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Quality of life in heart failure: New data, new drugs and devices

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Abstract

Quality of life (QoL) is a therapeutic goal in heart failure. There are many evidence based medicine therapies for improving QoL. In this study, data is presented on new pharmacotherapies and devices that impact QoL in the heart failure population. (Cardiol J 2024; 31, 1: 156–167)

Keywords: quality of life, heart failure, pharmacotherapy, devices

Introduction

Heart failure (HF) is a progressive disease which has a detrimental effect on quality of life (QoL). The prevalence of HF appears to be 1–2% in adults and is increasing due to the ageing of populations around the world, sedentary lifespan and comorbidities. In the 2021 guidelines of the European Society of Cardiology (ESC) for the diagnosis and treatment of acute and chronic HF, QoL is still considered a part of management strategy [1]. Like the 2016 ESC Guidelines [2], the treatment goals in HF are: improvement of the clinical status, functional capacity and QoL, prevention of hospital admission and reduction of mortality [1]. The aim of the study was to describe new data on QoL in light of innovative therapies in HF.

Definitions of QoL and evaluation methods in clinical studies

The World Health Organization defines QoL as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [3]. QoL consists of objective and subjective indicators. It is a multidimensional, individual outcome, composed of five dimensions: physical wellbeing, material wellbeing, social wellbeing, emotional wellbeing, as well as development and activity [4]. Central illustration presents QoL dimensions.

There are many instruments to assess QoL, like the Health-Related Quality of Life Questionnaire, World Health Organization Quality of Life Instrument, Short Form 36 Health Survey Questionnaire (SF-36), Quality of Life Scale [5]. Some of them are dedicated to HF: the Chronic Heart Failure Assessment Tool, Cardiac Health Profile of congestive heart failure, Chronic Heart Failure Questionnaire (CHFQ), Kansas City Cardiomyopathy Questionnaire (KCCQ), Left Ventricular Disease Questionnaire, Minnesota Living with Heart Failure Questionnaire (MLHFQ), and Quality of Life in Severe Heart Failure Questionnaire. Table 1 shows selected QoL questionnaires.

The use of some questionnaires has clinical potential. Assessments of KCCQ is used to identify high-risk patients and design their individual treatment plans. Patients with lower or worsening KCCQ scores demonstrate an increased risk of cardiovascular events and mortality [6]. Iqbel at al. [7] showed that the baseline QoL predicts mortality and hospital admissions — patients with worse

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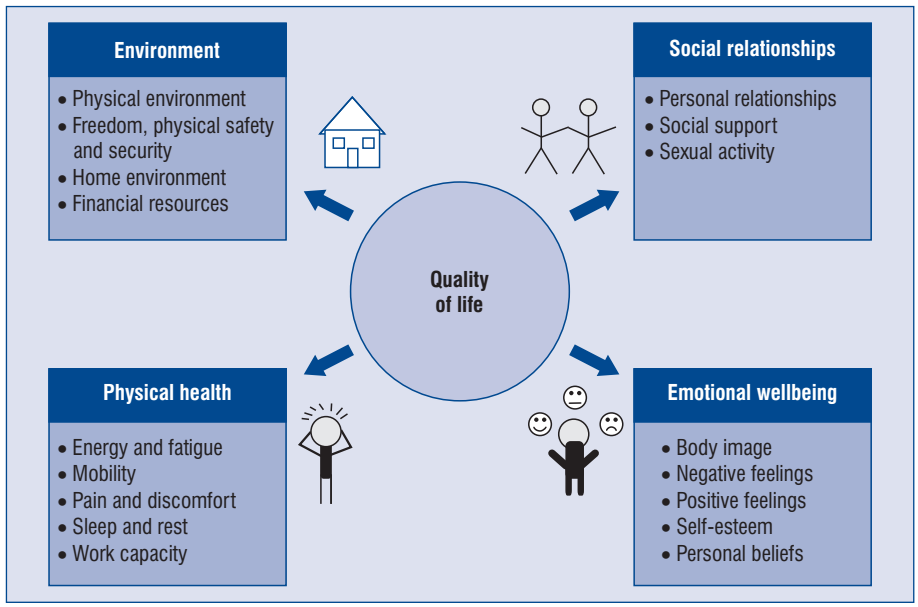

Central illustration: Dimensions of quality of life.

Table 1. Selected quality of life questionnaires.

