in Table 12. The recommended doses are shown in Table 13 (only those betablockers that have mortality trials in heart failure are included) [1].

Absolute contraindications of betablockers: asthma, severe forms of COPD, symptomatic bradycardia and hypotension should be respected. We always consider the risks and benefits in relative contraindications: diabetes mellitus with possible hypoglycaemia, less severe forms of COPD (perform spirometry before starting BB, than test BB), PAD.

### Table 12 – Recommendations for starting treatments with BB and recommendations in case of worsening during treatment.

<table>
<thead>
<tr>
<th>Practical recommendations for treatment with betablockers in CHF:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The patient must be clinically stable on established conventional therapy of heart failure (ACE inhibitors, diuretics, ev. digoxin). Patients in functional class NYHA IV must be hemodynamically stable (on oral diuretic therapy)</td>
</tr>
<tr>
<td>2. Start the treatment with a low dose, uptitrate slowly</td>
</tr>
<tr>
<td>3. Uptitrate dose every 2–4 weeks, if well tolerated. Try to achieve target dose. During every visit monitor BP and HR, clinical condition, ev. changes in weight (increased weight can signal fluid retention)</td>
</tr>
<tr>
<td>4. Inform the patient of the possibility of temporary worsening of symptoms when betablockers are started</td>
</tr>
<tr>
<td>5. We must acknowledge that patient improvement can be seen after 3–6 months of uninterrupted therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Steps to be followed in case of adverse effects:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In hypotension correct dose of ACEI or diuretics and slow down titration of BB</td>
</tr>
<tr>
<td>2. In temporary worsening HF when BB are started, increase dose of ACEI or diuretics and slow down titration until negative effects subside</td>
</tr>
<tr>
<td>3. Add digoxin, if patient not already on it</td>
</tr>
<tr>
<td>4. Do not abruptly discontinue BB, but leave a lower dose, which is better than no dose</td>
</tr>
<tr>
<td>5. Increase doses of BB slower to achieve maximal or maximal tolerated doses. Adverse effects that can limit dose include bradycardia, fatigue, weakness and gastrointestinal symptoms</td>
</tr>
</tbody>
</table>

### Table 13 – Recommended daily doses of betablockers in chronic heart failure.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1 × 1.25</td>
<td>1 × 10</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>2 × 3.125</td>
<td>2 × 25–50</td>
</tr>
<tr>
<td>Metoprolol ZOC</td>
<td>1 × 25</td>
<td>1 × 200</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>1 × 1.25</td>
<td>1 × 10</td>
</tr>
</tbody>
</table>

### Table 14 – Recommended daily doses of diuretics in chronic heart failure.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Initial dose (mg)</th>
<th>Max. daily dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>20–40</td>
<td>250–500</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>12.5–25</td>
<td>50</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>12.5–25</td>
<td>50</td>
</tr>
<tr>
<td>Indapamide</td>
<td>1.25–2.5</td>
<td>5</td>
</tr>
</tbody>
</table>

5.5.4. Diuretics

Diuretics combined with ACEI and betablockers are considered as core therapy in patients with pulmonary or systemic congestion. We do not give diuretics to asymptomatic patients, in absence of dyspnoea or oedema. In mild forms of heart failure, thiazide diuretics are the first line therapy, in more severe forms of heart failure loop diuretics (in our country most frequently furosemide) are chosen. In case of insufficient response, loop and thiazide diuretics can be combined [35].

**Recommendation I, level of evidence C.**

Diuretics are recommended in patients with HF and clinical signs or symptoms of congestion.

Diuretics have not been investigated in a double-blind mortality trial. The combination with drugs affecting the renin angiotensin system and betablockers is common [36].

**Recommendation I, level of evidence C.**

In severe forms of heart failure or in case of poor response to loop diuretics, a combination of loop and thiazide diuretics is favourable [37].

Dosing of diuretics is shown in Table 14.

The indication for diuretic use is to relieve signs of congestion and fluid retention. Dehydration should be avoided.

