

Underlying Disease – Specific Heart Failure Treatment

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Introduction

Acute or chronic heart failure is one of the most important entities among cardiac diseases. The treatment of heart failure becomes more and more disease-specific as new treatment options develop over time. Heart failure can occur due to ischemic cardiomyopathy, non-ischemic cardiomyopathy like specific forms of cardiomyopathies like dilated, hypertrophic, restrictive and arrhythmogenic one and special cardiomyopathies like acquired takotsubo cardiomyopathy.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy is characterized by the risk of sudden cardiac death and developing heart failure. Beneath therapeutic options like beta blocking agents, verapamil, surgical myectomy and septal ablation therapy a new pharmacologic agent is on the horizon: Mavacamten. Approval of mavacamten is supposed in the first period of 2021.

Beneficial effects of mavacamten can be considered for hypertrophic obstructive disease [1] and also for hypertrophic non-obstructive cardiomyopathy [2]. Especially for hypertrophic non-obstructive cardiomyopathy new options like ranolazine failed.

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy is characterized by fibro fatty replacement of myocytes. Fibrosis is the main feature causing ventricular arrhythmias, the risk of sudden cardiac death and progressive heart failure [3]. In order to prevent fibrosis ramipril is tested in the BRAVE study still waiting for the results [4]. The combination of valsartan and sacubitril had beneficial effects on soluble ST2 [5] and should be tested in a next step.

In phospholamban mutations leading to dilated cardiomyopathy or arrhythmogenic cardiomyopathy the compound of fibrosis is higher than in plakophilin-2 mutations [6]. Neither mineralocorticoid antagonists nor beta blocking agents are able to prevent fibrosis [7]. A study to assess the effect of eplerenon has been started at the University Hospital of Groningen, The Netherlands, to test the hypothesis, whether eplerenon is more effective than spironolactone [8]. Newer non-mineralocorticoid agents, called finerenon, should be tested as a next step. To use entresto should be a further attempt.

Amyloid Cardiomyopathy

Cardiac amyloidosis is characterized by fibril deposition in the myocardium which leads to structural and functional abnormalities and heart failure. Amyloid cardiomyopathy can lead to aortic valve dysfunction and pericardial effusion [9]. Cardiac light-chain amyloidosis and here dietary or wild-type transthyretin amyloidosis are the most prevalent forms of amyloid cardiomyopathy [10]. In transthyretin amyloid cardiomyopathy the amyloid stabilizer tafamidis leads to a significant reduction of mortality and cardiovascular morbidity [11]. Neurologic complications can be significantly reduced by patisiran and inotersen [12,13]. The question is whether these two drugs are effective in heart disease, too. Studies are started.

Fabry Disease

Fabry disease is a lysosomal storage disorder caused by mutations of the *GLA* gene that lead to a deficiency of the enzymatic activity of α -galactosidase [14]. Available therapies for Fabry disease include enzyme replacement therapy agalsidase alfa and agalsidase beta [15] and the chaperone migalastat [16].

Dilated Cardiomyopathy and Ischemic Cardiomyopathy

The by far largest group of heart failure patients are the group of ischemic cardiomyopathy and dilated cardiomyopathy. Therapeutic improvements are obtained by ACE inhibitors or AT1 receptor blockers [17], beta blocking agents [18], mineralocorticoid antagonists [19], the combination of valsartan and sacubitril (entresto) [20] and the relatively newly developed sodium-glucose cotransporter (SGLT2) inhibitors [21,22]. In dramatically reduced ejection fraction a rather low, but significant effect can be obtained by omecamtiv mecarbil [23] and danicamtiv [24]. Vericiguat, an oral soluble guanylate cyclase stimulator, reduced the composite end point of cardiovascular death or HF hospitalization vs. placebo [25].

In 2021 a new guideline for the treatment of heart failure is planned from the European Society of Cardiology suggesting the use of SGLT 2 inhibitors, empagliflozin and dapagliflozin, which reduce mortality and morbidity in heart failure.

A major problem is to treat heart failure with preserved ejection fraction, a problem which is relevant for at least 60% of cases. Spironolactone and sacubitril/valsartan just missed significant results. Ejection fractions between 50 to 57% and women, in general, had significant results. The guideline update should include these changes, too.

Both the diagnosis and treatment of heart failure with preserved ejection fraction, as well as management of advanced HF and acute HF, remain challenging.

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