	SF-36	KCCQ-23	WHOQOL-BREF	QOLS
Items	36	23	26	16
Domains	1. Physical functioning 2. Physical role limitations 3. Bodily pain 4. General health 5. Perceptions (energy/ /vitality) 6. Social functioning 7. Emotional role limitations 8. Mental health	1. Symptom frequency 2. Symptom burden and stability 3. Physical limitations 4. Social limitations 5. Quality of life; and self-efficacy	1. Physical health 2. Psychological 3. Social relationships 4. Environment	1. Material and physical well-being 2. Relationships with other people 3. Social, community and civic activities 4. Personal development and fulfillment 5. Recreation 6. Independence
Scale	0 to 100	0 to 100	0 to 100	16 to 112
Time to complete	10 minutes			5 minutes

SF-36 — The Short Form 36 Health Survey Questionnaire; KCCQ — Kansas City Cardiomyopathy Questionnaire; WHOQOL-BREF — The World Health Organization Questionnaire of QOL; QOLS — Quality of Life Scale

baseline QoL had a higher risk of mortality (hazard ratio [HR] 1.5, $p = 0.09$) and hospitalizations (HR 7.3, $p < 0.001$).

Impact of heart failure on QoL

Heart failure affects all fundamental spheres of human life at the same time. In the physical sphere, patients most often experience symptoms such as reduced general body efficiency, shortness of breath, fatigue, decreased energy levels, edema sleep problems. In the psychological sphere, HF patients are more likely to experience disorders at the emotional level, in particular strong anxiety and depression. In the social sphere, patients may experience deterioration of social contacts and

relationships with relatives, as well as difficulties in everyday work life.

Subjective assessment of QoL is also influenced by parameters such as gender and age. QoL is lower in women, which is consistent with the assessment of the QoL in the group of cardiac patients, as well as in younger patients. Among younger people, HF-related symptoms and treatment of the disease limit fulfillment of basic social roles, like starting a family or pursuing a professional career.

Quality of life in HF is significantly reduced not only by symptoms but also by numerous hospitalizations. Despite some improvement in reducing mortality in HF, the rehospitalization rate is still high, up to 30% in 60 to 90 days after discharge, regardless of ejection fraction (EF) [8, 9]. Thus, all therapies and procedures aimed at reducing the risk of HF hospitalization improve QoL.

Quality of life is also crucial in end-of-life care in HF. With every HF hospitalization the patient's condition and prognosis decline, which leads to advanced HF or death. In every patient with advanced stage of HF, palliative and end-of-life care should be considered. It can reduce the hospitalization rate and alleviate symptoms. End-of-life care should be focused on improving QoL of the patient and their family [10].

Impact of comorbidities on QoL

Many factors like comorbidities, the employment status, or social situation, influence both QoL and symptoms of HF. Comorbidities significantly reduce QoL in HF, mainly in older patients. However, the heart failure with preserved ejection fraction (HFpEF) phenogroup of young obese patients is considered to have the lowest QoL. Evangelista et al. [11] revealed that obese patients appeared to demonstrate higher values in MLHFQ (the higher score, the lower QoL), i.e., 48.5 ± 24.2 in mean ± standard deviation (SD) compared to normal weight patients (MLHFQ 39.4 ± 23.1) and the overweight group (MLHFQ 44.0 ± 24.70) with p value = 0.049 and worse depressive symptoms.

Many patients with HF suffer from diabetes. Concomitant diabetes worsens patient health status, increases the number of complications and reduces QoL. In CHMP-HF patients with heart failure with reduced ejection fraction (HFrEF) and diabetes mellitus exhibit worse results regarding health-related quality of life (HRQOL) compared to HFrEF patients without diabetes [12].

Benes et al. [13] study has shown that three common comorbidities (diabetes, chronic obstructive pulmonary disease, and chronic kidney disease) affect QoL in HFrEF patients. In this analysis, among patients with more comorbidities QoL was similar (evaluated with the MLHFQ). However, a multivariable regression analysis also showed that not the number of comorbidities in a stable advanced HFrEF patient but other factors like the New York Heart Association (NYHA) class, body mass index and furosemide daily dose affect their QoL [13].

Depression and anxiety disorders often occur in HF patients. Up to 20% of HF patients have depression. It may be responsible for aggravation of symptoms, increased hospitalization rates, reduced compliance, higher mortality and may also affect QoL. Nevertheless, depression often remains underestimated and untreated [14]. Psychological support and pharmacotherapies are considered. Selective serotonin reuptake inhibitors have proved to be safe in SADHART-CHF and MOOD-HF trials [15, 16]. Although they are recommended for patients with HF they did not significantly reduce hospitalization or all-cause mortality and show no significant improvement in depression when compared to placebo.

