Review Article

Current Therapeutic Options for Heart Failure in Elderly Patients

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Heart failure (HF) is a major and growing public health problem with high morbidity and mortality (Ponikowski et al., 2016). It affects 1-2% of the general population in developed countries, and the average age at diagnosis is 76 years. Because of a better management of acute phase and comorbidities, HF incidence is increasing in elderly patients, with a prevalence rising to 10% among people aged 65 years or older (Mozaffarian et al., 2014). Therefore, a substantial number of elderly patients need to be treated. However, because of clinical trial exclusion criteria or coexisting comorbidities, currently recommended therapies are widely based on younger population with a much lower mean age. In this review, we will focus on available pharmacological, electrical, and mechanical therapies, underlining pros, cons, and practical considerations of their use in this specific patient population.

1. Drug Therapy

Several issues must be considered in HF elderly patients undergoing pharmacological treatment. First, these patients suffer from multiple chronic diseases, which increase the likelihood of adverse drug reactions (hypotension, kidney dysfunction, and electrolytic disturbances) and often prevent the optimal recommended treatment, as is the case with severe chronic obstructive pulmonary disease and β-blockers. Also, patients with HF take many medications, which further increase the risk of adverse drug events and drug-drug interactions. Moreover, drugs pharmacokinetics and pharmacodynamics are influenced by age-related physiological changes of volume distribution. These aspects, in combination with the reduction in drug clearance, may affect to some extent the drug plasma concentration at steady-state, increasing the risk of drug accumulation and its side effects. Finally, the therapeutic plan may be affected by the age-related cognitive impairment, as well as social and economic factors, which impair the adherence to the medication regimen. Due to all the above reasons, several findings showed that elderly patients with HF had lower guideline based medical treatment prescription rates at discharge compared to younger patients [1–3].

To date, limited evidence has investigated the effects of the recommended systolic HF therapies in aged patients [4] (Table 1). However, data from small observational studies and substudies suggest that elderly patients derive similar benefits as younger patients [5–7].

β-Blockers are considered first-line therapy in the treatment of systolic HF. As the major randomized trials included a significant proportion of the elderly, the efficacy of β-blockers in the elderly is well-documented [8–14]. The SENIORS trial deserves a special mention [14]. It is a randomized controlled trial (RCT) that specifically evaluated the efficacy of nebivolol, a vasodilating β1-receptor blocker, in patients aged $\geq$ 70 years. Results showed a 14% relative risk reduction in the composite risk of all-cause mortality or cardiovascular hospital admission compared to placebo. The effect of nebivolol was similar in the subgroup of patients with chronic renal failure [15].

To avoid the major common side effects such as bradycardia or hypotension, β-blocker therapy should be initiated with the minimum recommended dose and uptitrated at intervals of no less than two weeks towards the target dose [16].

Angiotensin-converting enzyme inhibitors (ACEIs) benefits in elderly patients come from both major trials (Table 1)

Table 1: Major randomized clinical trials on HF drug therapy and elderly population.

Drug class	Trial	Patients number	Mean age (years)	Patients age ≥ 65	Patients age > 70	Primary endpoint RRR (%)	Age interaction
ACE inhibitors	SAVE [22] (captopril versus placebo)	2231	59	35%	15%	19% all-cause mortality	No (<55 versus 55–64 versus >65)
	SOLVD [21] (enalapril versus placebo)	2569	61	—	—	16% all-cause mortality	—
	ATLAS [20] (lisinopril low versus high dose)	3164	64	—	—	NS all-cause mortality	No (<70 versus ≥70)
	AIRE [19] (ramipril versus placebo)	2006	65	—	—	27% all-cause mortality	No (<65 versus ≥65)
	TRACE [18] (trandolapril versus placebo)	1749	67.5	33%	—	22% all-cause mortality	No (<65 versus ≥65)
Angiotensin receptor antagonists	CHARM-Overall [23] (candesartan versus placebo)	7599	66	34%	23%	(i) NS all-cause mortality (ii) 18% CV deaths or HF hospitalization	No (<65 versus >75–65 versus ≥75)
	CHARM-Alternative [23] (candesartan versus placebo)	2028	66	—	—	23% CV deaths or HF hospitalization	—
	ELITE II [25] (losartan versus captopril)	3152	71	100%	—	NS all-cause mortality	No (<70 versus ≥70)
	HEAAL [26] (losartan low versus high dose)	3846	66	26%	—	NS all-cause mortality	No (<65 versus ≥65)
	Val-HeFT [24] (valsartan versus placebo)	5010	63	47%	—	(i) NS all-cause mortality (ii) 13% all-cause mortality and morbidity	No (<65 versus ≥65)
B-blockers	CIBIS-II [10] (bisoprolol versus placebo)	2647	61	—	—	34% all-cause mortality	—
	COPERNICUS [11] (carvedilol versus placebo)	2289	63	—	—	(i) 35% all-cause mortality (ii) 24% all-cause mortality or all-cause hospitalization (i) 17% all-cause mortality	No (<65 versus ≥65)
	COMET [12] (carvedilol versus metoprolol tartrate)	3029	62	45%	—	(for carvedilol) (ii) NS for all-cause mortality or all-cause hospitalization	No (<65 versus ≥65)
	MERIT HF [13] (metoprolol succinate versus placebo)	3991	64	—	32%	34% all-cause mortality	No (upper tertile versus ≥ low + middle tertile)
	SENIORS [14] (nebivolol versus placebo)	2128	76	100%	100%	14% all-cause mortality or CV hospitalization	No (<75.2 versus ≥75.2)

