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## **Expert opinion of the Heart Failure Association of the Polish Cardiac Society and the Polish Psychiatric Association on the management of patients with heart failure and selected mental disorders (depression, anxiety disorders, sleep disorders, delirium)**

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**Expert opinion of the Heart Failure Association of the Polish Cardiac Society and the Polish Psychiatric Association on the management of patients with heart failure and selected mental disorders (depression, anxiety disorders, sleep disorders, delirium)**

**Short title:** Expert opinion of the HFA of the PCS and the PPA on the management of patients with HF

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**ABSTRACT**

The most common mental disorders in patients with heart failure (HF) include depression, anxiety disorders and sleep disorders, and in hospitalized HF patients — delirium. In patients diagnosed with HF, depression and anxiety are associated with an increased incidence of HF-related hospitalization and mortality. The vast majority of people with HF report poorer sleep quality and/or insomnia symptoms, which are associated with a decrease in exercise capacity and contribute to an increased risk of HF development. Delirium typically occurs in the course of acute HF, most often as hyperactive delirium. The occurrence of delirium in patients with acute HF adversely affects prognosis.

The basic pathophysiological mechanisms linking mental disorders with HF include oxidative stress, stimulation of the sympathetic nervous system and the immune system dysregulation.

Validated scales and questionnaires accepted by the Polish and European Psychiatric Association are applied to diagnose mental disorders. Basic antidepressants belong to selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors and drugs of other mechanisms of action. In addition to pharmacotherapy, psychological and psychotherapeutic interventions, psychoeducation, stress management and relaxation training, as well as spiritual care can also be applied. If the needs are more complex, palliative care should be considered at any stage of life with the disease, not only as the end-of-life care. The treatment of delirium, especially in hospitalized elderly patients, still remains a challenge.

This opinion defines the competencies of cardiologists and psychiatrists in mental disorders treatment in patients with HF and indicates how to manage patients in their treatment process. Diagnosis of mental disorders is essential for the appropriate treatment and improvement of the prognosis for patients with HF.

**Key words:** heart failure, psychiatric disorders, treatment

## **INTRODUCTION**

Heart failure (HF) is a syndrome that afflicts 1%–2% of the population and affects about 64 million people worldwide. The prevalence of HF is steadily increasing due to the aging of the population and increasingly better and effective treatments of many cardiovascular diseases [1, 2]. The mortality rate, however, remains high despite advances in HF treatment: about 50%–75% of patients with HF die within 5 years of diagnosis [1]. Heart failure is also associated with deteriorated quality of life, as well as frequent hospitalizations and high healthcare costs [1–3]. About 1.3 million people in Poland are estimated to suffer from HF. Of all the Organization for Economic Co-operation and Development (OECD) members, Poland is the country with the highest number of HF hospitalizations [4].

Patients with HF frequently suffer from mental disorders which lead to negative health and cardiovascular outcomes. Depression and anxiety disorders are the most commonly diagnosed mental health conditions in patients with HF [3]. Moreover, patients with HF often complain about sleep disturbances and/or insomnia, and elderly people are also afflicted by somatic delirium.

Depression is encountered in 42% of patients with HF, and a high severity of the condition is diagnosed in half of them [5]. Depression is more commonly encountered in women and is associated with a 32% higher risk of death and a 19% higher risk of cardiovascular events [5]. Up to 50% of patients with HF develop anxiety disorders, usually generalized anxiety disorder (GAD), less commonly post-traumatic stress disorder and panic disorder whereas clinically significant levels of anxiety are identified in almost 30% of patients. The comorbidity of depression and anxiety in patients with HF contributes to a significant reduction in the quality of life, an increased risk of ineffective cardiac treatment, a rise in the number of rehospitalizations and an elevated mortality rate [6–8]. Importantly, major depressive disorder is not only one of the potential consequences of HF, but it may also be a contributing factor to HF onset. The co-occurrence of anxiety can reduce the effectiveness of antidepressants and lead to persistent depression [3].

As many as 73% of patients with HF report poor sleep quality, and many of them have poor sleep continuity (34%–43%), difficulty falling asleep (23%–47%) and early awakening (35%–39%). What is also commonly observed is insomnia symptoms which are associated with an impaired functional performance, including diminished exercise capacity, a decreased distance walked in the 6-minute walk test (6MWT), and lower levels of self-rated physical fitness [9, 10]. The symptoms were also reported to be associated with an increased risk of HF development [11].

The available studies reported the incidence of delirium in patients with acute heart failure (AHF) to reach 17%–27% [12, 13]. Delirium is characterized by disturbances of consciousness and is typically observed in the early phase of AHF, but it can also be identified in a relatively later AHF phase, i.e. after 10 or more days. In more than 80% of patients with AHF, delirium is hyperactive, with increased motor activity, accompanied by mood swings, agitation and aggressive behavior. The prognosis of patients with AHF and delirium was reported to be worse than their counterparts without delirium [13].

Despite the significant adverse impact of anxiety, depression and sleep disorders on HF onset, progression and HF treatment effects, they are still insufficiently diagnosed and treated in this group of patients.

## **PATHOPHYSIOLOGICAL MECHANISMS OF BASIC MENTAL DISORDERS**

The prevalence of mental disorders such as depression and anxiety disorders are closely related to the pathophysiology of HF [14]. Higher HF risk in patients with mental disorders may result from

an interplay of a number of pathological processes, such as increased oxidative stress, lifestyle-related metabolic changes, autonomic nervous system (ANS) imbalance, hormone imbalance and immune dysregulation (Figure 1).

The available studies have revealed that mental disorders lead to increased oxidative stress and the activation of inflammatory processes which play a key role in HF development [15]. Increased production of reactive oxygen species (ROS) in HF contributes to the disease progression. However, normal antioxidant enzyme activity is preserved, which suggests the imbalance between ROS production and antioxidant defense mechanisms [16].

A relationship has been shown between mental disorders and lifestyle defined by an unhealthy diet, tobacco smoking and physical inactivity which all influence the development of cardiovascular diseases (CVDs) [17]. Some studies indicated an excessive consumption of sugar-sweetened beverages as a risk factor for depressive symptoms [18].

Mental disorders disturb the balance of the autonomic nervous system activity and adversely affect the cardiovascular system functioning [19]. The high risk of CVDs recorded shortly after the diagnosis of mental disorders may indicate a direct impact of stress-induced hypothalamic activation on the changes in sympathetic nervous systems. The sympathetic nervous system activation can potentially lead to an increased blood pressure, tachyarrhythmias, or a decrease in heart rate variability [19]. Pathophysiological processes which accompany stress may contribute to increased cardiac electrical instability, myocardial ischemia, atherosclerotic plaque rupture, and elevated prothrombotic readiness [20].

Some antidepressants and psychotropic drugs were found to produce hypertensive effects and entail the risk of complications associated with QTc prolongation [21, 22].

Depression is characterized by elevated levels of inflammatory markers such as C-reactive protein, interleukin-6, and fibrinogen. Their elevated levels were observed to correlate with an increased risk of CVDs development and they may contribute to increased susceptibility to HF in people with depression [23–24].

## **SCREENING FOR MENTAL DISORDERS IN PATIENTS WITH HEART FAILURE**

Correct diagnosis of depressive disorders in patients with chronic somatic diseases, including HF, can be challenging owing to the less typical picture of the disease. The symptoms predominantly include fatigue, exhaustion, insomnia, lack of appetite, decreased activity, worries about the future,

and decreased libido whereas low self-esteem, guilt, tearfulness, suicidal thoughts, and deep depression are recorded rarely. Mild severity of depression and the predominance of somatic symptoms cause physicians to attribute the patient's poor subjective well-being to their physical condition and medications taken [25]. The diagnosis of depression must rely on the examination of patients, contact with them and a thorough assessment of their mental state and psychological problems. Commonly used scales (e.g. PHQ-9) which measure the severity of depressive symptoms are also advisable, however, it should be remembered that although valuable, they are only auxiliary tools in the mental state assessment, and the score obtained does not suffice to authorize a diagnosis, being all the more insufficient to plan a therapeutic strategy.