Impact of exercise on QoL

The 2021 ESC HF guidelines recommend exercise rehabilitation and multiprofessional disease management for all patients in order to reduce HF hospitalization and to improve their QoL [1]. It has been proved that physical exercise in the form of structured exercise training improves exercise tolerance and QoL and reduces the risk of hospitalization. There are many studies which show positive impact of cardiac rehabilitation on HF patients. Taylor et al. [17] in their meta-analysis of randomized trials showed a statistically significant benefit of exercise on health-related QoL (measured with MLHFQ) and exercise capacity (tested by a 6-minute walk test [6MWT]), compared to the placebo group, after 12 months of follow-up.

Also, Palmer et al. [18] showed in a meta-analysis that exercise improves QoL, which is manifested with the score of 8.5 points in MLHFQ. Moreover, the physical function was improved, measured by 6MWT [18]. The HF ACTION study revealed that after 3 months of exercise rehabilitation, patients exhibited higher KCCS-overall summary score (OSS) (the mean: 5.21, 95% confidence interval [CI] 4.42–6.00) compared with the standard care group not undergoing exercise rehabilitation (3.28, 95% CI 2.48–4.090) and this

result was statistically significant ($p < 0.001$) [19]. The positive effect in the exercise group was also observed in the follow-up period.

Impact of pharmacotherapy on QoL

Heart failure with reduced ejection fraction (HFrEF)

There are many pharmacological therapies in HFrEF that improve QoL. The following four groups of fundamental pharmacological treatment are effective and they include: angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor-nephrilysin inhibitor (ARNI), sodium-glucose cotransporter-2 (SGLT2) inhibitors, beta-blockers and mineralocorticoid receptor antagonists (MRA).

ACEI and ARNI alleviate HF symptoms and increase exercise tolerance. The best effect for ACEI was visible in patients with the lowest left ventricular ejection fraction (LVEF) < 25% [20]. The drugs should be applied in maximum tolerated recommended doses. However, the PARADIGM-HF trial showed that sacubitril/valsartan contributed to a greater QoL improvement measured in the KCCQ clinical summary score (CSS) (+0.64 vs. –0.29; $p = 0.008$) and KCCQ-OSS (+1.13 vs. –0.14; $p < 0.001$) compared to enalapril [21]. In the PARASAIL study, in which 64.6% of patients were administered the maximum dose of sacubitril/valsartan 97/103 mg b.i.d. after 6 months, the improvement (slight, moderate, or marked) measured with the use of the patient global assessment at 4, 12 and 24 weeks of the study was 52.3%, 58.6% and 64.2%, respectively [22]. An improvement in QoL was also visible in decreasing MLHFQ total scores from the beginning of the study to 4, 12 and 24 weeks (with $p < 0.0001$ for all) [22].

Other studies suggest a positive effect of sacubitril/valsartan in patients equipped with an implantable cardioverter-defibrillator (ICD). This drug significantly prolongs survival without ventricular tachycardia and non-sustained ventricular tachycardia compared with ACEI/angiotensin receptor blocker (ARB) and increases in the number and percentage of biventricular stimulation (BiV) compared to patients treated with ACEI/ARB [23]. Moreover, results of the study revealed a lower number of adequate ICD discharges [23]. Another study suggests that sacubitril/valsartan reduces the risk of sudden cardiac death (SCD) and cardiac arrest compared to enalapril whether the patient had or had not been implanted with an ICD device [24]. The meta-analysis conducted by Fernandes et al. [25] also confirmed that ARNI therapy in HFrEF patients was associated with a reduced number of SCD events, ventricular arrhythmias and a reduced incidence of adequate ICD discharges. Patients treated with sacubitril/valsartan demonstrated increased BiV stimulation and reduced requirement for ICD [25]. These results are reflected in patients' QoL-reduced discharge rates and better control of arrhythmias are associated with an increase in a sense of caring and self-confidence, which leads to increased physical activity and improved KCCQ results.

Furthermore, in the CARVIVA HF trial, ivabradine added to carvedilol treatment demonstrated improvement in exercise capacity as measured in 6MWT and QoL ($p < 0.01$ vs. baseline for ivabradine and $p < 0.02$ for ivabradine with carvedilol) [26]. Docherty et al. [27], based on PARADIGM-HF and ATHMOSPHERE trials, have shown that lower HR values, contributed addition of ivabradine, reduced cardiovascular death and HF hospitalization as well as improvements in QoL, manifesting in higher KCCQ scores at 12 months ($p < 0.001$ in both) [27].