We can change the doses of diuretics in patients with good compliance according to their current condition, for example according to their daily weight.

We start therapy with low doses together with ACEI/ARB. In case glomerular filtration (GF) is below 0.5 ml/s, we do not add thiazide diuretics (they are ineffective), but we give loop diuretics instead (furosemide).

It is important to actively observe possible side effects: hypovolaemia, worsening of renal parameters, hypokalaemia, hypomagnesaemia, hyponatraemia, hyperuricaemia, impaired blood glucose, acid-base balance disorders, with amiloride hyperkalaemia.

In insufficient response, we increase the dose to twice daily, combine loop and thiazide diuretics. Aware patients to exclude use of other nephrotoxic agents e.g. NSAIDs.
Aquaretics—vasopresin antagonists (tolvaptan, conivaptan, lixivaptan), are being tested in clinical trials. They seem to be promising in patients with hyponatraemia and worsened heart failure, even though the EVEREST study has not yet proven their benefit when compared to loop diuretics [38].

5.5.5. Aldosterone receptor blockers

Hyperaldosteronism, which is a part of neuroendocrine activation and is associated with heart failure, causes the depletion of potassium and magnesium, fibrosis in the myocardium and blocks reverse reuptake of noradrenaline. It therefore worsens myocardial function and increases the predisposition to arrhythmias. It worsens endothelial function in blood vessels, it worsens compliance of arteries by increasing the amount of collagen and destroys the micro-circulation (vasculitis like changes). The increased level of aldosterone can be suppressed by the administration of ACEI/ARB only temporarily (aldosterone escape).

The RALES (Randomized Aldactone Evaluation Study), proved a positive effect of aldosterone antagonists on the prognosis and symptoms in patients with heart failure. A 30% reduction in mortality was observed.

Based on the results from the above study, therapy with low doses of spironolactone is indicated in patients with LVEF < 35%, and those in functional class NYHA III–IV or those who recently had an episode of circulatory decompensation and are treated with a loop diuretic. The recent EMPHASIS_HF trial with the new aldosterone antagonist eplerenone showed its positive effect even in less severe forms of heart failure [39].

The recommended doses of both drugs are 25 mg daily. In case of hyperkalaemia, the dose should be decreased by half, alternatively other concomitant therapy should be adjusted. The discontinuation of aldosterone blockers should be avoided if possible. In case of refractory heart failure without hyperkalaemia with the regular dose, the dose can be increased to 50 mg per day. Careful monitoring of potassium levels is needed as hyperkalaemia can occur (Tables 15 and 16) [40].

**Recommendation I, level of evidence A.**

### Table 15 – Strategies for administration of aldosterone receptor blockers.

<table>
<thead>
<tr>
<th>Patient NYHA II–IV or post MI with LV dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check plasma concentration of potassium (&lt;5 mmol/l) and creatinin (&lt;250 µmol/l)</td>
</tr>
<tr>
<td>Start with low dose of spironolakton 12.5–25 mg; eplerenon 25 mg</td>
</tr>
<tr>
<td>Check plasma concentration of potassium and creatinin after one week</td>
</tr>
<tr>
<td>The higher plasma potassium concentration above 5.0 mmol/l BRA reduce the dose to 50% for potassium above 5.5 mmol/l discontinue BRA</td>
</tr>
<tr>
<td>If symptoms of CHF persist after a month and lasts normokalemia increase BRA dose to 50 mg daily</td>
</tr>
</tbody>
</table>

**BRA contraindications:** Anuria, acute renal insufficiency, markedly decreased renal function, hyperkalemia, hyponatremia, porphyria, hypersensitivity to ingredients of BRA, pregnancy and lactation

5.5.6. Digoxin

From digitalis glycosides, in our country we exclusively use digoxin. There has been a single mortality/morbidity trial with digoxin, and this was done before betablockers were routinely used in chronic heart failure [41]. According to the DIG trial, digoxin does not affect all cause mortality. It decreases the number of hospitalisations for heart failure and it decreases the mortality for heart failure. Digoxin therefore improves symptomatic condition of patients with heart failure, but it does not affect their prognosis. The reduction of symptoms seems to be higher, in patients with more severe LV dysfunction and in more symptomatic patients [42].