TABLE 1: Continued.

Drug class	Trial	Patients number	Mean age (years)	Patients age ≥ 65	Patients age > 70	Primary endpoint RRR (%)	Age interaction
	RALES [29] (spironolactone versus placebo)	1663	65	—	—	30% all-cause mortality	No (<67 versus ≥67)
Aldosterone antagonists	*EPHESUS* [30] (eplerenone versus placebo)	6632	64	—	—	(i) 13% CV deaths or CV hospitalization (ii) 15% all-cause mortality	No (<65 versus ≥65)
	EMPHASIS-HF [31] (eplerenone versus placebo)	2737	69	—	—	37% CV deaths or HF hospitalization	No (<65 versus ≥65 and <75 versus ≥75)
Sacubitril-valsartan	*PARADIGM-HF* [27] (sacubitril-valsartan versus enalapril)	8399	64	50.1%	—	20% CV deaths or HF hospitalization	No (<65 versus ≥65)
Ivabradine	*SHIFT* [30]	6505	60	30.5%	—	18% CV deaths or HF hospitalization	No (<65 versus ≥65)
Cardiac glycosides	*DIG* [35] (digoxin versus placebo)	6800	63	—	30%	NS all-cause mortality	—
SGLT2 inhibitors	*EMPAREG* [36] (empagliflozin versus placebo)	7020	63	44.5%	—	14% CV deaths, nonfatal myocardial infarction, or nonfatal stroke	Yes (<65 versus ≥65)

SGLT2: sodium-glucose cotransporter 2; CV: cardiovascular; HF: heart failure; NS: nonsignificant; RRR: relative risk reduction.

and small community-size, observational studies [17–22]. All elderly patients without a history of allergy or intolerance to ACEIs should be treated, starting with low doses. In contrast, angiotensin receptor blockers (ARBs) should be considered only in patients who are intolerant to ACEIs due to cough, rash, or angioedema [23]. In this regard, main results and subsequently subanalyses of the VAL-HeFT [24], the CHARM [23], and other trials [25, 26] showed that increasing age did not influence the effect of ARBs on the outcomes. Recently, the PARADIGM-HF trial demonstrated that a new class of pharmacological therapy, which combines the neprilysin inhibitor sacubitril with the ARB valsartan reduces cardiovascular mortality and hospitalization for HF as well as all-cause mortality compared with enalapril alone [27]. The PARADIGM-HF enrolled a large proportion of patients aged ≥ 65 years; efficacy and safety (hypotension, renal impairment, and hyperkalemia) outcomes were similar across all age groups [28].

Concerning the use of aldosterone antagonist in the elderly, the RALES [29], the EPHESUS [30], and the EMPHASIS-HF [31] trials showed a decreased mortality risk, regardless of age. However, therapy with aldosterone antagonists requires a closer patient monitoring to prevent adverse events such as hyperkalemia, renal dysfunction, and hypotension, especially in elderly and very elderly patients.

Ivabradine can safely be prescribed in the elderly. The SHIFT trial demonstrated that, in HF patients with sinus rhythm, ivabradine reduces cardiovascular mortality and HF hospitalization in young as well as in elderly patients. Incidence of adverse events such as symptomatic bradycardia, asymptomatic bradycardia, and phosphenes similarly occurred in any of the age groups [32, 33].