Iron deficiency often affects HF patients and can decrease QoL. In the AFFIRM study, QoL was measured with KCCQ-12 at the baseline and after randomization [28]. A 4-week observation with KCCQ-OSS (KCCQ-12 OSS) and KCCQ-CSS revealed a higher improvement in ferric carboxymaltose in comparison to the placebo group: 2.9 (0.5–5.3, $p = 0.018$) for OSS, and 2.8 (0.3–5.3, $p = 0.029$) for CSS; in the adjusted mean difference (95% CI). According to the AFFIRM study, intravenous ferric carboxymaltose can alleviate symptoms and increase the functional capacity and QoL in HF patients with LVEF < 45%, as well as reduce the hospitalization rate in HF patients with LVEF < 50% [28].

Results from SGLT2 inhibitors trials are described in a separate section.

Heart failure with preserved ejection fraction (HFpEF)

Heart failure with preserved ejection fraction constitutes about 50% of all cases of HF. Prognosis in HFpEF is equally unfavorable as in patients with HFrEF. In the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist Trial) post-hoc analysis, 3 phenogroups were described [29]. Phenogroup 3 (patients with obesity, diabetes mellitus) had the lowest KCCQ overall score of 50 ± 22, compared to 55 ± 18 in phenogroup 1 and 58 ± 21 in phenogroup 2

Table 2. Outcomes of quality of life in EMPEROR-Reduced [34], EMPEROR-Preserved [35, 36], EMPULSE [38, 39] and DAPA-HF[43] trials.

EMPEROR-Reduced	Empagliflozin (n = 1863)	Placebo (n = 1867)	HR or absolute difference (95% CI)
Change in quality-of-life score on KCCQ at 52 weeks	5.8 ± 0.4	4.1 ± 0.4	1.7 (0.5–3.0)
No. of hospitalizations due to any cause	1364	1570	0.85 (0.75–0.95)
EMPEROR-Preserved	**Empagliflozin (n = 2997)**	**Placebo (n = 2991)**	**HR or absolute difference (95% CI)**
Total no. of hospitalizations for heart failure	407	541	0.73 (0.61–0.88)
Change in KCCQ clinical summary score at 52 weeks	4.51 ± 0.31	3.18 ± 0.31	1.32 (0.45–2.19)
Total no. of hospitalizations due to any cause	2566	2769	0.93 (0.85–1.01)
EMPULSE	**Empagliflozin (n = 265)**	**Placebo (n = 265)**	**HR or absolute difference (95% CI)**
≥ 5 point difference in the KCCQ-TSS change from baseline to day 90 (% wins)	35.91	27.48	
KCCQ-TSS improvement ≥ 10 points at day 90, n (%)	220.1 (83.1)	202.1 (76.3)	1.522 (0.927–2.501)
KCCQ-TSS change from baseline to day 90, adjusted mean (95% CI)	36.19 (33.28–39.09)	31.73 (28.80–34.67)	4.45 (0.32–8.59)
DAPA-HF	**Dapagliflozin (n = 2373)**	**Placebo (n = 2371)**	**HR or absolute difference (95% CI)**
Change in KCCQ-TSS at 8 months	6.1 ± 18.6	3.3 ± 19.2	1.18 (1.11–1.26)

CI — confidence interval; HR — hazard ratio; KCCQ — Kansas City Cardiomyopathy Questionnaire; TSS — total symptom score

($p < 0.001$) [29]. Phenogroup 3 also exhibited the highest rate of depression 197 (36%) compared to 64 (23%) in phenogroup 1 (the younger one) and 121 (19%) in phenogroup 2 (the older one) with $p < 0.001$ [29].

Until the introduction of SGLT2 inhibitors, there had not been a therapy improving prognosis in patients with HFpEF. Results of trials conducted earlier and meta-analysis of Zheng et al. [30], revealed that no single drug, including ACEI, MRAs and beta-blockers, administered to HFpEF patients, reduced HF hospitalization or cardiovascular mortality compared to placebo. Furthermore, neither exercise capacity nor QoL were improved in this population [30].

Sacubitril/valsartan administered in PARAGON-HF and PARALLAX-HF studies to population with HFpEF improved QoL measured in KCCQ and NYHA class at 8 months and 24 weeks, respectively, in comparison to valsartan in PARAGON-HF or individualized medical therapy (placebo, ACEI or ARB) in the PARALLAX-HF study [31, 32]. However, according to the 2021 ESC guidelines in HFpEF, before the SGLT2 inhibitors era, the optimal treatment of comorbidities and risk factors is recommended [1]. Results of EMPEROR-Preserved and DELIVER trials have completely changed our opinion on this issue and we believe that the goals of therapy in HFpEF patients should be defined in a similar way as those for HFrEF patients including QoL.