Along with depression, anxiety also poses a serious problem in patients with HF [26]. The comorbidity of anxiety hinders the patient adaptation to the situation linked to disease-related difficulties, it is associated with a worse quality of life and greater difficulties absorbing medical recommendations, and it hampers the progress of rehabilitation after an acute cardiac episode. Anxiety experienced by patients with cardiac diseases is a predictor of greater severity of symptoms of the underlying disease and, consequently, a higher degree of functional impairment. When assessing the anxiety level in patients with somatic diseases, particular attention should be paid to the patients' self-reports, as the measurement of symptoms regarded as the "indices" of anxiety (e.g. heart rate or blood pressure) are not reliable measures in patients with cardiovascular diseases [27].

## **SCREENING FOR MENTAL DISORDERS IN PEOPLE WITH HEART FAILURE AND SELF-REPORT SCALES**

The identification of psychopathological symptoms and their severity assessment in patients with HF should be based on clinical history and observation of the patient. However, the context of the treatment and the contact with the patient, especially in an outpatient setting or in the absence of a mental health specialist in the medical team, often makes it impossible to fully assess the patient's mental state. In such situations, it is advisable to use diagnostic questions and self-report scales of a screening nature. The scales facilitate the identification of patients with an increased level of symptoms indicative of psychological issues and allow to refer them to a comprehensive assessment of their mental state. Currently, several questionnaires are available as screening tools for mood, anxiety and sleep disorders. The scales feature good psychometric properties, which

allows for reliable and accurate identification of people who require additional psychological care or specialist psychiatric diagnosis and potential pharmacotherapy. When selecting the appropriate tool, it is advisable to use the versions adapted to the Polish population.

### **Assessment of depression symptoms**

In accordance with the current recommendations of scientific and clinical societies, such as the European Society of Cardiology or the British National Institute for Health and Care Excellence (NICE), and with reference to the guidelines of the Polish Psychiatric Association and recommendations developed as part of the implementation of the depression prevention program in Poland for 2016-2020, financed by the Minister of Health, it is noteworthy that regularly repeated screening for mental disorders is an important element of health care, especially for people with chronic somatic diseases, including HF [28–31].

When recognizing potential symptoms of depression, the aforementioned recommendations suggest the use of the following two depressive symptoms-related questions:

1. Over the last month have you often been bothered by feeling down, depressed or hopeless?
2. Over the last month have you often been bothered by little interest or pleasure in doing things?

They facilitate the recognition of depressed mood and anhedonia symptoms.

The questions are also included in the Patient Health Questionnaire (PHQ-2), which patients complete based on their feelings over the past two weeks. The questionnaire is most frequently recommended as a self-report screening test, it is easy to introduce into daily practice and clinical evaluation procedures in HF patients.

If depressive symptoms are confirmed in a screening test, an extended assessment of the patient mental status is worth considering by referring the patient to a specialist or by using scales that assess a larger number of symptoms, which allows for a more comprehensive picture of the patient psychosocial functioning. NICE suggests additional three questions regarding self-esteem, cognitive processes and suicidal ideation to be applied for people with somatic and PHQ-2-confirmed symptoms. Affirmative answers to the following questions should suggest that the patient be referred to specialist psychiatric diagnosis and care [29]:

1. Have you felt worthless in the last month?



2. Have you had trouble concentrating?
3. Have you had suicidal thoughts?

Other questionnaires included in **Table 1** [32–35] are also used to identify depression in people with HF. Among those listed in the table, the PHQ-9 questionnaire is the most frequently recommended. It is a simple self-report scale which includes 9 items concerning the depressive symptoms and 1 additional item about the feeling of being burdened by the symptoms and their impact on everyday functioning. A score of 5 points and above is indicative of an increasing risk of a depressive episode. Good psychometric properties of the Polish version of the PHQ-9 scale were confirmed and it is suitable for the adult population (18–60 years of age). Its availability in the public domain is another advantageous feature of the tool as the purchase of a license from the publisher is not required for the questionnaire to be used [34, 35].

The Hospital Anxiety and Depression Scale (HADS), originally developed for the hospital setting, is a self-administered questionnaire to assess the severity of anxiety (HADS-A) and depression (HADS-D). The Scale is composed of two subscales, each with 7 items rated from 0 to 3. A score of 8 points and above indicates an increasing risk of the assessed disorders. The HADS scale has been adapted to Polish population with psychosomatic disorders [36] as well as to the general population with elevated stress indicators [37].

### **Assessment of anxiety disorders symptoms**

A diagnostic interview towards symptoms of anxiety disorders should include two questions regarding the symptoms of increased anxiety levels:

1. Have you often felt nervous, anxious, or very tense over the past month?
2. Over the past month, have you often been unable to stop worrying or to control it?

The questions facilitate the recognition of the potential existence of anxiety disorders in the patient.

The patient answers the questions based on the feelings experienced in the last two weeks. The presence of the above symptoms implies that the patient should be referred for their mental status extended evaluation, and psychiatric or psychological care. Currently available questionnaires for the assessment of symptoms of severe anxiety and anxiety disorders are included in **Table 1** [33, 34]. Among the scales available in Poland, the Generalized Anxiety Disorder (GAD-7)

questionnaire is the most frequently recommended to diagnose somatic patients. The GAD-7 scale includes 7 items used to assess the anxiety level, as well as the risk of generalized anxiety disorder. The questions in the scale enable the assessment of the sense of anxiety, tension, nervousness, worry, as well as the ability to control these feelings and the problems with relaxation. Affirmative answers to these questions facilitate the identification of people who require additional psychological care or specialist psychiatric diagnosis. A score of 5 points and above indicates an increasing risk of anxiety disorders. The scale has good psychometric properties, it was designed to assess the severity of anxiety symptoms in the adult population and the questionnaire is available in the public domain [34, 38].

### **Screening for sleep disorders**

Screening for sleep disorders is rarely performed as a routine diagnostic procedure in HF patients' health status assessment, although the relationship between sleep deficits and the somatic and mental status of cardiac patients is of considerable clinical significance [39, 40]. The assessment regards the period of three weeks back (chronic insomnia). Attention should be paid to difficulties in daytime functioning and feeling rested in the morning.

One of the following questions which are also included in the PHQ-9 scale with regard to depressive symptoms, can be used to assess sleep disorders:

1. Do you have trouble sleeping?
2. Do you have problems with falling asleep, interrupted sleep or sleeping too much?

A number of questionnaires are available to assess the presence and severity of sleep disorders symptoms, and they are presented in **Table 1** [40, 41]. The Insomnia Severity Index (ISI) or the Athens Insomnia Scale (AIS) are advisable as screening questionnaires for sleep disorders due to their good diagnostic properties and short completion time. The AIS includes 8 questions about the amount and quality of sleep and physical and mental well-being [42]. Its Polish version has been validated for use in the Polish population and its good psychometric properties have been demonstrated. The ISI, on the other hand, includes 5 questions about the severity of sleep problems, the impact of sleep disorders on daily functioning and quality of life, and the degree of worry about sleep disorders. Its good psychometric properties have also been confirmed [43].

## **Screening for delirium**

The tools which have proven useful in practice include the Mini Mental State Examination (MMSE) scale applied in dementia assessment or Polish adaptation of the Confusion Assessment Method (CAM), designed for non-psychiatrically trained staff to identify and recognize delirium at the patient's bedside [44]. The Schuurmans Delirium Observation Scale (DOS) (interpretation: three or more symptoms indicate delirium), which includes the following items, is also considered to be of great use [45]:

1. falls asleep during a conversation or activity;
2. easily distracted by external stimuli;
3. not holding attention in conversation or activity;
4. does not complete the question or answer;
5. gives answers that do not match the question;
6. slow to respond to instructions;
7. he/she thinks he is somewhere else;
8. he/she does not know what time of day it is now;
9. does not remember recent events;
10. restless/agitated/nibbling;
11. removes cannula, probes, catheters, etc.;
12. easily or rapidly changes emotionally (fear/anger/irritability);
13. he/she sees, hears things that are not there.