The DIG trial has showed that digoxin reduces the risk of hospitalization with a higher risk of toxic effect and withdrawals in the elderly. In this regard, a serum digoxin concentration of 0.5–0.9 ng/ml is sufficient [34, 35].

Lastly, the EMPA-REG OUTCOME (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients) demonstrated that empagliflozin, an inhibitor of sodium-glucose cotransporter 2 (SGTL2), significantly reduces the risk of CV deaths, nonfatal myocardial infarction, or nonfatal stroke in subjects with type 2 DM and established CV disease with a greater benefit in those over 65 [36]. Also, empagliflozin was associated with a risk reduction of the secondary composite endpoint of HF hospitalization or CV death with a consistent benefit across subgroup age and in patients with and without baseline HF [37]. Although many factors may explain the effects of empagliflozin on HF and CV death, including osmotic diuresis, reduction of plasma volume, and sodium retention, the real mechanism is uncertain. Empagliflozin has shown a good safety profile. However, a higher risk of volume deletion-related adverse events and of urinary infections may be expected in elderly patients.

A significant interest is growing in diastolic or "preserved" HF that involves elderly patients who suffer from multiple comorbidities such as hypertension or atrial fibrillation. Unfortunately, besides a symptomatic benefit derived from diuretic therapy, to date, there is no evidence showing that the use of ACEIs/ARBs, aldosterone antagonist, or beta-blockers reduced mortality or morbidity in diastolic HF [38].

2. Anemia and Iron Deficiency

Anemia is commonly reported in chronic HF, especially in specific populations such as women, patients with renal impairment, and, even more importantly, elderly patients [39]. In this latter subgroup, anemia is most commonly due to iron deficiency, renal impairment, or inflammatory chronic diseases [40]. Anemia accompanying chronic HF nearly doubles the rate of death over three years in elderly patients, with patients with high hematocrit values being more likely to die from sudden cardiac death and patients with low hematocrit values being more likely to die for worsening HF [41].

Nowadays, several treatments are available in order to correct anemia and iron deficiency in elderly patients with HF. Two trials have shown the efficacy of intravenous iron in improving HF-related symptoms. In FERRIC-HF, 35 patients were randomized to iron sucrose or control [42]. Treatment with iron sucrose for four months resulted in an improvement in patients clinical status, peak VO_2, NYHA class, and treadmill exercise time. The same inclusion and exclusion criteria of the FERRIC-HF were used in the largest trial published so far on HF and iron deficiency: the FAIR-HF trial [43]. In this trial, ferric carboxymaltose was compared with placebo in 459 patients with HF and iron deficiency, while a diagnosis of anemia was not necessary. Patients treated with ferric carboxymaltose reported improved symptoms according the Patient Global Assessment (OR 2.51; 95% CI 1.75–3.61) and lower NYHA class when compared to the control group (OR 2.40; 95% CI 1.55–3.71). Similar benefits were seen between patients aged ≥ 69.7 years and <69.7 years for both Patients Global Assessment and NYHA class. Treatment with ferric carboxymaltose was associated with improvements also in the 6-minute walk test and in quality of life, while rates of adverse events and mortality were similar between the two groups.

3. Implantable Cardioverter-Defibrillator (ICD)

According to current guidelines, an implantable cardioverter-defibrillator (ICD) is recommended in symptomatic HF (NYHA classes II-III) associated with systolic dysfunction (LVEF ≤ 0.35) despite ≥3 months of treatment with optimal pharmacological therapy and in patients expected to survive for more than one year in good functional status [38]. Many RCTs have shown a significant reduction in sudden cardiac death (SCD) with a prophylactic ICD implant in ischemic cardiomyopathy [44–46] while primary prevention in nonischemic cardiomyopathy has recently been questioned, especially in older patients [47]. Unfortunately, the mean age of patients enrolled in these trials is always below 65 years, with the only exception of the MUSTT trial [48]. Moreover, no trial yet had tried to evaluate outcomes in patients aged ≥ 65 years, with some trials actively cutting

off the very elderly (≥80 years) as an exclusion criterion [49]. Therefore, only indirect evidence is currently available regarding primary prevention ICD implant as an effective tool in elderly patients (Table 2). The majority of the RCTs demonstrated no significant interaction between age categories and ICD efficacy in preventing all-cause death, with the DANISH study as the only notable exception, where the authors described a significant decrease of all-cause mortality in patients aged ≤ 59 years, while ICD provided no benefit in patients aged 60 years or older [47].