Lastly, diuretics are recommended in the I class in both HFrEF and HFpEF patients with volume overload to improve QoL and exercise capacity as well as alleviate symptoms by reducing congestion [1, 33].

SGLT2 inhibitors and QoL

Results of changes in QoL for SGLT2 inhibitors therapy are presented in Table 2.

In the EMPEROR-Reduced study [34], QoL was assessed with KCCQ at the beginning of the study and at 12, 32, and 52 weeks after randomization. Patients receiving empagliflozin demonstrated a significant improvement in KCCQ-CSS (by 1.94, 1.35, and 1.61 points), in the total symptom score (TSS) by 2.52, 1.64, 1.69 points and OSS by 1.77, 1.30, and 1.52 points at 12, 32 and 52 weeks compared to placebo. Moreover, patients treated with empagliflozin scored more than 5 points in

KCCQ-CSS (odds ratio [OR] 1.20 [1.05–1.37]), ≥ 10 points (OR 1.26 [1.10–1.44]), and more than |15 points (OR 0.75 [1.12–1.48]). Benefits of improved QoL was also visible at 3 months and continued for at least a year. Patients treated with empagliflozin were 20% to 40% more likely to exhibit an improvement in the NYHA class and 20% to 40% less likely to experience deterioration in the NYHA class. The clinical benefit was already seen on day 28 after randomization and continued in the follow-up [34].

The EMPEROR-Preserved study [35] revealed that empagliflozin is effective in patients with HF and EF > 40%. It decreased the risk of death from cardiovascular cause and hospitalization due to HF by 21%, reduced the risk of all hospitalizations by 27% and improved QoL. Table 2 shows selected EMPEROR-Preserved outcomes.

Quality of life was assessed with KCCQ at the beginning of the study and after 12, 32, and 52 weeks. Patients receiving empagliflozin demonstrated a significant improvement compared to those receiving placebo in KCCQ-CSS by +1.03, +1.24, and +1.50 points, TSS by 1.77, 1.53 and 2.07 points and in the OSS by 1.77, 1.53 and 2.07 points at 12, 32 and 52 weeks [36]. Already at 12 weeks, patients treated with empagliflozin scored more than 5 points in KCCQ-CSS (OR 1.23, 95% CI 1.10–1.37), ≥ 10 points (OR 1.15, 95% CI 1.03–1.27), and more than 15 points (OR 1.13, 95% CI 1.02–1.26) [36].

In the EMPEROR-Preserved study, the effect of empagliflozin was manifested in baseline KCCQ tertiles (Table 3). Improved QoL was also visible at 32 and 52 weeks, and was observed for at least a year [36]. Patients treated with empagliflozin were 20% to 50% more prone to demonstrate an improvement in the NYHA class. The effect was already seen at 12 weeks after randomization and continued for at least 2 years [37].

Empagliflozin also improves QoL in patients with acute HF, as it was revealed in the — EMPULSE study [38, 39]. Clinical benefits after taking empagliflozin were 36% higher in comparison to results obtained in the placebo group (stratified win ratio 1.36; 95% CI 1.09–1.68; p = 0.0054). Clinical benefits included: a decreased risk of cardiovascular death and decreased hospitalization due to HF as well as improved QoL. Such results were achieved irrespective of EF or concomitant diabetes [38].

In the EMPULSE trial, QoL was assessed using a difference in the change from baseline in the KCCQ-TSS at 90 days. The average change in KCCQ-TSS from baseline to 90 days was 36.2 (95% CI 33.3–39.1) in the empagliflozin group and 31.7 (95% CI 28.8–34.7) in the placebo group [39]. The clinical benefit was observed very early, already after 15 days and stayed to 90 days. At day 90, patients treated with empagliflozin exhibited better results in KCCQ-TSS, Physical Limitations (PLS), QoL, CSS and OSS in comparison to

Table 3. Effect of empagliflozin on outcomes by baseline KCCQ tertiles in EMPEROR-Preserved [36] and EMPULSE trial [39].

