The relevance of specific heart failure outpatient programs in the COVID era: an appropriate model for every disease

Matteo Beltrami¹,²*, Simone Bartolini¹, Massimo Milli¹, Alberto Palazzuoli²

¹Cardiology Unit, San Giovanni di Dio Hospital, 50142 Florence, Italy
²Cardiovascular Diseases Unit, Department of Internal Medicine, Le Scotte Hospital, University of Siena, 53100 Siena, Italy
*Correspondence: beltrami.matteo1@gmail.com (Matteo Beltrami)

DOI: 10.31083/j.rcm2203077

This is an open access article under the CC BY 4.0 license (https://creativecommons.org/licenses/by/4.0/).

Submitted: 31 May 2021 Revised: 19 July 2021 Accepted: 28 July 2021 Published: 24 September 2021

Heart Failure (HF) is characterized by an elevated readmission rate, with almost 50% of events occurring after the first episode over the first 6 months of the post-discharge period. In this context, the vulnerable phase represents the period when patients elapse from a sub-acute to a more stabilized chronic phase. The lack of an accurate approach for each HF subtype is probably the main cause of the inconclusive data in reducing the trend of recurrent hospitalizations.

Most care programs are based on the main diagnosis and the HF stages, but a model focused on the specific HF etiology is lacking. The HF clinic route based on the HF etiology and the underlying diseases responsible for HF could become an interesting approach, compared with the traditional programs, mainly based on non-specific HF subtypes and New York Heart Association class, rather than on detailed etiologic and epidemiological data. This type of care may reduce the 30-day readmission rates for HF, increase the use of evidence-based therapies, prevent the exacerbation of each comorbidity, improve patient compliance, and decrease the use of resources. For all these reasons, we propose a dedicated outpatient HF program with a daily practice scenario that could improve the early identification of symptom progression and the quality-of-life evaluation, facilitate the access to diagnostic and laboratory tools and improve the utilization of financial resources, together with optimal medical titration and management.

Keywords
Heart failure, Hypertrophic cardiomyopathy, Dilated cardiomyopathy, Ischemic cardiomyopathy, Valvular heart disease, COVID-19, Telemedicine, Heart failure outpatient programs

I. Introduction
Heart Failure (HF) is the leading cause of outpatient visits in the Medicare system [1]; the increased prevalence of HF reflects a major health burden with respect to age-adjusted rates of first hospitalization, poor overall survival, and premature mortality when compared to the most common forms of cancer [2, 3]. Several items remain poorly explored; they include: (1) readmissions for worsening HF most often occur during the early months post-discharge (30 to 50% within the first 30–90 days) or in the last months before death, with similar trends among patients with heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) [4]. (2) The EVEREST Trial clearly shows that one-third of all hospitalizations are due to non-HF-related causes, another third are due to ischemic or arrhythmic reasons, and the remaining are related to incomplete decongestion during hospitalization [5]. (3) Despite the re-hospitalization rates for HFpEF (rates for HFrEF are similar), the mechanisms leading to destabilization and the risk profile are quite different [6]. In HFpEF, more than half of hospitalizations are not related to any specific cardiac causes, due to the exacerbation of the underlying comorbidities; conversely, hospitalizations for cardiovascular reasons are much more prevalent in HFrEF [7]. Therefore, the vulnerable phase represents the period when patients go from a sub-acute to a stabilized chronic phase; transitional care programs reduce 30-day readmission, optimize the use of evidence-based therapies, improve the patient’s necessary knowledge of the disease and save financial resources [8–11]. The structure and organization of HF clinics need a multidisciplinary team, physician- and nurse-directed, with easy access to available slots for laboratory and imaging exams and to other specialists with expertise in treating patients with HF [12]. Most care programs are based on the main diagnosis and the HF stages, but a model focused on specific HF etiology is lacking. For all these reasons, we propose a dedicated outpatient HF care that could improve the early identification of symptom progression and the quality-of-life evaluation, facilitate the access to diagnostic and laboratory tools and improve the utilization of evidence-based medications, with the aim of reducing HF hospitalizations. We also suggest a specific model to organize an optimal network between hospital clinics, outpatient visits, peripheral medical support and patient care.