Santangeli and colleagues, pooling together the results of five randomized clinical studies, found that ICD was not associated with a significant reduction in mortality in patients aged ≥ 60 years (HR 0.81; 95% CI 0.62 to 1.05) while a pronounced 35% reduction in mortality was seen in patients aged < 60 years (HR 0.65; 95% CI: 0.50–0.83) [50]. The authors therefore concluded that prophylactic ICD implant did not improve survival in elderly patients.

Just a year after, another meta-analysis by Kong et al. tested the effectiveness of primary prevention ICD on patients aged ≥ 65 years and ≥75 years [51]. While selected studies differed from previous meta-analysis, the authors found a significant improvement in overall survival after ICD implant in patients aged ≥ 65 years (HR 0.62; 95% CI 0.49–0.78) and, although of lesser magnitude, even in patients aged ≥ 75 years (HR 0.70; 95% CI 0.51–0.97).

More recently, another meta-analysis questioned the usefulness of ICD for primary prevention demonstrating no difference in survival between patients aged ≥65 years and <65 years in a pooled analysis of 6 trials (RR 0.93; 95% CI 0.73–1.20) [52, 53]. Three studies provided data for patients aged ≥ 75 years and <75 years, and again a significant difference was found with this alternative cut-off.

Procedure safety in elderly and very elderly has also been discussed, but, unfortunately, most of the largest clinical trials did not report complications stratified by age [46, 53]. Prospective data and clinical registries [54] showed an incidence of complications in the elderly around 10%, with pocket hematoma being the most common. Serious complications are even rarer (less than 5%), with no significant difference between elderly and nonelderly subpopulations.

Potential survival improvement in elderly patients is hampered by many mechanisms, such as a higher number of comorbidities and lower life expectancy and quality of life. Moreover, the proportion of sudden cardiac death in this population is lower, as noncardiac causes of death increase in prevalence with older age [55]. Nonetheless, sudden cardiac death's prevalence increases with advanced age so that ICD implant could be associated with a greater overall survival benefit [56].

4. Cardiac Resynchronization Therapy (CRT)

Current guidelines on cardiac pacing and cardiac resynchronization recommend the use of cardiac resynchronization therapy (CRT) in patients with systolic HF, LVEF ≤ 0.35, wide QRS duration, and New York Heart Association (NYHA) functional classes II–IV [57].

In these patients, CRT has been demonstrated to reduce all-cause mortality [53, 58] and HF hospitalization [59, 60] (Table 2), while reducing left ventricular volumes, increasing left ventricular ejection fraction, and improving NYHA class, 6-minute walking test, quality of life, and peak oxygen consumption [61]. Moreover, clinical and echographic response to CRT seems to reduce clustered and unclustered ventricular arrhythmias in a recent propensity-score matched analysis [62].

Although the proportion of elderly patients with systolic dysfunction and HF is increasing dramatically in the last few decades, this specific subpopulation is scarcely represented in randomized controlled trials [60, 61], mostly due to the numerous comorbidities and the intrinsic difficulties related to enrolment. Therefore, direct data on the benefit of CRT in elderly patients is still limited.

In the COMPANION trial [58], CRT reduced the absolute risk of death and hospitalization by 12% when compared to optimal medical therapy alone. In these patients, age by itself was not an independent predictor of rehospitalization, as instead were chronic renal failure, atrial fibrillation, and ischemic cardiomyopathy. Similar results come from a pooled post hoc analysis of the NYHA III-IV patients of the MIRACLE and MIRACLE-ICD trials, in which CRT benefit on functional class and LVEF was consistent across every age group, even in patients over 75 years [63].

Data on NYHA I-II elderly patients is still more limited. A prespecified, post hoc analysis of the MADIT-CRT study aimed to investigate the effect of CRT on the composite endpoint of death and HF hospitalization during 3-year follow-up [64]. Multivariate analysis showed that CRT was associated with a significant reduction of the composite primary endpoint only in patients aged 60–74 (HR 0.55; 95% CI 0.41–0.72) and ≥75 years (HR 0.57; 95% CI 0.37–0.87), while no significant benefit was seen in patients under 60 years.