EMPEROR-preserved outcome	Hazard ratio (95% CI)
Cardiovascular death or HF hospitalization	
KCCQ-CSS	
Tertile 1 (< 62.5)	0.83 (0.69, 1.00)
Tertile 2 (62.5–83.3)	0.70 (0.55, 0.88)
Tertile 3 (≥ 83.3)	0.82 (0.62, 1.08)
KCCQ-TSS	
Tertile 1 (< 66.7)	0.85 (0.70, 1.04)
Tertile 2 (66.7–87.5)	0.76 (0.60, 0.96)
Tertile 3 (≥ 87.5)	0.71 (0.55, 0.93)
KCCQ-OSS	
Tertile 1 (< 61.2)	0.81 (0.67, 0.98)
Tertile 2 (61.2–82.3)	0.72 (0.57, 0.92)
Tertile 3 (≥ 82.3)	0.82 (0.62, 1.08)
Total number of HF hospitalizations	
KCCQ-CSS	
Tertile 1 (< 62.5)	0.82 (0.61, 1.08)
Tertile 2 (62.5–83.3)	0.62 (0.44, 0.88)
Tertile 3 (≥ 83.3)	0.70 (0.49, 1.00)
KCCQ-TSS	
Tertile 1 (< 66.7)	0.86 (0.64, 1.14)
Tertile 2 (66.7–87.5)	0.71 (0.51, 0.99)
Tertile 3 (≥ 87.5)	0.56 (0.39, 0.79)
KCCQ-OSS	
Tertile 1 (< 61.2)	0.82 (0.62, 1.08)
Tertile 2 (61.2–82.3)	0.64 (0.45, 0.90)
Tertile 3 (≥ 82.3)	0.65 (0.45, 0.93)
EMPULSE	
All-cause death or HF events, or 5-point or greater difference in KCCQ-TSS change	
KCCQ-TSS < 27.1	1.49 (1.01, 2.20)
KCCQ-TSS ≥ 27.1 and < 52.1	1.37 (0.94, 1.99)
KCCQ-TSS ≥ 52.1	1.48 (1.00, 2.20)

CI — confidence interval; CSS — clinical summary score; HF — heart failure; KCCQ — Kansas City Cardiomyopathy Questionnaire; OSS — overall summary score; TSS — total symptom score

placebo (95% CI); respectively, 4.45 (0.32, 8.59), p = 0.03; 4.80 (0.00, 9.61), p = 0.05; 4.66 (0.32, 9.01), p = 0.04; 4.85 (0.77, 8.92), p = 0.02; and 4.40 points (0.33, 8.48), p = 0.03 [39].

Data obtained in EMPEROR-Preserved, EMPEROR-Reduced and EMPULSE studies show that empagliflozin significantly improves QoL in a wide spectrum of HF patients, regardless of EF. Very few therapies have been previously shown to improve symptoms and the functional status in the early post-discharge period. Apart from empagliflozin, the only other pharmacotherapies include intravenous ferric carboxymaltose, ivabradine (OPTIMIZE Heart failure care program) and sacubitril/valsartan [28, 40, 41].

Another SGLT2 inhibitor, recommended in HFrEF, is dapagliflozin [42]. In the DAPA-HF study, in the group receiving dapagliflozin, the TSS in KCCQ was higher than that observed in the placebo group by 2.8, 2.5 and 2.3 points (p < 0.0001), from baseline to 8 months [43]. More often patients receiving dapagliflozin had increased in KCCQ results for at least 5 points in the total score than in the placebo group (58.3% vs. 50.9%; OR 1.15; 95% CI 1.08–1.23) and less frequently experienced important deterioration (25.3% vs. 32.9%; OR 0.84; 95% CI 0.78–0.90; p < 0.001 for both comparisons) [43].

Kosiborod [44] analyzed DEFINE-HF and PRESERVED-HF trials and concluded that dapagliflozin improved QoL in patients with HF irrespective of EF [44]. Patients receiving dapagliflozin at 12 weeks demonstrate a greater improvement in KCCQ-CSS (effect size: 5.0; 95% CI 2.6–7.5 points; p < 0.0001) compared to the placebo group [44]. There was also an improvement, manifested in scores of KCCQ-PLS (effect size: 5.0; 95% CI 1.8–8.2 points; p = 0.0023), KCCQ-TSS (5.0; 95% CI 2.3–7.7 points; p = 0.0003), and KCCQ-OSS (3.7; 95% CI 1.3–6.1; p = 0.003), despite LVEF [44].

The recently published DELIVER study confirmed a positive effect of dapagliflozin in HF patients with EF > 40%. Patients who were administered dapagliflozin had a greater chance of improvement in the NYHA class compared to placebo patients. The result was seen as early as at week 4 [45]. The beneficial impact of dapagliflozin on QoL was also seen in improvement of KCCQ--TSS compared to the placebo group in month 8 (win ratio 1.11; 95% CI 1.03–1.21; p = 0.009; mean placebo-corrected difference between baseline and month 8 in survivors, 2.4 points; 95% CI 1.5–3.4) [46]. A prospective analysis of the DELIVER trial showed that frailer patients demonstrated a higher improvement of QoL, while having worse KCCQ score at baseline [47]. On the basis of a pooled meta-analysis of DAPA-HF and DELIVER, dapagliflozin is the second most effective drug, after empagliflozin, which improves QoL in the whole spectrum of HF, regardless of EF [48].