## **INITIAL DIAGNOSIS AND VERIFICATION OF THE MOST COMMON MENTAL DISORDERS IN PATIENTS WITH HEART FAILURE**

### **Episode of depression**

An episode of (mild, moderate or severe) depression is diagnosed when the symptoms remain for at least 2 weeks and cause significant functional impairment. The most commonly reported symptoms include depressed mood, anhedonia, lack of energy, increased fatigue, somatic complaints, non-specific “tension”, pain and anxiety symptoms, including free-floating, generalized anxiety. Other symptoms are listed in [Table 2](#).

Recurrent depressive disorder is recognized after the second episode of depression.

Dysthymia is defined as a chronic sub-depressive condition (characterized by less severe depressive symptoms, duration of at least 2 years, without significant functional impairment).

Diagnosis of depression (including differential diagnosis) should involve basic laboratory tests that are helpful before treatment implementation (complete blood count, the level of glucose, urea, creatinine, serum sodium and potassium, liver enzymes (AST, ALT, GGTP), thyroid-stimulating hormone).

## **Anxiety**

Anxiety is a natural emotional response while being, at the same time, a warning signal that allows us to react and gain experience. When the response is disproportionate to the stimulus, it becomes the cause of individual suffering and deteriorated functioning. Anxiety disorders can take many different forms: phobias (agoraphobia, simple and specific phobias); anxiety disorders with panic attacks, generalized anxiety, somatic symptom disorders, and psychoactive substance use disorders. Anxiety disorders (especially panic attacks) are a common reason why patients seek emergency medical help.

Somatic, psychiatric and behavioral symptoms are assessed during the evaluation of patients' mental status and observation of their behavior (Table 2).

The diagnostics are complemented by a somatic and psychiatric history as well as basic laboratory tests (complete blood count, electrolytes, glucose, thyroid-stimulating hormone levels), electrocardiography. Anxiety disorders are differentiated from psychotic disorders and psychoactive substances-induced conditions (psychedelic state, the so-called "bad trip", during substance use, or the withdrawal syndrome). In order to verify the initial diagnosis many anxiety-inducing somatic diseases must be excluded: hyperthyroidism, hyperparathyroidism, pheochromocytoma, hypoglycemia, cardiac diseases (arrhythmias, myocardial infarction, circulatory failure, mitral valve prolapse, hypertension), neurological diseases (inner ear dysfunction, epilepsy), chronic obstructive pulmonary disease, asthma, and even the intake of thyroid hormones, corticosteroids, analgesics and anesthetics, antidepressants or antipsychotic drugs.

## **Sleep disorders**

Insomnia is defined as disturbances in the quantity, quality or the time of sleep, including difficulties in sleep initiation and continuity, early wake-up, experienced at least three times a week for at least a month, which leads to poor subjective well-being and deteriorated daytime functioning. Sleep disorders can take the form of dyssomnia and parasomnia (Table 2).

Sleep disorders are the most commonly reported concerns which can sometimes be excessively reported and need to be objectively verified.

The AIS scale is useful, however, what is crucial in the diagnostic process of sleep disorders is a detailed interview pertaining to the mental state (the occurrence of depressive, anxiety, psychotic disorders), neurological status (i.e. stroke, dementia, Parkinson's disease, headaches and injuries, polyneuropathy), as well as somatic diseases (arrhythmias, ischemic disease, circulatory failure, chronic obstructive pulmonary disease, asthma, peptic ulcer disease, irritable bowel syndrome, diabetes, thyroid dysfunction, rheumatoid arthritis, fibromyalgia, bruxism and others). The potential impact of mucosal decongestants, stimulants, narcotic analgesics, antidepressants, and cardiovascular medications (especially beta-blockers and diuretics) should also be taken into account. Polysomnography is recommended if sleep apnea or narcolepsy is suspected. Understanding the nature of insomnia symptoms and their relationship to daytime symptoms and functional performance is essential for targeted treatment of sleep disorders in patients with HF.

## **Delirium**

Delirium is a non-specific etiologically organic brain syndrome manifested by disturbances of consciousness of varying intensity and duration, usually with acute or subacute onset, impaired attention, disturbed thinking and perception and loss of the ability to assess environmental stimuli, which results in disorganized speech and functioning, and inadequate behavior. The mental status evaluation includes the assessment of the characteristic symptoms listed in Table 2.

Delirium requires differentiation from psychoses, including schizophrenia, organic hallucinosis (where disturbances of consciousness are not observed but psychotic symptoms occur) and dementia (in the course of which episodes of delirium may occur) and complicated withdrawal syndrome (stimulation of the vegetative system with sweating, facial redness, dilation of the pupils; exaggerated tendon reflexes). In each case, it is essential to perform a physical examination, including neurological assessment, and full laboratory diagnostics, including toxicology. If meningeal symptoms are found, a cerebrospinal fluid test is to be performed. Occasionally, when

the underlying cause cannot be identified, it is diagnostically helpful to perform heavy metals tests, tests for syphilis, HIV, ammonia concentration in hepatic encephalopathy or arterial blood gases in hypoxia and acid-base imbalance, and neuroimaging tests (computed tomography, magnetic resonance imaging).

## **PHARMACOLOGICAL TREATMENT OF MENTAL DISORDERS IN PATIENTS WITH HF**

### **Treatment of depression and anxiety in heart failure**

Cardiologists or family doctors are typically the first medical specialists that encounter the symptoms of mental disorders in a patient with HF. The situations when patients promptly recognize the initial symptoms and spontaneously report to a psychiatrist are rare. Moreover, despite the growing awareness of the significance of mental disorders, patients often avoid psychiatrists and psychiatric treatment and seek "alternative therapy options". It is therefore the role of the physician (a cardiologist or family doctor) to early identify mental disorders and then implement treatment individually or upon consultation with a psychiatrist. There is no doubt that the basic principle the physician should be guided by is substantive and immediate action. Below, we present proposals for the hospital and outpatient clinic interventions. Most of the procedures overlap, however, obtaining both the patient's consent to a quick psychiatric consultation and the consultation itself are significantly easier when patients are being hospitalized, which is worth taking advantage of (Figure 2).

### ***Situations when psychiatric consultation is absolutely necessary***

Pursuant to Article 10 of the Code of Medical Ethics, the physician should not exceed his/her capacities and knowledge in undertaking diagnosis and therapy, therefore, the doctor's lack of certainty as to the diagnosis and treatment is the basic (and actually exclusive) and absolute indication for a psychiatric consultation [46]. Nevertheless, it seems appropriate to seek advice from a psychiatrist in the event of diagnostic complexity (e.g., when bipolar disorder or psychotic symptoms are suspected), in cases where suicidal thoughts are difficult to exclude, in pregnant and lactating women, and in patients who have previously been ineffectively treated psychiatrically. In the event of a threat to the patient's life due to suicidal thoughts, hospitalization is vital.

## ***Psychotropic drug selection***

### *Safety of antidepressants*

The safety of antidepressant medications in the management of HF has been extensively demonstrated in the available meta-analyses [47, 48]. First-line drugs in both depressive and anxiety disorders therapy in patients with HF include selective serotonin reuptake inhibitors which are characterized by high efficacy and a very good safety profile. The SADHART study demonstrated the safety of sertraline application in cardiovascular diseases [49, 50]. The study reported that early initiation and a fairly high dosage of the analyzed agent demonstrated its efficacy in 85% of patients, i.e., a higher number than in everyday clinical practice. The list of safe antidepressants also includes other SSRIs: citalopram, escitalopram, and the less commonly used paroxetine [47, 50]. Mirtazapine is a very commonly applied medication, especially in the elderly, although few studies have confirmed its safety [51]. In patients with a high risk of ventricular arrhythmias, bupropion is also considered to be a safe option [52], however, from the author's subjective standpoint, SSRIs should remain the first-line medication. When warfarin is incorporated in HF management, it should be remembered that prolongation of prothrombin time could be a potential consequence. The use of escitalopram is contraindicated in patients with QT interval prolongation.