The results of the DIG trial are supported by a metaanalysis of smaller studies [43].

A clear indication for chronic digoxin therapy is chronic symptomatic heart failure with systolic dysfunction of left ventricle with atrial fibrillation with rapid ventricular response. In asymptomatic systolic LV dysfunction and atrial fibrillation, digoxin can be used for rate control, but digoxin only influences heart rate at rest, and not during exercise. Therefore betablockers are the drugs of choice, if needed they can be combined with digoxin.

**Recommendation I, level of evidence C.**

The administration of digoxin in heart failure and sinus rhythm remains contradictory. Digoxin still has a wide popularity for some of its benefits. It can be administered once per day, it had good short and long term tolerance, tachyfylaxation does not occur, and it is inexpensive. The current consensus is that digoxin can be beneficial in sinus rhythm in patients with manifested heart failure and more severe left ventricular systolic dysfunction. It should be tried in these patients, and if it leads to clinical improvement, it should be administered regularly. If it does not lead to clinical improvement, it should be discontinued.

**Recommendation IIa, level of evidence B.**

In heart failure with preserved ejection fraction (HFPEF), digoxin is indicated only for control of heart rate with simultaneous atrial fibrillation with rapid ventricular response. There are no benefits in sinus rhythm.

**Recommendation IIb, level of evidence B.**

Digoxin is not suitable in heart failure during acute myocardial infarction and sinus rhythm, as its effect is unpredictable and it can cause serious arrhythmias. It is contraindicated in significant bradycardia, second- or third-degree heart block, sick sinus syndrome (in the absence of a permanent pacemaker), carotic sinus syndrome, WPW syndrome, obstructive hypertrophic cardiomyopathy, hypokalaemia, hypercalcaemia and in case of previous intolerance of digoxin. Digitalization is ineffective in chronic cor pulmonale,

### Table 16 – Recommended daily doses of BRA in chronic heart failure.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Initial dose (mg)</th>
<th>Maximal daily dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone</td>
<td>12.5–25</td>
<td>25–50</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>25</td>
<td>25–50</td>
</tr>
</tbody>
</table>
in mitral stenosis and preserved sinus rhythm, pericardial tamponade and constrictive pericarditis.

**Recommendation I, level of evidence B.**

Before starting treatment with digoxin, renal functions and potassium levels must be determined. The usual daily dose is 0.125–0.250, in older patients 0.0625–0.125. For chronic treatment, a booster dose is not needed. Digoxin is eliminated almost completely by the kidneys, and its clearance is similar to that of creatinine. It is therefore important to reduce daily dose in patients with renal failure, according to given nomograms and equations. Certain drugs can interfere with the pharmacokinetics of digoxin and they can increase plasma digoxin levels twofold (chinitidine, propafenone, amiodarone, verapamil and others). Therefore the adjustment of the daily dose is needed. The therapeutic blood levels of digoxin are 0.6–1.2 ng/ml [44].

5.5.7. **Antiaggregation, anticoagulation**

Clinical data from observational trials show that patients with chronic heart failure have a higher risk of thromboembolism (deep vein thrombosis, pulmonary embolism, peripheral arterial embolizations and ischaemic brain infarctions) [45].

Thromboembolic events are the third most common cause of death in patients with chronic heart failure [46,47]. The cause is not only the frequently present atrial fibrillation but also the activation of coagulation due to platelet dysfunction, endothelial dysfunction and inflammatory activation not only in patients with atrial fibrillation, but also in patients with sinus rhythm. These disorders are proportional to the level of left ventricular dysfunction and severity of symptoms [48]. The effectivity of antiaggregation therapy in patients with heart failure and sinus rhythm is debated, as acetylsalicylic acid (ASA) can decrease the effect of ACE inhibitors by decreasing Prostaglandin synthesis in the kidney and this unfavourable interaction can lead to an increase in worsening of heart failure [49,50].