Finally, the CHIEF-HF remote, patient-centered randomized, placebo-controlled trial determined superiority of canagliflozin administered at daily doses of 100 mg daily over placebo in improving the KCCQ-TSS at 12 weeks — the difference between the two groups was 4.3 points (p = 0.016) [49]. Results were similar irrespective of occurrence of EF and diabetes status.

Quality of life and implantable devices

Implantable devices, together with pharmacotherapy, have a considerable impact on QoL of patients. Although the primary goal of all implantable devices is to improve patient survival and prognosis, their implantation can have both a positive and a negative impact on patients' lives. Depending on the type of the implanted device, improvement can be observed immediately (as in the case of a pacemaker), gradually increasing over time (as in the case of left ventricular assist device) or only under special conditions (as in the case of an ICD). Some of them may take the form of bridging or continuous therapy, and some are only supposed to monitor patients' condition. Guidelines for their application must be adequately determined so that they can serve the proper purpose. Issues regarding adequate ICD discharges are described in this paper in the section on ARNI.

Cardiac resynchronization therapy (CRT) is a cardiac pacing method used in patients with left ventricular systolic dysfunction and non-synchronous ventricular activation, which provides simultaneous or near-simultaneous electrical activation of both ventricles. A special CRT pacemaker or a device which can be applied via a cardioverter-defibrillator is used. These devices are characterized by an additional lead whose purpose is to stimulate the left ventricle. This therapy can improve performance and reverse adverse ventricular remodeling, improve QoL, reduce the number of hospitalizations and improve survival rates. However, patients should be appropriately selected. In cases of preserved LVEF ≥ 50% EF, no significant improvement after administering CRT therapy has been found. The PACE trial after 1 and 2 years did not improve the quality of life compared to right ventricular pacing alone [50, 51].

When analyzing implantable devices, it is important to consider devices whose purpose is to improve the heart valve function. Surgical repair is the gold standard in treatment of severe degenerative mitral regurgitation. However, an impact of application of transcatheter repair with the Mitra-clip device should be also considered. Lim et al. [52] report that such intervention in patients with excessive surgical risk is safe and brings good clinical outcomes, including reduced hospitalizations, functional improvement and improved QoL [52]. Significant improvements were found in SF-36 QoL questionnaire scores for both physical and mental components for almost all SF-36 subscales at each time point, except for body pain and the role-emotion scale at day 30. Similarly, both surgery and transcatheter valve replacement are possible for severe aortic stenosis. The second option is an acceptable alternative for patients at high surgical risk. Current evidence demonstrates that transcatheter aortic valve implantation (TAVI) will provide a significantly better prognostic benefit in inoperable patients [53]. The SURTAVI trial evaluated both interventions in patients with a moderate surgical risk [54]. Regardless of the choice of the treatment modality, both surgery and TAVI implantation improved clinical condition, which was observed in the assessment of the NYHA scale. Besides, they also improved QoL, as measured by the KCCQ questionnaire. Moreover, a greater proportion of patients treated with TAVI showed improvement as early as 1 month after the procedure.

It should also be stressed that in recent years we have observed that the number of younger patients receiving TAVI who show a longer life expectancy is increasing. It can be assumed that patients will survive their bioprostheses and the number of repeated interventions after TAVI will increase. Transcatheter heart valve failure, treated with transcatheter aortic valve implantation (TAVI--in-TAVI), will become increasingly common. More research is needed to assess how this intervention will affect the QoL of these patients.

Quality of life and implantable devices — Left ventricular assist device

Left ventricular assist device (LVAD) systems are used as a bridge to transplantation, destination therapy, recovery or to candidacy. LVAD is a special pump that supports the left ventricle by transferring the blood through a mechanical device from the ventricle into aorta Recently, more than half of LVAD implantations has become a destination therapy. Maclever and Ross [55], having analyzed a review of LVAD clinical trials, showed that patients with LVAD demonstrated an early improvement in KCCQ 1 to 3 months after implantation, which stayed for the time of device support. Besides, HeartMate II–DT (destination therapy) arm of HeartMate II trial KCCQ score improved from baseline 27 to 63 in 3 months with $p < 0.001$ [56].