2. Management of heart failure based on its etiology
2.1 Dilated cardiomyopathy management
2.1.1 HF in de novo dilated cardiomyopathy and advanced HF

Dilated cardiomyopathy (DCM) is one of the most frequent causes of HFrEF worldwide, and HF is a common clinical presentation [13]. Compared to other HF etiolo-
gies, DCM patients are younger and with lower left ventricle ejection fraction (LVEF) at diagnosis; women show better survival rates than men in relation to a better left ventricle (LV) systolic function. Outpatient visits should be scheduled every 3 months—or monthly—in subjects recently diagnosed or hospitalized who need therapy up titration and patients with left bundle branch block, high arrhythmic burden potentially candidates for cardiac resynchronization therapy (CRT), or with implantable cardioverter defibrillator (ICD). Cardiac magnetic resonance (CMR) is indicated in all patients at the first diagnosis of DCM, with a diagnostic and prognostic implication. In 30 to 40% of non-ischemic DCM, LV fibrosis is localized in the mid-myocardial septum; however, the characteristics of fibrosis are variable and can involve other locations, such as the LV free wall [14]. The presence and extension of LV fibrosis are both related to adverse cardiovascular outcomes [15]. CMR is recommended to assess the exact LV systolic dysfunction prior to CRT/ICD implantation in patients who are candidates for a LV assist device or Heart Transplantation (HT). Together with ischemic heart disease (ICM), DCM is the most common indication for HT in younger subjects (less than 60 years old). A dedicated pathway addressing the advanced HF management and a HT surgery center may be recommended [16]. In this context, cardiopulmonary exercise testing (CPET) provides an objective evaluation of the functional capacity and represents the key to defining the clinical severity and to stratifying the outcomes. CPET is essential for the anaerobic threshold measured by V-slope analysis of VO\textsubscript{2} and VCO\textsubscript{2}, exercise oscillatory ventilation and ventilatory efficiency (VE) with peak oxygen consumption (peak VO\textsubscript{2}), and VE/VCO\textsubscript{2} assessment. All these parameters reflect the pathophysiological changes seen in HF and are significantly associated with cardiovascular outcomes in DCM [17]. Peak VO\textsubscript{2} provides incremental benefits to LVEF, natriuretic peptide (NP) and late gadolinium enhancement (LGE) in the DCM populations, which highlights its potential utility in multi-parametric models [18]. Moreover, peak VO\textsubscript{2} is strongly associated with the onset of pulmonary hypertension (PH). Abnormal exercise capacity (calculated by the metabolic equivalent of the task) and PH are associated with a higher VE/VCO\textsubscript{2} slope, resulting in severe ventilation/perfusion mismatching and gas exchange abnormalities [19].

A dedicated nursing staff with HF skills may measure and record weight and blood pressure (BP), and provide patients with an education regarding their daily diuresis and body weight. The physician organizes the follow-up based on disease stability and progression (including booking the next visit, laboratory exams and second-level imaging tools).

2.1.2 HF in dilated cardiomyopathy with recovery of left ventricular ejection fraction

The clinical course of HF in DCM may be variable; however, around 40% of DCM patients show a significant LV reverse remodeling. Complete functional LV systolic recovery and reverse LV remodeling can be achieved if a correct etiology has been performed, especially following a guidedirected medical therapy [20]. Female sex, a higher LVEF at baseline, a reduced LV dimension, and a limited LGE area are all associated with positive LV reverse remodeling [21]. Outpatient visits should be scheduled every 6 months in subjects in stable clinical condition and with recovered LVEF. Holter ECG should be scheduled every 6 months, or more frequently, in the presence of a high arrhythmogenic burden. In these patients, a CMR should be repeated every 5 years, and should be performed during follow-up in case of HF progression and relevant worsening of LV/right ventricle systolic function. Exercise echocardiography (EE) provides a wealth of additional information during follow-up, such as functional capacity, BP curve, PH, mitral regurgitation (MR) and arrhythmias, and should be prescribed especially in case of HF symptoms during the stress test [22]. The 6-minute walking test (6-MWT) is a simple test capable of identifying variations in exercise tolerance with prognostic utility. Commonly available and simple, this test is a valid alternative to the more complex VO\textsubscript{2} in detecting changes in the functional capacity. The repetition after specific training program could also be useful to confirm the benefit for peak VO\textsubscript{2} of exercise tolerance, increased distance walked and METs [23] (Fig. 1).