We recommend administration of ASA to all patients with proven ischaemic aetiology of heart failure, with doses between 75 mg and 160 mg/day. Caution is needed in patients with refractory heart failure and frequent decompensations where we consider risk versus benefit.

**Recommendation IIa, level of evidence B.**

In patients with atrial fibrillation, anticoagulation therapy is indicated, as it strongly decreases the number of thromboembolic events when compared to placebo and ASA.

Anticoagulation therapy is indicated in patients CHF and

- History of systemic or pulmonary embolism.
- With atrial fibrillation—dabigatran is indicated in patients with atrial fibrillation and heart failure.
- Intracardial thrombus.
- After an extensive Q myocardial infarction of anterior wall with aneurysm.
- Significant left ventricular dilatation of nonischaemic aetiology.
- With LVEF below 20%.

Target INR for effective anticoagulation is 2.0–3.5. Anticoagulation therapy with INR<2.0 is ineffective.

Heparin or preferably low molecular weight heparins are the drug of choice during acute decompensations, pulmonary embolism, recent intracardial thrombus, venous thrombosis, preoperative and postoperative treatment.

**Recommendation I, level of evidence A.**

5.5.8. **Hypolipidemic therapy**

There is no reason to stop statin therapy in patients that are already treated with a statin for example for a previous myocardial infarction in secondary prevention. On the other hand, there is no reason to start patients on statin therapy due to chronic heart failure.

5.5.9. **If channel blockers**

In patients with heart failure and sinus rhythm, heart rate at rest above 70/min is considered as a negative prognostic factor. The trials BEAUTIFUL and mainly SHIFT, proved positive effect of ivabradin, a drug that inhibits If channels in the sinus node, and therefore decreases the heart rate, without having other negative effects on the myocardium [51,52].

Ivabradin is indicated in patients with compensated heart failure and sinus rhythm, who have heart rate at rest above 70/min, even if on maximal tolerated dose of betablockers. It must be differentiated if present tachycardia is a compensatory mechanism in patients with low cardiac output. The recommended starting dose is 2 mg × 2.5 mg, the maximal daily dose is 2 mg × 7.5 mg. According to EMA, the recommended heart rate to start ivabradin is 75/min. (EMA citation).

**Recommendation I, level of evidence B.**

5.6. **Recommendations for pharmacological therapy of systolic cardiac dysfunction**

The principles of pharmacological therapy of chronic systolic heart failure are summarised in Table 17.

5.7. **Elimination methods**

Haemodialysis is used in severe kidney dysfunction and there, where the elimination of excessive fluids is required. The basic principles are diffusion and filtration. Diffusion is the exchange of substances according to the concentration gradient on the semipermeable membrane (SM). During ultrafiltration, water and substances dissolved in it cross the SM according to the pressure gradient [53,54].

For patients that mainly need removal of fluids, without the need for haemodialysis, continual elimination methods are available. In this case we mainly use ultrafiltration.

The indication is acute pulmonary oedema and congestive heart failure accompanied by renal insufficiency due to hypoperfusion, without the ability to eliminate the retained fluids (subacute and chronic pulmonary oedema, anasarca resistant to pharmacological treatment). Chronic nephropathy (ischaemic kidney disease, diabetic nephropathy, chronic tubulointerstitial nephritis), drug damage (antibiotics, NSAIDs) may participate.
5.8. Recommendations for cardiac resynchronization therapy in patients with heart failure

Current recommendations for cardiac resynchronization therapy (CRT) in patients with heart failure are based on Guidelines for cardiac pacing and resynchronization therapy with pacemaker/defibrillator function of Czech society of Cardiology issued in 2009 and newly published Guidelines on device therapy in heart failure of European society of Cardiology from 2010 [55,56].