### *Principles of the drug selection.*

The two basic criteria for the medication selection are the drug safety and the current configuration of the patient's symptoms. The doctor's experience is also a selection criterion of some significance and, although important in practice, it is underreported in literature. The most beneficial strategy for a cardiologist or a family doctor is their good knowledge of 2–3 antidepressants and anxiolytics to use them freely in indisputable cases (Table 3). The available reports on the safety of antidepressants in cardiovascular diseases suggested that sertraline or escitalopram should be used as the therapeutic strategies of first choice. Good antidepressant and anxiolytic efficacy of both medications has been reported (although they differ in the registered indications for the treatment of anxiety disorders). Advice on a potential third drug choice poses a greater challenge, but a significant number of depressive patients with predominant anxiety or sleep disorders tend to opt for at least one antidepressant with a strong sedative or hypnotic effect. Such clinical features are

found in e.g., mitrazapine, mianaserin and trazodone. Even though these drugs are frequently used, their application in HF patients has been scarcely investigated.

### *Drug posology*

Ineffectiveness of pharmacotherapy with antidepressants and anxiolytics does not always result from incorrect drug selection, but most frequently from too low dosage or too short drug use duration. Treatments should be carried out with the lowest effective dose, i.e. the general rule of dosage is: "*start low, go slow..., but go!*" It is good practice to administer half of the minimum dose for several days, then set the dose at the lower limit of the therapeutic window and monitor the treatment outcomes and adverse drug reactions (Table 3). When no response is observed, the dose should be increased every 2–3 weeks (with continuous monitoring of drug efficacy and tolerance) until remission, maximum permissible dose or intolerance threshold are achieved. Drug intolerance or no response to the maximum tolerated dose for 2–3 weeks are the indications to change the medication. The treatment of depression should not only aim at alleviating the symptoms, but also achieving remission, as the persistence of residual symptoms is associated with a 2–3 times higher risk of relapse, a shorter timespan to the next episode, a larger number of episodes, a higher risk of suicidal ideation, and worse functioning [53].

### *Treatment duration*

Mental disorders in HF are usually chronic and require a long-term treatment. In practice, the maintenance dose is usually equal to the dose with which remission was achieved. Potential dose reduction should not be considered until several months of remission (which should not be confused with a relief of symptoms). Any potential dose reduction should be managed cautiously and very slowly, preferably spreading it out over many months. The decision to discontinue an antidepressant in a patient with HF is always very difficult thus prior to such a decision, at least the following rationale should be acknowledged:

- a chronic, debilitating disorder is already a serious stressor, and thereby a depression and anxiety-maintaining factor;
- there are common pathogenetic processes of anxiety and depression as well as cardiovascular diseases, and achieving remission is not synonymous with extinguishing these processes;



- it should be considered whether the benefits for the patient from drug withdrawal outweigh the risk of relapse of depression/anxiety.

### **Management of sleep disorders**

Sleep disorders in patients with HF may result from an underlying pathology, i.e., dyspnea which is induced/intensified in the supine position and when skeletal muscles are relaxed. Obviously, sleep-inducing drugs will be ineffective in such patients. In other cases, it should always be considered whether insomnia is a separate disorder or a symptom of a depressive or anxiety syndrome. Patients with reduced introspection frequently report only shortened and fragmented sleep out of all depressive symptoms, or from the anxiety symptoms they only recognize sleep disorders. It is also not uncommon (especially for males) to dissimulate depressive disorders and to accept only the diagnosis of sleep disorders. It is for these two reasons that insomnia often appears to be a symptom of a more serious disorder and prompts to a discussion on a long-term treatment. Antidepressants with hypnotic effects (mirtazapine, mianserin, trazodone, agomelatine) are recommended in these cases.

Although this chapter discusses pharmacological therapies, we cannot omit to underline that before sleep-inducing drugs are included, the patient's daily routine must be analyzed and education on sleep hygiene must be provided. If behavioral interventions prove ineffective and no indications for the inclusion of antidepressants are found, the patient should be encouraged to consult a psychiatrist. Hypnotics (zolpidem, zopiclone, eszopiclone, zaleplon) should be administered only for a very short period (up to 4 weeks including a period of slow tapering). Unfortunately, in practice, these time limits are not respected, which leads to addiction. If sleep-inducing drugs are used during hospitalization, the discharge card should include the information that they cannot be applied for a long-term treatment of insomnia disorder.

### **Treatment of delirium**

Therapeutic management of disorders of consciousness requires:

1. identification of the causes and attempts to eliminate them;
2. general somatic condition assessment, supported by a detailed medical history taken from relatives or staff;
3. analysis of previously used drugs and verification of indications for their continuation, taking into account drug-drug interactions;

4. regular control of the patient's mental state and behavior with constant supervision and follow-up:
  - reduction of sensory-stimuli surplus (sound, light),
  - ensuring an optimal circadian rhythm (*clear day vs. night differences in lighting and the number of stimuli*),
  - cognitive deficits reduction at the level available to the patient,
  - emotional overload avoidance;
5. systematic control of the somatic condition and prevention of further complications by:
  - ensuring the best possible brain perfusion,
  - monitoring the levels of hydration, glucose, oxygen saturation, electrolytes, proteins, and other abnormalities identified in laboratory test,
  - treatment of infections, in particular the urinary and respiratory tract infections,
  - treatment of thromboembolic complications and decubitus ulcers related to immobilization caused by somatic status and/or the use of mechanical restraint,
  - management of consequences of falls, especially in restless patients,
  - pain reduction.
6. early mobilization and rehabilitation with the patient-adjusted stimulation (prevention of daytime sensory deprivation, calm environment facilitating orientation in time, place and situation, nighttime stimulus control). Providing the maximum activity available to the patient (preferably *active exercises if it is not possible — passive ones*).
7. psychotropic drugs application only in significant agitation, aggression and disorganized behavior (**Table 4**). Their use is justified only when non-pharmacological treatment is ineffective:
  - hypokinetic delirium is not an indication for neuroleptic drugs administration, and the improvement of cerebral circulation and cholinergic transmission should be sought, in hyperkinetic delirium, neuroleptics (e.g., haloperidol, quetiapine) are used, and in sudden agitation - dexmedetomidine, haloperidol are applied,
  - benzodiazepine derivatives and Z-type drugs should be avoided as they may prolong delirium course,

- most studies on the use of neuroleptic drugs in the elderly report an increased risk of death (although delirium poses a higher risk), so once sedation is achieved, the dose should be reduced quickly and the medication should be discontinued.

In significant agitation, with disorientation, anxiety or aggression, the use of direct coercion by the patient's isolation and immobilization with two or four magnetic belts should be considered. The procedure is described in the regulation of the Minister of Health. When mechanical restraint is used, the fact must be reported to the hospital management immediately and constant monitoring of the patient's condition and recording it every 15 minutes in an appropriate observation form must be performed.

### **Management of mental disorders in patients with heart failure**

Treatment of mental disorders in patients with HF entails the need to take into account both drug-drug interactions and potentially reduced drug tolerance. On the other hand, mental comorbidities in HF, especially depressive disorders, increase the importance of achieving remission for overall health status. There is evidence that remission of depression improves the prognosis in cardiovascular diseases by reducing the risk of major adverse cardiac events (MACE) and that active post-hospital mental health care reduces the number of rehospitalizations [54, 55]. Therefore, delayed implementation of antidepressant treatment or avoidance of dose increases should not take place.

Psychiatric management of a “drug naive” patient does not differ from the one described above. However, patients are often referred to a psychiatrist after unsuccessful attempts at treatment or with an unusual picture of the disease. The psychiatric visit should involve the diagnosis verification and the antidepressant/anti-anxiety treatment analysis including the adequacy of drug selection and posology, as well as the duration of therapy with appropriate doses. If improper dosage or inappropriate therapy duration are found, re-administration of previously used drugs at the correct doses should be considered. In cardiac patients, only the conviction that first-line drugs are actually ineffective should be a prerequisite for the inclusion of other substances.