2.2 Hypertrophic cardiomyopathy management

2.2.1 HF in HCM 'classic phenotype' and left ventricular outflow tract obstruction

Patients affected by hypertrophic cardiomyopathy (HCM) develop more frequent HF symptoms when the hypertrophic phenotype is clearly expressed and when left ventricular outflow tract (LVOT) obstruction and/or atrial fibrillation (AF) occur [24, 25]. Based on the HCM course and progression, outpatient check-up should be scheduled every year in patients with "classic" phenotypes. Holter ECG should be considered every year in all patients with HCM; consequently, in subjects with higher arrhythmogenic burden, suspected AF, unexplained syncope, a longer loop for 7 days or subcutaneous loop recorder implantation is recommended. Patients with signs and symptoms of HF due to LVOT should be evaluated every 3–6 months, to optimize medical treatment (b-blockers and dysopiramide) and re-check the indication for myectomy or a novel therapy such as mavacampten [26]. EE is commonly performed as a routine test in patients with HCM, primarily to measure the dynamic LVOT gradients provoked by physical exercise every 6 months in obstructive HCM patients and every two years in all remaining HCM patients [27, 28]. EE can add important management data and prognostic information, including functional capacity, BP response, pulmonary pressure changes and arrhythmias [29, 30]. LV diastolic pressure could markedly increase during exertion, causing exertional dyspnea and increased exercise intolerance; the diastolic function under stress should be reported in all patients subjected to EE. CMR should be recommended at diagnosis in all patients with HCM. The LGE extent and distribution significantly correlates with the
Management of patients with CMD and HF
(Family history, clinical evaluation, ECG, natriuretic peptides, six minute walking test)

1) LVEF
  - 40% ≤ LVEF ≤ 49%
  - LVEF ≥ 50%

2) Diastolic function
  - LA size (LAVI)
  - LA function (E wave, A wave, E/A ratio, DT)
  - TDI analyses (Septal E’, Lateral E’, E/E’ ratio)
  - Pulmonary vein atrial reversal velocity
  - Peak velocity of TR jet by CW Doppler

3) Mitral/tricuspid regurgitation

Exercise Echocardiography/CPET
(symptoms, peak oxygen consumption, VE/VO2 slope, diastolic dysfunction, dynamic mitral regurgitation, exercise induced PH)

TEE (in case of percutaneous/surgical intervention)

CMR (LVEF, reduction of LV wall thickness, LGE)

1) 1/3 months follow up after diagnosis/recent hospitalization or therapy up titration or CRT/ICD implantation
2) 6 months in patients in stable clinical condition or with "recovery LVEF"

Advanced HF → consider evaluation for HT or long-term mechanical circulatory support as bridge to HT

Fig. 1. The diagram describes the management of patients with Dilated Cardiomyopathy and Heart Failure: patients may be screened according to baseline LVEF and subsequent changes. Indeed, some patients may experience a systolic function recovery, a consistent percentage remain stable, and others have progressive deterioration with scarce response to therapy. Outpatient visits should be scheduled every 3 months or monthly in subjects recently diagnosed or hospitalized who need therapy up titration and patients with left bundle branch block, high arrhythmic burden potentially candidates for CRT, or with ICD. Outpatient visits should be organized every 6 months in subjects in stable clinical condition and with recovered LVEF. EE/CPET provides functional capacity, anaerobic threshold, BP curve, PH, MR and arrhythmias, and should be prescribed especially in case of HF symptoms during effort and prior to HT. CMR is indicated in all patients at the first diagnosis of DCM. CMR should be repeated every 5 years, and should be performed earlier during follow-up in case of HF progression and relevant worsening of LV/right ventricle systolic function. CMD, Dilated cardiomyopathy; ECG, Electrocardiogram; LA, Left atrial; LAVI, Left atrial volume index; DT, Deceleration time; TDI, Tissue doppler imaging; LVEF, Left ventricle ejection fraction; CMR, Cardiac magnetic resonance; TEE, Transesophageal Echocardiography; HF, Heart Failure; HT Heart Transplantation; CRT, Cardiac resynchronization therapy; ICD, Implantable cardioverter defibrillator; PH, Pulmonary Hypertension; LGE, Late gadolinium enhancement; CPET, Cardiopulmonary exercise test; TR, tricuspid regurgitation; CW, Continuous wave; LV, Left ventricular.

prognosis and identification of typical patterns of sarcomeric forms (thick-filament involves more frequently the anteroseptal wall, with mid-wall distribution, and thin filament the mid-wall distribution, with atypical sites). CMR can provide surgical information in patient referred to myectomy, such as the exact extension of hypertrophy, the presence of mitral valve apparatus abnormalities, or accessory chordae tendineae/papillary muscles and recognized apical aneurysms and thrombi, with implications affecting the outcomes [31].