In contrast to previous guidelines, this update is focused on the clinical state of the patients with heart failure, analyses the results of newly published important clinical trials in this area and introduces the indications of CRT in patients in NYHA II functional class.

Meta-analysis of clinical trials with less symptomatic patients (NYHA I–II) and patients with advanced heart failure (NYHA III–IV) clearly shows that CRT is an effective therapy in adequately selected patients with any NYHA class [57].

It should be emphasised that there is still no clear predictor of long term efficacy of CRT as well as the definition of so-called non-responders to this treatment despite the use of sophisticated echocardiographic and other imaging and electrophysiological methods [58].

The indication for cardiac resynchronization therapy remains highly individual, with regard to clinical state, comorbidities, pharmacological treatment and the overall perspective of the patient.

Optimally indicated CRT should be based on consensus of the arrhythmologist and heart failure and echocardiography specialists.

The clinical effects of long-term CRT, where CRT-P or CRT-D (biventricular pacemakers or implantable cardioverter-defibrillators) were implanted, have been evaluated in a large number of randomized multi-centre trials and registries [59–62].

Meta-analyses were also published [63], suggesting that the most efficacious option to reduce mortality in patients with heart failure and low left ventricular ejection would be a CRT-D.

The most common inclusion criteria were: NYHA functional class III or IV despite optimal pharmacological treatment, left ventricle ejection fraction LVEF ≤ 35%, sinus rhythm (SR), left ventricular (LV) dilatation but with varying definitions, and QRS duration ≥ 120/≥ 130 ms [64].

The results support the use of resynchronization therapy to improve morbidity (but not mortality) in ambulatory class IV patients with the exception of patients eligible for cardiac transplantation, where the aim is to reduce the mortality before the surgery.

Key points:

- Left ventricle dilatation is no longer required in a recommendation.
- NYHA class IV patients should be ambulatory.
- Reasonable expectation of survival with good functional status for more than 1 year for CRT-D.
- Evidence is strongest for patients with typical left bundle branch block (LBBB).
- Similar level of evidence for CRT-P and CRT-D in primary prevention.

Recommendations in patients with heart failure in NYHA III–IV functional class.

Patients in NYHA III–IV classes, with LVEF ≤ 35%, QRS ≥ 120 m, sinus rhythm, optimal pharmacotherapy (NYHA class IV patients should be ambulatory). CRT-P or CRT-D are recommended to reduce mortality and morbidity.

Class of recommendation I, level of evidence A.

Four trials—MIRACLE ICD II [65], MADIT-CRT [66], REVERSE [67] and RAFT [68, 69] assessed the role of CRT in patients presenting with mild or no manifestations of heart failure, low LVEF and wide QRS complex.

Currently there is no convincing evidence that CRT should be indicated in patients with no or transient, mild symptoms (NYHA I), and the recommendation is restricted to patients in NYHA II.

Key points:

- Three recent, randomized, prospective, multicenter trials (MADIT-CRT, REVERSE a RAFT) in mild HF demonstrated reduced morbidity.
- Improvement primarily seen in patients with QRS ≥ 150 ms and/or typical LBBB.
• In MADIT-CRT, women with LBBB demonstrated a particularly favourable response.
• In MADIT-CRT the extent of reverse remodelling was concordant with and predictive of improvement in clinical outcome.

Recommendations in patients with heart failure in NYHA II functional class.

Patients in NYHA functional class II, with LVEF ≤ 35%, QRS ≥ 150 ms, sinus rhythm, optimal pharmacotherapy. CRT-D is recommended to reduce morbidity and prevents the progression of heart failure.

Recommendations are restricted to patients with HF in NYHA II, QRS ≥ 150 ms, in whom very good response to treatment is expected. Patients with a secondary prevention indication for an ICD should receive CRT-D.

**Class of recommendation I, level of evidence A.**

Approximately one-fifth of patients receiving CRTs in Europe have permanent atrial fibrillation. The prevalence of AF in patients with HF is linked to the severity of the disease: 5% in NYHA I as compared with 25–50% in NYHA III/IV patients. Some patients with permanent AF may resume SR during long-term treatment or following successful left atrial ablation.