More recent, prospective observational studies aimed directly at the elderly population showed similar results. In a recent study on "real world" CRT implants, patients over 75 years of age performed as good as their younger counterparts in functional improvement, LVEF, and quality of life while showing a more pronounced reduction of LV end-systolic volume and a much greater QRS reduction over 12-month follow-up [65]. Thus, although there is still no definition of response to CRT that is commonly accepted, patients aged > 75 years have the same chance to meet the proposed clinical and ecographical criteria as their younger counterparts [63–65].

Resynchronization therapy offers significant advantages in the elderly, as it does not require uptitration and is not limited by poor compliance or drug interaction. However, it is still widely underused in common clinical practice, as it requires proper facilities and a dedicated out-of-hospital assistance.

5. Left Ventricular Assist Device

Left ventricular assist device (LAVD) is becoming a mainstream therapy for advanced HF. At the beginning, it was

TABLE 2: Major randomized clinical trials on HF device therapy and elderly population.

	Trial	Patients number	Mean age (years)	Patients age ≥ 65	Patients age > 70	Primary endpoint RRR (%)	Age interaction
	MUSTT [22]	704	67			55% all-cause mortality / 74% arrhythmic mortality	No (<60 versus 60–69 versus ≥70)
	MADIT II [21]	1232	64	—	35%	31% all-cause mortality	No (<65 versus ≥65)
ICD	DEFINITE [20]	458	58	34%	—	35% all-cause mortality / 80% arrhythmic mortality	No (<60 versus ≥60)
	DINAMIT [19]	674	61		—	NS all-cause mortality / 68% arrhythmic mortality	No (<65 versus ≥65)
	SCD-HeFT [19]	2521	60	23%	—	35% all-cause mortality	No (<65 versus ≥65)
	DANISH [36]	556	64			13% all-cause mortality (not significant)	Yes (≤59 versus 60–67 versus ≥68)
	COMPANION [23]	1520	67	56%		(i) 20% all-cause mortality or HF hospitalization	No (<65 versus ≥65)
CRT	CARE-HF [23]	813	66			(i) 37% all-cause mortality or HF hospitalization / (ii) 36% all-cause mortality	No (<66.4 versus ≥66.4)
	RAFT [26]	1798	66	57%	—	(i) 25% all-cause mortality or HF hospitalization / (ii) 25% all-cause mortality	No (<65 versus ≥65)
	MADIT-CRT [23] LBBB subgroup	1817	64	53%		(i) 53% all-cause mortality or HF hospitalization	No (<65 versus ≥65)

CRT: cardiac resynchronization therapy; HF: heart failure; ICD: implantable cardioverter-defibrillator; NS, nonsignificant; RRR: relative risk reduction.

thought as a bridge to heart transplant (HTx) in critically advanced HF patients refractory to medical therapy and with a high probability of death while waiting for HTx. Nowadays, the use of LVAD has assumed different connotations, from bridge to transplant to bridge to decision, or bridge to recovery or destination therapy (DT) [38, 66].

Thought HTx remains the gold standard in advanced HF treatment, LVAD implant as a destination therapy (DT) has become a frequent solution. The sixth annual report of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) has shown that the proportion of patients receiving a mechanical support device as DT is increased from 28.6% in 2008–2011 to 45.7% in 2014 [67].

Over time, LVAD implantation increase interested more patients aged 65–74 years compared with patients older than 75 years, although a substantial increase was also seen in this latter group [68].

Several reasons explain the LVAD breakthrough as DT. Firstly, There are the limited availability of donors and the common restriction to patients aged under 70 years [69], in an HF population with a mean age of 80 years at first diagnosis [70]. Moreover, elderly patients frequently present comorbidities that further restrict the indications to HTx. The REMATCH trial [71] was the first study showing the benefits of LVAD in patients with NYHA IV class compared to optimal medical therapy. In this trial, the LVAD group had a 48% reduction in the risk of death from any cause. Moreover, LVAD therapy resulted in a statistically significant increase in both one-year (52% versus 25%) and two-year (23% versus 8%) survival compared with controls, regardless of age. Older patients, however, showed a lower survival (47%) compared to patients aged under 60 years (74%) after one year.