2.2.2 HF in HCM “adverse remodeling and overt dysfunction”

Once it has occurred, the HCM-phenotype usually has a benign course, but a small proportion of patients, accounting for 15–20% of the total population, present an unfavorable clinical profile, with slow and progressive adverse ventricular remodeling, which results in 5–10% of patients with overt LV dysfunction expressing two different morphofunctional patterns: the “hypokinetic-dilated” variant, characterized by volume increase and LVEF impairment (<50%); and the “hypokinetic-restrictive” variant, characterized by a small and stiff LV, with severe diastolic dysfunction, regardless of any systolic function deterioration. In patients with “adverse remodeling” and “overt dysfunction phase”, the outpatient follow-up needs to be scheduled every 3–6 months [32]. The use of serial CMR, usually every 5 years (or every 2 years in patients with progressive disease), can provide valuable information to help the patient’s management, with
Management of patients with HCM and HF
(Family history, clinical evaluation, ECG, natriuretic peptides)

2D Echocardiography

- 1) LVEF (50%≤LVEF≤50%)
- 2) Diastolic function
  - LA size (LAVI)
  - LA function (E wave, A wave, E/A ratio, DT, IVRT)
  - TDI analyses (Septal E’, Lateral E’, E/E’ ratio)
  - Pulmonary vein atrial reversal velocity
  - Peak velocity of TR jet by CW Doppler
- 3) LVOT obstruction at rest and during Valsalva
- 4) mitral regurgitation

HCM progression: “adverse remodeling” and “overt dysfunction phase”

Exercise Echocardiography
- (symptoms, functional capacity, LVOT obstruction, diastolic dysfunction, dynamic mitral regurgitation, exercise induced PH)

TEE 3D Echo

Symptoms+LVOT obstruction
- Nadolol+dipiridamole if ineffective → Surgical miectomy (or Mavacampten?)

Fig. 2. The scheme proposes the management of patients with hypertrophic cardiomyopathy and heart failure: according to non invasive hemodynamic assessment and arrhythmic burden, the clinical evaluation may be tailored individually. Outpatient check-up should be scheduled every year in patients with ‘classic’ phenotypes, every 3–6 months in patients with signs and symptoms of HF due to LVOT and in patients with “adverse remodeling” and “overt dysfunction phase”. EE is commonly performed to measure the dynamic LVOT gradients every 6 months in obstructive HCM patients and every two years in all remaining HCM patients. The use of serial CMR, usually every 5 years or every 2 years in patients with progressive disease, can provide valuable information to help the patient’s management, with particular regard to LGE progression and LV wall thickness reduction. CPET should be prescribed in patients with suggestion of disease progression, in order to optimize treatment and refer to HT earlier. ECG, Electrocardiogram; LA, Left atrial; LAVI, Left atrial volume index; DT, Deceleration time; CMR, Cardiac magnetic resonance; TEE, Transesophageal Echocardiography; HCM, Hypertrophic cardiomyopathy; TDI, Tissue doppler imaging; LVOT, Left ventricle ejection fraction; HF, Heart Failure; HT Heart Transplantation; PH, Pulmonary Hypertension; LGE, Late gadolinium enhancement; CPET, Cardiopulmonary exercise test; TR, tricuspid regurgitation; CW, Continuous wave; LV, Left ventricular.

particular regard to LGE progression and LV wall thickness reduction [33]. The progression of LGE has proven to be a strong predictor of several clinical outcomes, such as LVEF ≤50% and the occurrence of HF. Extensive LGE has been identified as a risk factor for sudden cardiac death (SCD) and adverse remodeling. Emerging techniques, such as gadolinium extracellular volume (ECV) fraction by T1 mapping, allow the quantification of interstitial fibrosis; an increased ECV seems to correlate with a more advanced disease status and ventricular arrhythmias [34]. Shortened T1 mapping is also correlated with elevated filling pressures and dyspnoea, suggesting a relation between a degree of diffuse fibrosis and diastolic dysfunction [35]. CPET is useful to identify patients at high risk of disease progression and early mortality from HF, with the measurement of VE, anaerobic threshold and peak VO₂. CPET should be prescribed in all patients with a clinical and imaging suggestion of disease progression, in order to optimize treatment and refer to HT earlier [36].

Recent data from large international registries has shown a low mortality rate, with rare occurrence of SCD compared to earlier descriptions [37], however the SCD risk score and other risk factors—such as genetic positive variants, LGE, LV apical aneurism, end-stage HCM—should be punctually reconsidered during each visit (Fig. 2).