It should be emphasised that patients with symptomatic HF, AF, and an LVEF of ≤ 35% may satisfy the criteria for ICD implantation. The presence of QRS prolongation would favour implantation of a CRT-D in these patients.

In that the evidence is limited in AF and most of the patients included in trials had a very wide QRS width, we restrict recommendation for CRT-P/CRT-D to QRS ≥ 130 ms.

**Key points:**

- Approximately one-fifth of CRT implantation in Europe are in patients with permanent AF.
- NYHA classes III–IV symptoms and LVEF of ≤ 35% are well established indications for ICD.
- AV nodal ablation may be required to assure adequate pacing.
- Evidence is strongest for patients with an LBBB pattern.
- Insufficient evidence for mortality recommendation.

Recommendations in patients with HF and permanent atrial fibrillation.

Patients in NYHA classes III–IV, LVEF ≤ 35%, QRS ≥ 130 ms and pacemaker dependency induced by AV nodal ablation, CRT-P/CRT-D should be considered to reduce morbidity [70].

**Class of recommendation II, level of evidence B.**

Patients in NYHA class III–IV, LVEF ≤ 35%, QRS ≥ 130 ms. CRT-P/CRT-D should be considered to reduce morbidity.

**Class of recommendation II, level of evidence C.**

Although prospective randomized controlled studies specifically addressing the issue of CRT in patients with a narrow QRS complex are currently lacking, there are several retrospective observational series or small prospective trials demonstrating a clinical benefit of upgrading to biventricular pacing with long-standing right ventricular pacing, severe ventricular dysfunction, NYHA functional class III symptoms, regardless of QRS duration [71,72]. This may indirectly indicate that preservation and/or restoration of an intrinsic, near-normal activation sequence by biventricular pacing should be pursued regardless of rhythm.

**Key points:**

- In patients with a conventional indication for pacing, NYHA III/IV symptoms, an LVEF of ≤ 35%, and a QRS width of ≥ 120 ms, a CRT-P/CRT-D is indicated.
- RV pacing will induce dyssynchrony.
- Chronic RV pacing in patients with LV dysfunction should be avoided.
- CRT may permit adequate up-titration of beta-blocker treatment.

Recommendations in patients with heart failure and a concomitant class I pacemaker indication are summed up in Table 18.

### 5.9. Artificial heart and ventricular assist devices

Mechanical assist devices are pumps that are partially able to take over the heart’s function and restore sufficient cardiac output (Table 19).

Currently there is a whole range of systems for short- and long-term ventricular assistance [73]. In patients with advanced chronic heart failure, nonpulsatile implantable left ventricular assist device (LVAD) is most frequently implanted [74]. LVAD is used as a bridge to heart transplantation (CTX) in patients in end-stage heart failure and in patients with progressive clinical deterioration and expectation of short survival (Table 20). Further indications are severe pulmonary hypertension [75] and cardiac cachexia as a result of low cardiac output in candidate for cardiac transplantation. Contraindications for ventricular assist devices are shown in Table 21.

Health care of patients with implanted LVAD should be complex, consisting of close cooperation of specialized nurse, physician and a technician. Infection or bleeding during the anticoagulant therapy is the most common complication. Patients with LVAD do not necessarily have to be hospitalised, although they are placed on top positions on the heart transplant waiting list. Short-term assist devices are used in emergency situations—after a cardiac surgery, in CTX as a right ventricle assist device in patients with pulmonary hypertension. Correctly indicated mechanical assist device improves the prognosis for patients and enables a successful CTX.