If good common sense is used i.e., tricyclic antidepressants, unproven drug combinations, too high dosage are avoided and drug-drug interactions are not ignored, the drug selection in this group of patients does not differ from other populations. It is worth remembering that patients with

HF are usually well monitored and possible cardiac side effects are quickly detected. The cardiologists who provide care for this group of patients are less concerned about the necessity to modify the basic treatment than about the patient's anxiety that disorganizes the treatment or their inhibition which hinders rehabilitation. That is why to act quickly is of great importance. In patients with anxiety and sleep disorders, mirtazapine should be considered, and if contraindicated, trazodone could be applied. Selective serotonin and norepinephrine reuptake inhibitors: venlafaxine and duloxetine may offer a good option in patients with inhibition and concomitant pain. With regard to duloxetine, it is noteworthy that it has been shown that the risk of MACE is not increased by the treatment, but by the very fact of depression [56]. As far as cardiac safety and antidepressant dosage are concerned, we must mention a study of 2013 which questioned the FDA warnings about the risk of abnormal heart rhythms, including *torsade de pointes*, when citalopram is prescribed at doses exceeding 40 mg [57]. The study demonstrated that higher doses of citalopram were associated with lower risks of ventricular arrhythmias and lower all-cause mortality. Consistent observations were recorded for sertraline, where no significant relationship was found between the daily dose and all-cause mortality [58].

The conclusion from these studies is unequivocal: depression treatment should be performed with an effective dose.

### **COORDINATED CARE FOR PATIENTS WITH HF AND MENTAL DISORDERS**

The concept of coordinated heart failure care (Polish: KONS) focuses on patients hospitalized for decompensated HF who are offered post-hospital medical supervision provided by outpatient specialist care (Polish: AOS) and primary health care (Polish: POZ). Patients with HF and comorbid mental disorders pose a particular challenge for cardiologists, and, unfortunately, too often mental disorders remain unrecognized and untreated. The quality of care in this area would certainly be improved if screening for the initial diagnosis of the most common mental disorders comorbidities could be provided under KONS in decompensated HF patients admitted to hospital, by using simple tools of self-report scales, as well as by providing consultations with a psychiatrist, psychologist or psychotherapist. Under the KONS program, cardiologists could play a linking role in the defragmented care (Figure 3). They could also initiate basic treatment for mild symptoms of mental disorders most often co-occurring with HF in accordance with local therapeutic protocols.

## **NON-PHARMACOLOGICAL, PSYCHOLOGICAL AND PSYCHOTHERAPEUTIC INTERVENTIONS**

### **Psychological and psychotherapeutic interventions**

When treating people with HF and comorbid mental disorders, it is important to build relationships based on trust and respect, and to remember that the diagnosis of mental disorders can be a source of anxiety for the patient and cause fear of stigmatization, which can affect the patient's attitude towards mental disorders treatment. Skillful communication of the observed symptoms, diagnosis and treatment options, with an emphasis on their importance for the quality of life and the effectiveness of HF treatment are therefore of vital importance in the therapy.

In addition to pharmacotherapy, effective treatment of mental disorders in people with HF may require the inclusion of psychological or psychotherapeutic care. The psychological interventions objectives include distress reduction, quality of life improvement, and support for patients' adaptation and motivation for self-care. Their effectiveness in reduction of anxiety and depressive symptoms and improvement of health-related quality of life has been demonstrated in reports on a variety of psychological and psychotherapeutic interventions. The available studies also support the impact of psychological care of patients with HF on their prognosis and hospitalization frequency thereby suggesting its importance in the multidisciplinary care provided for this group of patients [59, 60].

Psychological interventions in this group should be evidence-based and tailored to the patient's current needs and the treatment goals. It is recommended that psychological and psychotherapeutic assistance is provided by specialists with confirmed competence in psychological interventions and experienced in somatic patients care. Psychological strategies that may impact the quality of life of patients with HF and mental disorders include psychoeducation, psychological counseling, stress reduction and relaxation training, including mindfulness-based interventions, meditation, biofeedback and psychotherapy.

Due to the specificity of HF treatment, short-term intervention methods could be incorporated into the inpatient therapy. Psychotherapy is more advisable to be implemented on an outpatient basis as a longer therapeutic alliance is needed. Prolonged hospitalization is an exception to the rule, e.g., psychotherapy can be provided along the circulatory support.

### **Psychoeducation**

Educational interventions in people with HF and comorbid mental disorders have an impact on their understanding of the interrelationships between somatic and mental conditions and on reduction of their fear of revealing their emotional problems, which may increase the chances for therapy initiation. In the conversation with the HF patient concerning their mental health, it is advisable to emphasize the psychopathological symptoms impact on the quality of life and coping with everyday situations, as well as on the course of the underlying disease and the effectiveness of treatment, the risk of further decompensation and prognosis. Psychoeducational interventions provided for patients and their relatives are important for the increase in their awareness of HF, the quality of life improvement, and reduction of the burden of depressive and anxiety symptoms [61–63]. Psychoeducation is also applicable in somatogenic delirium in cardiovascular decompensation to create conditions that enhance the sense of security (Table 5).

When the disorders of consciousness subside, it is important to properly educate both the patients and their relatives about the specifics of the disorders. Patients should be informed that these disorders are relatively common in HF exacerbation, and medical staff should be aware that patients' potential inadequate behavior is a natural consequence of their condition. It is also essential to assure the patient that the occurrence of this type of disorder does not indicate the onset of a long-term mental condition, which is what the majority of patients are often concerned about.

### **Stress management and relaxation training**

Stress management training is a method of developing skills to recognize and reduce the symptoms of emotional tension and stress-induced physiological arousal. Its objective is to develop the skills to cope with difficult situations in a constructive way, i.e. developing mental resilience. Stress reduction methods applied in patients with HF and comorbid mental disorders include, among others, mindfulness-based interventions or meditation training. They facilitate the reduction in depressive and anxiety symptoms, improve health-related quality of life, and may also affect the patient's somatic state, which diminishes the risk of rehospitalization and improves prognosis [64, 65]. The relaxation training and psychological care incorporated in cardiac rehabilitation programs lead to improved quality of life and reduced symptoms of mood disorders and anxiety in patients with HF. Thus, referring a patient with HF and mental disorders to cardiac rehabilitation is worth considering as one of comprehensive treatment components.

## **Psychological counseling**

Psychological counseling is a method of psychological support to improve intra- and interpersonal functioning in the course of life. Such interventions aim to reduce the risk of persistent anxiety symptoms or mood disorders and to help patients restore their belief in their ability to effectively cope with the current situation and its consequences for their daily life. The process involves assistance for the patient in developing the best and most effective coping strategies for current distress-causing difficulties. The psychological counseling principles assume that it is a short-term help, which makes it particularly useful in several-day in-hospital patient care.

## **Psychotherapy**

Psychotherapy is the most effective of non-pharmacological interventions for people with HF and comorbid mental disorders, and psychotherapeutic interventions have been recorded as an important component of cardiac patient care, including those with HF [66]. Psychotherapy is a deliberate and planned psychological intervention intended for people with mental disorders aimed at alleviating or removing the disorder symptoms and improving mental and social functioning, supporting the individual's or family's aspirations for health and development. The advantage of psychotherapy is the adjustability of its course to the needs and capabilities of the patient. It facilitates the development of coping skills with the symptoms of mental difficulties, which can be helpful in various situations and reduce the risk of symptoms recurrence. Moreover, there is no evidence of adverse effects of psychotherapeutic interventions in this group of patients, which may be indicative of the intervention safety [3, 67].

In the multitude of therapeutic approaches for people with HF, it is advisable to select the cognitive-behavioral approach as its effectiveness in cardiac patients has been documented most extensively. The cognitive-behavioral approach, the essence of which is the identification and modification of maladaptive thinking patterns and behaviors, enables patients to increase their abilities to better cope with the symptoms of mental disorders and life difficulties. When applied in patients with HF, it allows to reduce the symptoms of depressive and anxiety disorders, improves health-related quality of life and reduces the risk of rehospitalization for HF [68].

Mindfulness Based Interventions offer a promising technique for developing stress management skills. Numerous studies have shown that classic mindfulness programs such as Mindfulness Based Stress Reduction and Mindfulness Based Cognitive Therapy can effectively

reduce symptoms of depression, anxiety, stress, chronic pain, or sleep disorders that are frequently concomitant with HF [69, 70].