2.3 Infiltrative cardiac disease management
2.3.1 HF in transthyretin amyloidosis

Cardiac amyloidosis (CA) has exponentially increased among patients misdiagnosed as undifferentiated HFpEF, thanks to more advanced imaging tools, that are capable of recognizing matrix extracellular deposition with higher ac-
curacy than in the past. A remarkable concentric hypertrophy, paradoxical low-gradient aortic stenosis, or unexplained LV hypertrophy are all potential conditions associated with patchy amyloid deposition into myocardial tissue [38]. Transthyretin amyloid (ATTR) can be managed with emerging therapies, such as stabilizing molecules (tafamidis - AG10) and genetic silencers (patisiran and inotersen), which show a reduction in mortality accomplished by a relative reversal of LV mass [39]. In the meantime, the most common clinical picture of CA remains the advanced HF symptoms and recurrent congestion; the management still remains a challenge, often requiring high-dose diuretics and frequent hospitalizations, with a poor prognosis and a high healthcare burden. Thus, innovative outpatient programs and the earliest possible referral to an experienced center are crucial in order to assess the optimal treatment and patient care. Outpatient visits should be scheduled after 1 month from hospital discharge, and then every 6 months in chronic patients, including NP, troponin and Holter ECG every 6 months. 2D echocardiography is the primary imaging tool to be used in the follow-up of patients with amyloidosis. Diastolic function is invariably impaired, and the degree of dysfunction is related to the HF symptoms and the progression of the disease. Severe diastolic dysfunction, leading to the onset of AF, is the most common cause of destabilization in these patients. LVEF is not a reliable indicator of systolic function in CA, because it reflects radial contraction, which is often preserved until the end-stage disease. Longitudinal function is typically affected earlier than radial contraction, and indices of longitudinal function can be used as early disease markers. The longitudinal strain measurement shows the typical impairment of the basal segments, with sparing of the apical segments. New CMR techniques such as ECV can recognize interstitial fibrosis, a hallmark of CA. ECV level provides better prognostic information than LGE, and correlates with amyloid burden, disease severity, and with systolic and diastolic dysfunction markers [40] (Fig. 3).

2.3.2 HF in light chain amyloidosis

In case of amyloid light-chain (AL) amyloidosis, the main actor is the hematologist. The main role of the cardiologist is to evaluate the cardiac assessment for initial hematologic strategies, with the monitoring of HF symptoms and systolic function during chemotherapy and with the use of supportive HF treatment. Outpatient visits should be scheduled every month during the initial hematological treatment, and then every 3/6 months. Holter ECG, complete blood count, basic biochemistry, NP, troponin and serum free light chain quantification is requested upon each visit [41].

2.4 Ischemic cardiomyopathy management

2.4.1 Ischemic cardiomyopathy in patients with HFpEF without LV remodeling

ICM has a spectrum of clinical changes and pathophysiological states, which eventually lead to congestive HF, ranging from myocardial stunning, hibernation and scarring [42]. Remodeling is primarily achieved by myocardial fibrosis, which results in decreased cardiac function, arrhythmia, and possible cardiac conduction system impairment, leading to HF [43, 44]. Outpatient visit should be scheduled 1 month from the hospital discharge in patients with de novo HF, reduced LV systolic function and LV remodeling, or in patients with complex anatomy and multivessel disease and further evaluation of revascularization after imaging test for inducible myocardial ischemia [45]. Data from the STICH (Surgical Treatment for Ischemic Heart Failure) trial show that a ≥10% improvement of LVEF at 24 months is independently associated with a reduced mortality, and did not differ between patients receiving CABG and medical therapy or medical therapy alone [46]. However, revascularization in patients with well-established criteria for symptoms—despite an optimal medical therapy—and for prognosis are associated with a marked decrease in HF admissions. The up-titration of the medical therapy (such as sacubitril/valsartan and beta-blockers) and/or the indication for CRT/ICD implantation needs to be evaluated monthly during the early post-discharge period, followed by a trimestral evaluation. CMR should be proposed to all patients with ICM and HF as a therapeutic option (CRT/ICD implantation) and in order to evaluate myocardial viability integrating LV wall thinning, distribution of LGE and low-dose dobutamine stress CMR [47]. The infarct size has been identified as a predictor of adverse outcomes and adverse LV remodeling in STElevation myocardial infarction (STEMI). Our previous study showed the linear relationship between scar extension, regional wall motion abnormalities and LVEF [48]. This data is more significant in patients with transmural myocardial infarction (MI); conversely, patients with non-transmural MI show a less significant relationship. In line with the current findings, patients with transmural MI experienced greater systolic dysfunction than patients with sub-endocardial scar. LV enlargement and lower LVEF are much more relevant in patients with larger scar extension. The scar size is strictly related not only to adverse cardiac remodeling, but also to cardiovascular events [49]. Scar recognition is also a potential predictor of arrhythmogenic substrates. Scar extent, end-diastolic volume and regional wall motion abnormalities could improve the risk stratification of patients with previous STEMI. Patients with transmural MI are at higher risk of adverse outcomes, including recurrent MI, longer hospitalization, stroke, ventricular arrhythmias, and cardiac arrest [50].