**Class of recommendation I, level of evidence A.**
5.10. Non-surgical revascularization

There are no data from multicentre trials assessing the benefit of percutaneous coronary revascularization in patients with chronic heart failure. However, smaller studies suggest functional and prognostic benefit of myocardial revascularization (for both coronary bypass grafting and percutaneous coronary intervention) in case of dysfunctional but viable (hibernating) myocardium supplied by significantly stenotic coronary artery. If angina pectoris or exertional ischaemia is present, indication criteria for myocardial revascularization in chronic ischaemic heart disease should apply and these patients should be considered at higher risk. Class of recommendation I, level of evidence C.

5.11. Surgery

Surgery is indicated when surgically correctable conditions of heart failure are present. Patients with acceptable risk profile for surgery should be considered.

5.11.1. Myocardial revascularization

Coronary angiography is indicated in patients with ischaemic left ventricular dysfunction and myocardial revascularization should be considered. Proof of viable myocardium supplied by stenotic or occluded coronary arteries is an important factor in favour of revascularization. The most frequent methods of myocardial viability assessment are dobutamine stress echocardiogram, myocardial perfusion scintigraphy and magnetic resonance imaging. In correctly indicated patients, symptomatic improvement and increase of LVEF may be expected. Randomized trial STICH proved decreased hospitalisation and death rate during 5 years following intervention [76]. Class of recommendation I, level of evidence B.

5.10. Non-surgical revascularization

There are no data from multicentref trials assessing the benefit of percutaneous coronary revascularization in patients with chronic heart failure. However, smaller studies suggest functional and prognostic benefit of myocardial revascularization (for both coronary bypass grafting and
indicated. In patients with atrial fibrillation, MAZE procedure and/or atrial reduction should be considered.

**Class of recommendation IIa, level of evidence C.**

5.11.2. Aneurysmectomy

In symptomatic patients with LV aneurysm, aneurysmectomy is indicated, most frequently in anterior wall and interventricular septum area.

**Class of recommendation IIb, level of evidence B.**

In patients with vast anterior wall akinesis indicated for surgery, LV endoventriculoplasty may be considered. In randomized trials there is no evidence of prognosis improvement after this procedure.

**Class of recommendation IIb, level of evidence B.**

5.11.3. Mitral valve surgery

In patients with ischaemic left ventricular dysfunction and severe mitral valve regurgitation, mitral valve surgery should be considered when coronary revascularization is an option.

**Class of recommendation I, level of evidence C.**

Surgical correction in patients with non-ischaemic left ventricular dysfunction may improve symptoms.

**Class of recommendation IIa, level of evidence C.**

5.11.4. Aortic valve replacement

It is recommended in patients with severe aortic valve stenosis, as well as in patients with both aortic valve stenosis and LV dysfunction. Severe aortic regurgitation may be considered for replacement before important LV dilatation and remodelling occurs.

**Class of recommendation I, level of evidence C.**

5.12. Heart transplantation

Heart transplantation is an accepted treatment for patients in end-stage heart failure with no alternative form of medical therapy [77]. Patients in NYHA class IV (or advanced III) with severe LV dysfunction (EF < 20%) and poor prognosis should be considered. End-stage heart failure is mostly due to ischaemic heart disease or dilated cardiomyopathy. Dyspnoea and fatigue are most limiting factors. Patients with severe angina pectoris or severe rhythm disturbances with no alternative treatment options may exceptionally be considered for CTX.

In patients in NYHA III class, expectation of survival and prognosis is decisive. The assessment should be comprehensive, including spiroergometry. Indications for CTX are summarised in Table 22. Peak VO₂ ≤ 10 ml/kg/min is a clear indication for CTX, with peak VO₂ above 14 ml/kg/min, the CTX is usually not necessary. When the values are between 10–14 ml/kg/min, the presence of hyperventilation helps assess stratification (VE/VCO₂ slope > 35 represents worse outcome).

Indications for cardiac transplantation are summed up in Table 23.

Contraindications for cardiac transplantation are shown in Table 23.