The negative impact on the patients' lives may relate to possible complications. Implantable devices are foreign bodies so they may induce a local and/or systemic infection. In some cases, apart from administering hospital antibiotic therapy, it may also be necessary to remove the device, which may have a negative impact not only on the health but also on the well-being of the patient. Bleeding from the gastrointestinal tract or into the central nervous system is another significant complication. This is due to the application of anticoagulants and changes in the circulatory system, possibly caused by less physiological continuous flow in most LVAD systems. On the other hand, implantable devices can also lead to blood clots that in turn lead to strokes. It should also be mentioned that potential mechanical complications, e.g., damage to the device, damage to the electrodes, the action of electromagnetic radiation, which may lead to malfunction of the device and other complications. To prevent the above potential side effects, patients are required to avoid certain activities, involving as submersing in water, such as swimming or having a bath in a bathtub. They are not allowed to practice contact sports, do jumps and undergo magnetic resonance imaging examinations. Every patient has to learn about their own device, keep additional batteries and supplies and put on new sterile dressings every day. All those factors may have an influence on their QoL.

Discussion

Quality of life in patients with HF depends on many physical and psychological factors, including disease stage, age, sex, comorbidities, social and economic status, therapeutic processes, mental state, etc. Many studies show that QoL of patients with HF is relatively poor in comparison to QoL of healthy patients or patients with other diseases, like thalassemia, diabetes, certain types of cancer. Lower QoL correlates with longer hospitalization and higher mortality rates and generates costs for healthcare systems, families and patients. Also, patients with more severe HF symptoms and no social support demonstrated worse QoL.

Due to the lack of understanding of HF and its effects in the general population, there is a lot of anxiety about the disease progression in both patients and their caregivers. It would be useful if psychosocial care and support of such patients were better defined, as it happens in other life-limiting diseases, such as cancers. In this area, patient associations and support groups can play a role in helping the patients understand their disease, treatment and expectations. Fortunately, for some time now, due to new treatment methods, the prognosis and survival rate in patients with HF has been significantly improving, hereby also improving their QoL [56–62].

It is very important for a patient to understand and accept HF and closely cooperate with the doctor during disease treatment. Symptoms of the disease appear in a different order in different HF patients, which makes the disease unique for each patient. Gaining a relevant knowledge about the disease is one of the first steps in treating HF and improving the quality of patients' lives. Diligent monitoring of symptoms is highly important. The patient should be aware of possible symptoms like dyspnea, weight loss or gain, which, if measured every day, can help to prevent deterioration of disease symptoms. Sedentary lifestyle can negatively affect the disease itself and QoL. Yet, patients often isolate themselves and limit their activities as they fear disease progression or sudden death. Therefore, due to the chronic nature of HF, it is extremely important to be supported by the family and friends as it may also improve QoL [63, 64].

It is important that patients with HF should not only receive optimal pharmacotherapy and treatment with implantable devices but also be provided with appropriate care, multidisciplinary care including, among others, rehabilitation, education, and psychosocial support. Recently, due to the pandemic of COVID-19 and its consequences, some chronically ill patients had poorer access to medical care. Hence, their therapy might not have been optimal, and their prognosis and QoL decreased.

The importance and potential perspectives of QoL were highlighted in the results of a cohort study conducted by Greene et al. [65] on 2,872 US outpatients with HFrEF. Changes in KCCQ-OSS from baseline to 12 months have a greater prognostic value than changes in the NYHA class. Greene et al. [65], on the basis of clinical practice-based population, revealed that an improvement by 5 or more points in KCCQ-OSS was independently associated with decreased mortality (HR 0.59; 95% CI 0.44–0.8; $p < 0.001$) and mortality or HF hospitalization (HR 0.73; 95% CI 0.59–0.89; $p = 0.002$), whereas such a correlation was observed in the improvement of the NYHA class.

Innovative treatment options are constantly being designed for HF patients [66–68]. They improve their prognosis and QoL. However, some patients, despite receiving made-to-measure pharmacological treatment and implantable devices, do not demonstrate expected benefits. It should be remembered about providing such patients with palliative care.

Lastly, the adopted treatment program in HF should focus equally well on improving the prognosis and providing care at physical, psychological and social levels. Patients should be partners for medical personnel and should themselves take optimal, integrated decisions regarding offered procedures that are supposed to protect their health and lives. Regular assessment of patients' QoL and health promotion are key measures to increase their prognosis and survival.

Conclusions

Quality of life in HF is an extremely important element of the course of the disease and treatment process. The higher level of QoL is associated with the better acceptance of the disease and better prognosis. A new therapeutic option, especially pharmacotherapy (ARNI, SGLT2 inhibitors or ferric carboxymaltose) and devices, enable to improve QoL in HF.

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