Beneficial effects of cognitive behavioral therapy for insomnia were observed in patients with HF. The therapy models reduce sleep disorders symptoms, fatigue and daytime sleepiness, and improve physical well-being in this group of patients [71, 72]. Methods based on behavioral interventions (Brief Behavioral Treatment for Insomnia) are also effective in reduction of sleep disorders symptoms. However, it should be taken into account that previous studies in people with HF have been conducted in small samples [73]. Nowadays, online psychotherapy is also one of available intervention options. Contact with a psychotherapist via the available technologies allows people with severe HF symptoms or difficult access to a specialist (e.g., due to their place of residence) to receive appropriate help. Online interventions can have a positive impact on the self-care of people with HF and favorably affect their mental state.

## **STRATEGIES FOR PATIENT INVOLVEMENT AND ACTIVATION IN THE TREATMENT PROCESS**

The patient's acceptance of HF and the consequent necessary adjustment of their lifestyle are difficult and as such are stress-generating factors. To follow complex recommendations and self-care demands necessary to maintain physiological and emotional stability can often overwhelm the patients and lead to their confusion and passivity.

Making the patient a partner and an active party involved in their health issues is actually a significant element of care in which the patient regains a sense of control over the illness and life, and also provides an opportunity to engage their healing potential. The main assumption of the patient empowerment paradigm is to give the patient the right to shared decision-making and a leading role in the treatment process, taking into account the patient's preferences and capabilities [74]. Mindfulness training or other psychotherapeutic interventions offer patients with HF the opportunity to develop effective psychological or behavioral coping strategies for stress and diseases that facilitate their long-term motivation and commitment to the therapeutic process, which translates into improved quality of life and treatment outcomes. Informed and empowered patients are therefore able to take care of themselves and engage in health-promoting activities on their own. Training in coping strategies to handle the change and difficult situations in order to



reduce psychological stress should be implemented as part of comprehensive care for patients with HF [75].

The complexity of health care for patients with HF renders health education of patients and their caregivers crucial for an effective treatment process. The patient's knowledge of the disease allows them to better understand their situation, enables their acceptance of the disease, reduces anxiety and tension, and also facilitates their understanding of the expectations and requirements they face. Furthermore, it promotes patients' active involvement in the treatment process, their informed choices making, recommendations and treatment adherence, trust and good communication with medical personnel [76]. One of the main goals of HF education is to develop self-care skills. Self-care is defined as a natural decision-making process which enables the patient to choose behaviors that support their physical stability by monitoring the disease symptoms, adhering to recommendations or choosing a healthy lifestyle, as well as responding appropriately to the emerging symptoms of the disease.

### **SPIRITUAL CARE FOR PATIENTS WITH HEART FAILURE**

Holistic and appropriate care for patients with HF should include, not only their somatic and psychological health, but also their spiritual welfare. The spiritual dimension is currently becoming more widely accepted as an integral part of medical care since, international research has shown that, properly conducted spiritual care significantly increases the effectiveness of the healing process [77]. According to the definition of the Polish Association for Spiritual Care in Medicine, spirituality includes "a dimension of human life which refers to transcendental and other existentially important values" [78]. It concerns three features of human life.

Firstly, a religious aspect which consists of the patient's relationship with God (if they are believers), religious customs and practices, and community life. The patient should not be deprived of this type of care at any stage of treatment. Experience shows that patients are more reconciled to their clinical condition when pastoral support from members of their faith group is continued.

Secondly, and beyond the purely confessional context, spiritual experience affords possible answers to existential questions that arise in patients with HF concerning the meaning of life, suffering and death, and importantly, the dignity of the person with deteriorating health. Patients often ask themselves, "Who am I as a person who is sick and yet still free and responsible? How can I live with hope in the difficult situation I find myself in? Am I still capable of reconciliation

and forgiveness, love and joy?” etc. Human beings are the only ones to search for meaning (which was especially pointed out by Viktor Frankl), and, if people do not find meaning, they suffer more profoundly and quickly succumb to thoughts that can lead to increased anxiety, depression and even suicidal thoughts [79].

Thirdly, properly understood spirituality touches on the values that people live by, especially in regard to their relationship with themselves and other people. This extends to their attitude to work, nature, art and culture, and influences their moral and ethical choices. In other words, the spiritual dimension encompasses the whole of life. Thus, patients may feel the need to talk about literally everything, from seemingly trivial issues to those that touch the deepest roots of their personality.

Consequently, spiritual care should not be confined to exclusive ministries (e.g., dispensing sacraments) but should go beyond the sphere of religious observance. It should be provided by trained specialists in spiritual care, both lay people and clergy, operating in specially appointed teams. They should be ready, not only to facilitate the patients’ compliance with religious obligations and rituals, but also, to be able to engage in conversations about the most difficult topics of a transcendental and supernatural nature, going beyond the practice of psychological counselling. It is necessary to note that when spiritual care is provided, it is imperative that a neutral position should be adopted and that respect for the patient’s worldview should always be observed.

## **PALLIATIVE CARE IN HEART FAILURE**

Palliative care is a multidisciplinary approach aimed at maintaining or improving the quality of life of people with potentially life-limiting conditions (at any stage of the disease advancement, where indicated) and their relatives, by addressing health-related needs in physical, emotional and mental, social and spiritual areas. The so-called palliative approach is often sufficient in less complicated situations and it includes elements of palliative care provided by all members of the treatment team. More complex issues or needs may require a collaboration of a multiprofessional, specialist palliative teams which are composed of, among others, a nurse, doctor, psychologist, physiotherapist, chaplain, as well as a social care worker [80–82]. The American Heart Association, guidelines for the management of HF published last year strongly recommend (class 1 recommendations) palliative interventions for all the patients, involving, (in addition to the elements mentioned above), high-quality clinical communication, including information on

prognosis [83]. Proper treatment of physical symptoms, support in satisfying social needs and the search for answers to spiritual dilemmas can prevent or support the treatment of emotional burdens and disorders. Nowadays, the major emphasis of palliative care is placed on the support for patients and their relatives in the process of communication on future health, the expected further disease course and potential burdens as well as the patient's preferred scope and intensity of treatment and the care in health deterioration. Open communication allows for the patient active involvement in medical decision-making, reduces anxiety levels and improves understanding of one's own health status and expected changes. Advance Care Planning is a lengthy process of communication with the person with a disease, which allows for reconsideration and definition of the accepted treatment intensity, the treatment limits and the choice of location of end-of-life care provision. If, for some reason, the limits of the treatment intensity cannot be established with the patient, and the patients have lost their decision-making capacity or ability to express their decisions, in order to enable the care that does not prolong suffering, the active treatment discontinuation should be considered as the ongoing treatment bears the hallmarks of futile therapy, i.e. it involves life-sustaining treatment of terminally ill patients, it prolongs dying and entails excessive suffering or violation of dignity. The management protocol for such cases has been described by the Working Group of the Polish Society of Internal Medicine for Futile Therapy in Internal Medicine Departments. Limitation of futile therapy may involve withholding new therapies, no increase in the intensity or withdrawal from the ongoing therapy [84]. All of the above-mentioned elements of palliative care as a complement to optimal cardiovascular therapy allow patients and their relatives to live as actively as possible and improve the compatibility of the treatment with the patient's preferences. Therefore, they contribute to the improvement of the quality of life and the increase in satisfaction with treatment, and they can prevent or alleviate emotional burdens and mental disorders, both in the patients and their relatives

## **SUMMARY**

This expert opinion is a summary of the current state of knowledge on the occurrence of mental disorders such as depression, anxiety, sleep disorders and delirium in patients with HF as well as the options of therapeutic interventions. The available literature indicates a significant impact of the above disorders on the quality of life, disease progression, involvement in the treatment process, the number of hospitalizations and mortality in patients with HF. In the light of the latest data, the

most effective therapeutic management of patients with HF should include interventions which pertain to physical, mental and spiritual well-being. As the prevalence of mental disorders in the population of patients with HF is high, screening for their occurrence should be performed in the vast majority of patients with HF by cardiologists or primary care physicians, and cooperation with psychiatrists, psychologists and spiritual care specialists should be an indispensable element of therapy. In addition to pharmacotherapy, the available therapeutic options also include psychological and psychotherapeutic interventions, psychoeducation, stress management training, relaxation training and spiritual care. Therefore, it seems necessary to increase efforts to raise the awareness of mental disorders and their importance in the population of patients with HF, as well as to improve the access to specialists and develop effective collaboration of cardiologists, psychiatrists and psychotherapists.