Patients after heart transplantation require continuous long-term care provided by specialized cardiology centre in cooperation with a cardiologist. The greatest complications during first months following surgery are graft rejection and infections, hypertension, obesity, hyperlipidemia, osteoporosis, renal failure, cardiac allograft vasculopathy and increased incidence of malignancies. Heart transplantation significantly improves patients' quality of life and prognosis. Perioperative mortality is approximately 10%, 1-year survival 80% and 5-year survival around 70%. The heart transplant programme is limited, depending on number of donors, therefore this treatment can be offered only to a fraction of patients suffering from heart failure.

**Class of recommendation I, level of evidence C.**
5.13. Palliative care of patients with end-stage heart failure

Chronic heart failure leads, sooner or later, to death. It may be sudden, based on malignant arrhythmia or pulmonary embolism, or terminal failure of the heart as a pump. In the latter case the close cooperation of health care professionals, the patient and close relatives is necessary to comfort the dying patient. Patients in terminal phase must be free of agonising pain and dyspnoea and their fear of dying should be moderated. In case the patient has an ICD, its inactivation may be offered. The use of opiates, inotropic agents and high-dose diuretics to alleviate the symptoms should not be feared [78–81].

6. Heart failure management programs

Any physician should be able to diagnose acute heart failure, ensure basic treatment and refer the patient to the closest intensive care unit at the internal medicine department or coronary care unit at cardic centre. Most ambulances are equipped with 12-lead ECG, often connected to the closest coronary care unit or invasive angiography department and in case of acute coronary syndrome with heart failure, take the patient directly to one of these specialized centres.

Should the first contact physician discern signs of heart failure in his patient, clinical examination, ECG, chest X-ray and basic laboratory tests should be performed and the patient referred to a cardiologist? The cardiologist should ensure the echocardiogram, BNP or NT-pro-BNP testing and consider further specialized exams.

A patient with chronic heart failure should be taken care of by a cardiologist cooperating with the general practitioner. The heart failure issue has become important to such an extent, that it is advisable to establish specialized outpatient centres and departments within inpatient cardiology departments. In patients with severe left ventricular dysfunction or advanced/end-stage heart failure, it is necessary to refer them to a heart transplant centre.

Patients with left bundle branch block in NYHA III or IV class, or patients in NYHA I–III class with malignant arrhythmias should be referred to a centre specialized in resynchronization therapy and implantation of ICDs. In patients with advanced heart failure possibly eligible for heart transplantation, it is recommended to contact the heart transplant centre, where the resynchronization or and ICD implantation could be performed as a bridge to transplantation.

Patient with stable heart failure should be taken care of by general practitioner, including drugs prescription. The general practitioner manages the timing of further check-ups, which should be indicated with any clinical deterioration. With every check-up the history should be updated, clinical examination with blood pressure and pulse measurement performed. An ECG, chest X-ray and basic laboratory tests should be carried out at least once a year. At least once in 6 months a check-up by a cardiologist should be arranged. The cardiologist indicates specialized examinations such as echocardiography and other.

The health condition of patients with heart failure may often require hospitalisation. These patients should be hospitalised at cardiology units within internal medicine departments at the catchment area hospital. According to the results of the EURO HEART SURVEY, 25% of patients hospitalised at internal medicine departments in Czech Republic have chronic heart failure and the in-hospital mortality is 7%.

Patients being prepared for prospective heart transplantation should be examined on an inpatient basis in heart transplant centres. In Czech Republic these are currently Cardiology Department, Institute of clinical and experimental medicine (IKEM) in Prague (Klinika kardiologie, IKEM, Praha) and 1st Department of Internal Medicine, Cardioangiology, St. Anne’s University Hospital Brno (I. interní-kardioangiologická klinika FN u sv. Anny v Brně). The surgery itself is performed at Cardiovascular surgery clinic IKEM Prague (Klinika kardiovaskulární chirurgie Praha) and Cardiovascular Surgery and Transplant Centre in Brno (Centrum kardiovaskulární a transplantační chirurgie Brno). The resynchronization therapy and implantation of ICDs is performed by most of larger hospitals (University Hospital, Hospital Na Homolce, IKEM Prague etc.).

References

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