Despite these initial and encouraging data from REMATCH [71], advanced age has subsequently been identified as a risk factor for death in patients with LVAD [72, 73]. Elderly patients tend to recover more slowly from surgery. They are generally more prone to complications, as bleeding or infections. However, advancing age significantly affects prognosis of those older patients with critically ill conditions at LVAD implantation: in contrast to INTERMACS 1-2 level patients, the 1-year survival for ambulatory heart failure patients is less dramatically affected by older age [67].

Therefore, therapeutic decision is hard and burdened by limited and sometimes contrasting literature.

In 2004, Jurmann et al. published their experience about LVAD in patients older than 65 or older than 60 with contraindications to HTx, characterized by a highly critical hemodynamic status [74]. The cumulative survival rate for the global population was 63% at 30 days, 30% at 180 days, and 22% at two years, comparable with survival rates of the REMATCH trial at the same time points. Older age, by itself, was not a determinant of survival in this series [74].

More recently, different authors [75–78] have analyzed the outcomes in elderly patients, using different age threshold. All the studies reported no significant difference in survival rate of older patients compared to younger ones. Kim et al. [78] performed an analysis of the Mechanical Circulatory Support Research Network (MCSRN) registry showing age is not a significant predictor of mortality when dichotomized (above and below 70 years) while it predicts prognosis if considered as continuous variable, with a 20% increased risk of death per decade of life. Moreover, authors reported preoperative creatinine as the most powerful predictor. Success of LVAD treatment is strongly related to a careful selection of patients based on a scrupulous preoperative risk assessment and a correct choice of implantation timing [76].

The opposite side of the debate is represented by the retrospective analysis of INTERMACS registry that showed a significant difference in 2-year survival between patients aged ≥70 years (63%) and patients aged ≤70 (71%). Moreover, age was an independent predictor of mortality during follow-up [79]. Authors, however, stressed that 63% survival at 2-year was still a very good result for elderly when compared with medical management.

In conclusion, data in elderly population are exiguous and not univocal. However, age alone should not be considered as an absolute contraindication to mechanical support or a synonym of poor outcome. A detailed evaluation and risk stratification of HF elderly patients are needed to find the right candidate to LVAD implant while waiting for specific clinical trials with the aim of defining distinct strategies for assessment, care, and therapy of this population.

A huge number of variables have been identified over time to be associated with increased mortality in advanced HF patients. However, no single parameter may be used for prognostic assessment: therefore the utility to consider a multiparametric score [80, 81]. Recognized tools as the Seattle HF risk score and the Heart Failure Survival Score stratify outpatients and are used to predict their 1-year survival in medical therapy with reasonable confidence, highlighting those patients at higher risk of death as preferable candidates to LVAD.

Moreover, the challenge of last years has been in identifying risk scores to predict long-term survival after LVAD implantation. In this context, the most useful ones are represented by the Model for End-Stage Liver Disease score (MELD score) and the Heartmate II risk score [82, 83].

To conclude a detailed evaluation and risk stratification of HF elderly patients are needed to find the right candidate to LVAD implant, while waiting for specific clinical trials with the aim of defining distinct strategies for assessment, care, and therapy of this population.

6. Palliative Treatments in End-Stage HF

When HF enters end-stage, patients experience greater physical and spiritual suffering despite maximal medical therapy and usually die of progressive pump failure within one year. Due to epidemiological changes, end-stage HF increasingly involves aged patients whose associated comorbidities exacerbate symptoms and increase the complexity of management. In this clinical scenario, there is a natural transition of goal treatments from life prolongation to end of life care with the focus on symptoms control, improved quality of life, and emotional support for the patient and his family [84, 85]. To address these needs, palliative care includes both pharmacological (opioid therapy, continuous

intravenous positive inotrope support, and antidepressant) and nonpharmacological approaches (hemofiltration, exercise training, and physiological interventions). Consistent with the aim of preserving the quality of life during the dying process, when the end of life is approaching, progressive withdrawal of conventional therapy and ICD inactivation may also be required [84, 85]. To date, although timing and nature of all these approaches are still not completely clear, palliative strategies for patients with end-stage HF are strongly discussed and recommended by all major cardiology associations [84, 85].

7. Conclusions

Heart failure is a complex syndrome and is predominantly a disease of the elderly, increasing its prevalence with the increasing age. Although older patients are less represented in clinical trials, all HF therapies, from drugs to devices, are still recommended in this population. However, the choice of the best treatment should be personalized, considering more aspects beyond HF such as comorbidities, frailty, social, and economic background and quality of life.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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