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**Table 1.** Selected mental disorders screening questionnaires

<b>Disorder</b>	<b>Abbreviation</b>	<b>Full name of the questionnaire</b>
<b>Depression</b>	PHQ-9 HADS BDI-II	Patient Health Questionnaire Hospital anxiety and depression scale, depression subscale Beck Depression Inventory
<b>Anxiety disorders</b>	GAD-7 HADS	Generalized Anxiety Questionnaire Hospital anxiety and depression scale, anxiety subscale
<b>Sleep disorders</b>	PSQI ISI AIS	Pittsburgh Sleep Quality Questionnaire Insomnia Severity Index Athens Insomnia Scale
<b>Delirium</b>	MMSE MOS/CAM DOS	Mini Mental State Examination Entanglement Assessment Method Schuurmans Phantom Observation Scale

**Table 2.** Symptoms observed in patients with depression, anxiety, sleep disorders and delirium

<b>Type of disorder</b>	<b>Symptoms</b>
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<b>Depressive episode</b>	<b>Basic</b>	<ul style="list-style-type: none"> <li>– Depressed mood unaffected by external events</li> <li>– Elevated morning negative mood</li> <li>– Anhedonia — loss of pleasure and interest</li> <li>– Lack of energy and increased tiredness, excessive fatigue</li> </ul>
	<b>Additional</b>	<ul style="list-style-type: none"> <li>– Low self-esteem</li> <li>– Lack of self-respect</li> <li>– Feeling of guilt</li> <li>– Trouble concentrating</li> <li>– Resignation and suicidal thoughts</li> <li>– Occasional psychotic symptoms — hypochondriac delusions, guilt, punishments (in a severe episode)</li> <li>– Psychomotor drive changes — retardation or agitation</li> <li>– Eating disorders (lack or excessive appetite)</li> <li>– Sleep disorders (falling asleep, characteristic waking up 2–4 hours earlier than usual and inability to fall asleep again)</li> </ul>
<b>Anxiety</b>	<b>Somatic</b>	<ul style="list-style-type: none"> <li>– Pale or red skin, sweating</li> <li>– Increased heart rate, increased blood pressure</li> <li>– Hyperventilation with a feeling of shortness of breath</li> <li>– Tremors in the limbs, paresthesia, increased muscle tone</li> <li>– Pain, including headaches, abdominal pain</li> <li>– Diarrhea, pollakiuria</li> </ul>
	<b>Mental</b>	<ul style="list-style-type: none"> <li>– Feeling terrified, threatened, on edge</li> <li>– Fear of sudden death, fear of diseases</li> <li>– Exaggerated fear reactions</li> <li>– Feeling apprehensive and tense</li> <li>– Panic, fear of another panic attack and growing fear of its consequences</li> <li>– Generalized, persistent anxiety often concerns everyday matters and loved ones, and the fears are unjustified and inadequate</li> </ul>
	<b>Behavioral</b>	Avoiding situations in which anxiety has appeared, striving to reduce it
<b>Sleep disorders</b>	<b>Dyssomnia</b>	<ul style="list-style-type: none"> <li>– Nonorganic insomnia</li> <li>– Nonorganic hypersomnia</li> <li>– Nonorganic circadian rhythm sleep-wake disorders</li> <li>– Nocturnal respiratory dysfunction</li> <li>– Narcolepsy</li> </ul>

	Parasomnia	Episodic sleep disturbances, with symptoms occurring during certain stages of sleep or during partial or complete awakening (somnambulism, night terrors, nightmares)
<b>Delirium</b>	Disorientation	<ul style="list-style-type: none"> <li>– Allopsychic (as to time, place, situation)</li> <li>– Psychic (as to oneself and in deeper states)</li> </ul>
	Psychomotor drive disturbances	<ul style="list-style-type: none"> <li>– As agitation and excessive sensitivity to stimuli</li> <li>– Activity reduction, slowness and drowsiness (may be alternating)</li> </ul>
	Mood disorders	<ul style="list-style-type: none"> <li>– With irritability and mood swings</li> <li>– Depression</li> </ul>
	Perception impairment	– With visual and auditory hallucinations, and others (less frequently)
	Thinking impairment	– Disorganized thinking and delusions
	Cognitive impairment	<ul style="list-style-type: none"> <li>– Inadequate focusing of attention and general reactivity to stimuli</li> <li>– Impairment in following simple commands: understanding, interpretation and adequacy of reactions</li> </ul>
	Variability	– Fluctuation of symptoms during the day with the evening and night increase in severity

**Table 3.** Medications used to treat depression

Substance	Dose [mg] (initial/ therapeutic basis)	Dosage frequency	Key warnings	Comments
Agomelatine	25/50	Once daily in the evening	ALAT and ASTAT levels should be controlled	Antidepressive and anxiolytic effects. Circadian rhythm- regulating properties

Bupropion	150/150–300	Once daily	Potential increase in blood pressure. Do not combine with nicotine transdermal systems. May aggravate sleep problems and anxiety, a risk of seizures	Antidepressive effects. Safe in cardiac arrhythmias
Duloxetine	30/60–120	Once daily in the morning	No significant impact on the cardiovascular system, but contraindicated in patients with uncontrolled hypertension	Antidepressive, anxiolytic and analgesic effects
Escitalopram	5/10–20	Once daily	Contraindicated in patients with recognized QT prolongation, otherwise as with sertraline	Antidepressant and anxiety effects, limited number of drug-drug interactions
Fluoxetine	10/10–20	Once daily in the morning	No significant cardiovascular side effects. Due to the long half-life of the active metabolites, do not include another SSRI until two weeks after discontinuation	Antidepressive effects
Mirtazapine	7.5–15/15–45	Once daily in the evening	Bone marrow suppression has been reported. It can impair glycemic control	Antidepressive and anxiolytic effects. Pronounced sedative and hypnotic effects, also in small doses
Paroxetine	10/20–50	Once daily	As for sertraline. CYP2D6 inhibitor has quite numerous interactions. Contraindicated when combined with metoprolol	Antidepressive and anxiolytic effects, slightly less tolerated than other SSRIs. Not recommended for women planning pregnancy
Sertraline	25/50–200	Once daily	Increased risk of bleeding when combined with anticoagulants and NSAIDs. Increased risk of hyponatremia, especially in older adults	Antidepressive and anxiolytic effects. Most extensively investigated for its safety in cardiac patients. Safe in kidney failure



Trazodon	25-50/75–300	Once daily in the evening	Potential increase in conduction and rhythm disorders and decrease of blood pressure	Antidepressive and anxiolytic effects. Pronounced sleep-inducing effect, even in small doses
Vortioxetine	5–10/20	Once daily	No effect on heart rate, blood pressure or QTc interval.	Antidepressive and anxiolytic effects. Improves cognitive functions. Safe in somatic diseases.

Notes on anti-anxiety medications:

- Pregabalin, an anxiolytic, should be applied with caution in patients with severe HF (Summary of Product Characteristics). Exacerbation of previously stable HF has been reported.
- Hydroxyzine is believed to have a similar impact on the QTc interval prolongation as other first-generation antihistamines; therefore, it should be applied with caution.
- Benzodiazepine derivatives and so-called non-benzodiazepine hypnotics are relatively safe but are contraindicated in patients with acute respiratory failure. When used regularly, they are associated with a high risk of addiction and its consequences.

Abbreviations: ALAT, alanine aminotransferase; AspAT, aspartate aminotransferase; SSRI, selective serotonin reuptake inhibitors

**Table 4.** Psychotropic drugs used on an ad hoc basis in the treatment of delirium

Drug (available forms)	Dosage <sup>a</sup>	Comments
Haloperidol (tab., liq., amp.)	0.5–5 mg p.o., every 6 hours, max. 30 mg/day  In uncooperative patients: haloperidol 2.5–5 mg i.m. or i.v. every 0.5 to 2 hours, max. 15 mg/day	ECG check-up; if the QT interval is prolonged during treatment — reduce the dose, when the QTc interval is longer than 500 msec — discontinue  Electrolyte levels control before and during treatment  Hypokalemia and hypomagnesaemia increase the risk of ventricular arrhythmias and should be controlled prior to haloperidol therapy initiation  Risk of extrapyramidal symptoms, e.g., stiffness and/or tremor
Risperidone (tab., orodispersible tab., liq.)	0.5–2 mg every 0.5–2 hours, max. 6 mg/day	Risk of extrapyramidal symptoms; caution: hypokalemia, which increases the risk of ventricular arrhythmias, should be controlled before the treatment initiation
Quetiapine (tab.)	12.5–300 mg/day	ECG control

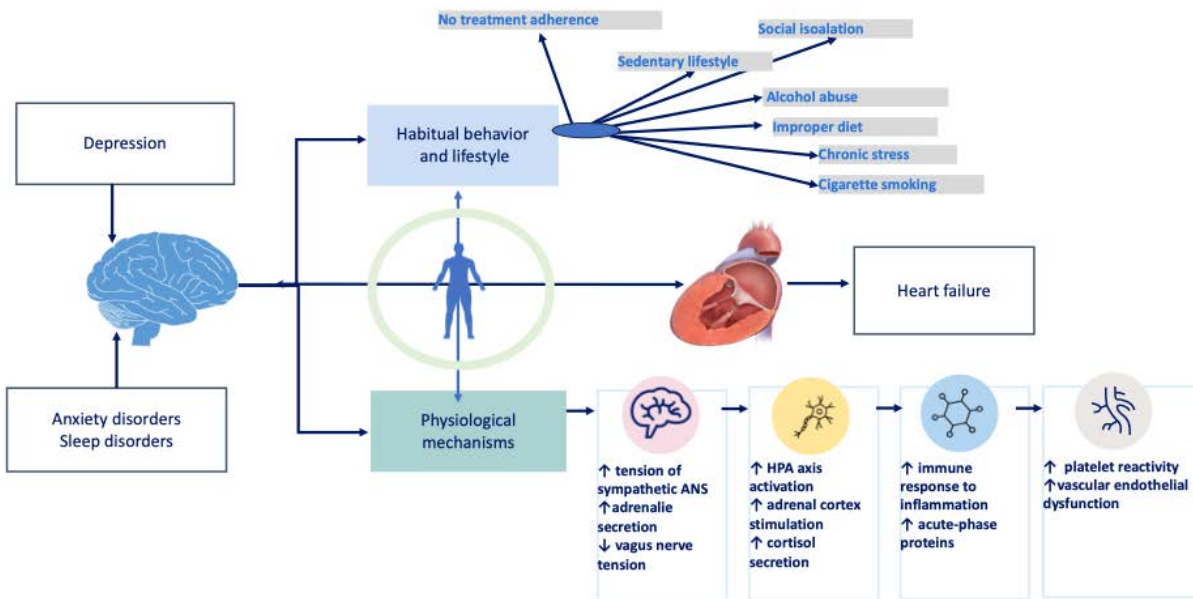
Olanzapine (tab., amp.)	5–10 mg p.o., every 1/2–2 hours up to max. 20 mg/day 5–10 mg i.m. every 2–4 hours to max. 30 mg/day	Particularly recommended in delirium superimposed on dementia, risk of hypotension
Lorazepam <sup>b</sup> (tab., amp.)	3–4 × 1–2,5 mg p.o. max. 10 mg/day	
Clonazepam <sup>b</sup> (tab., amp.)	1 mg every 2–6 hours, max. 20 mg/day i.v. or i.m., when no venous access is possible, repeating as needed	Administered especially in alcoholic delirium, complicated withdrawal syndrome, with the risk of seizures
Tiapride (tab.)	50–300 mg/day	Used mainly in behavioral disorders and delirium superimposed on dementia, cardiologically safe
Dexmedetomidine	0.2–1.5 µg/kg/h	

<sup>a</sup>Dose modification is necessary in the elderly, patients with hepatic and renal failure, as well as, for example, the dose of olanzapine in women or non-smokers. <sup>b</sup>Used only to treat delirium in the course of withdrawal syndrome  
Abbreviations: EKG, electrocardiogram; i.m., intramuscular; i.v., intravenous; p.o., per os

**Table 5.** Non-pharmacological interventions to increase the sense of security

<p>Limiting the staff caring for the patient to several selected people</p> <p>Attempts to maintain natural circadian rhythms</p> <p>Not transferring the patient between rooms (unless absolutely necessary)</p> <p>Regular information on auto- and allopsychic orientation (even several times daily)</p> <p>Education of the patient and relatives regarding the observed disorders of consciousness</p>
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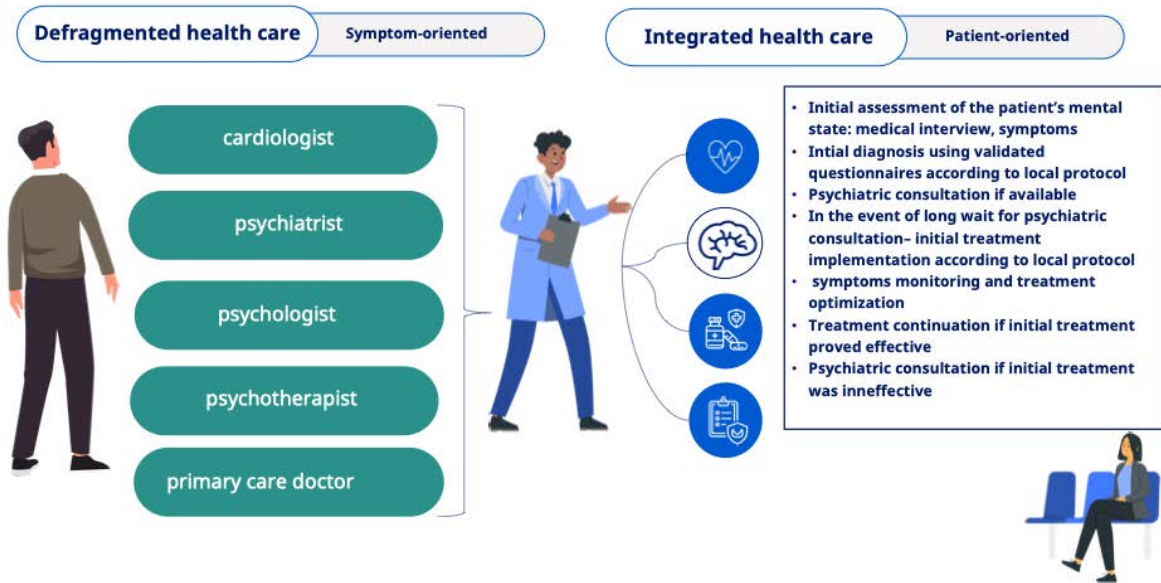
Screening Questions for the Most Common Mental Disorders	
Assessment of depressive symptoms	Have you often been anxious over the past month due to your depression, depressed mood, or feelings of hopelessness? Have you been bothered by feeling lower interest or pleasure in various activities in the past month?
Assessment of increased anxiety symptoms	Have you often felt nervous, anxious, or very tense over the past month? Over the past month, have you often been unable to stop worrying or to control it?
Assessment of sleep disorders	Do you have trouble sleeping? Do you have trouble with falling asleep, interrupted sleep or sleeping too long?



**Figure 1.** Pathophysiological relationships between mental disorders and heart failure development

Screening for most common mental health comorbidities in patient with HF (cardiologist, GP)

**Figure 2.** Algorithm for the management of suspected mental disorders in patients with HF during hospitalization and in outpatient settings



**Figure 3.** Patient-centered approach: health care for patients with heart failure and psychiatric disorders