2.4.2 Ischemic cardiomyopathy in patients with HFpEF without LV remodeling

In chronic patients with preserved LVEF and without LV remodeling, outpatient visits should be scheduled every 6 months to assess clinical status, NP, LVEF and the optimization of the treatment of risk factors, as well as to further evaluate myocardial revascularization. Scar identification is important not only in patients with impaired systolic func-
The diagram proposes the management of patients with transthyretin amyloidosis and heart failure: the clinical evaluation may be settled according to disease evolution and treatment response. Outpatient visits should be scheduled after 1 month from hospital discharge, and then every 6 months in chronic patients, including NP and troponin. 2D echocardiography is the primary imaging tool to assess the common echocardiographic characteristics of the disease, to evaluate the presence of aortic stenosis and the degree of diastolic dysfunction that is related to the HF symptoms and the progression of the disease. LVEF is not a reliable indicator of systolic function, which is often preserved until the end-stage disease. The longitudinal strain measurement shows the typical impairment of the basal segments, with sparing of the apical segments. ATTR can be managed with emerging therapies, such as stabilizing molecules and genetic silencers, which show a reduction in mortality accomplished by a relative reversal of LV mass. Innovative outpatient programs and the earliest possible referral to an experienced center are crucial in order to assess the optimal treatment and patient care.

This observation agrees with another study evaluating scar and wall motion in patients with healed MI, identifying scar as a better predictor of all-cause mortality than LVEF or LV size. In patients with ICM, HF and smaller sub-endocardial scar, the prognosis is more frequently related to non-cardiac comorbidities, such as older age, diabetes, and chronic kidney disease, with less frequent hospitalizations for cardiac causes. EE is a well-established technique to assess myocardial ischemia/viability, functional evaluation, and MR under stress. EE represent the most cost-effective imaging tool to evaluate inducible ischemia, with important data (large area of ischaemia >10% LV) to guide myocardial revascularization. The interpretation of the EE may be difficult in patients with previous MI, LV dysfunction, and multiple vessel disease. Stress CMR constitutes an accurate functional non-invasive test in ICM, due to its ability to identify myocardial perfusion, inducible ischemia and LGE. All these data are good prognosticators, and CMR may be well suitable also in CABG patients. Stress CMR should be proposed in patients with poor echocardiographic acoustic window, sub-maximal exercise test with significant reduction of diagnostic accuracy or impossibility to exercise. Stress CMR shows better sensitivity and negative predictive values, with an accurate assessment of inducible ischemia in single-vessel and multi-vessel coronary disease than Single Photon Emission Computed Tomography (SPECT). Stress CMR, according to local availability, should be preferred, due to its strongest predic-
tors for cardiovascular events, regardless of the cardiovascular risk factors and the angiographic outcome.

2.5 Valvular heart disease management

2.5.1 HF in aortic stenosis

The prompt recognition and effective treatment of congestive HF in patients with valvular disease are of the utmost importance for the practicing physician. Aortic stenosis (AS) is a progressive disease that characteristically remains asymptomatic for decades, but once its symptoms occur, survival is severely compromised. Historical data have shown that the time from the onset of the symptoms to death is about two years in patients who develop HF symptoms, three years in those who present with a syncope, and five in those presenting with anginal symptoms [53]. The continued improvement in transcatheter heart valves and implantation techniques resulted in a consistent decrease in the overall rates of all-cause death at 1 year among 31% of patients in the inoperable cohort of the PARTNER IB trial treated with TAVR [54], to 7% in SURTAVI trial targeting patients with an intermediate risk [55], and 5% in the all-comers NOTION trial [56]. The survival rate in patients with asymptomatic severe AS and preserved LVEF is similar to that of age-matched controls, with a low risk of sudden death. However, few echocardiographic parameters are associated predictors of symptoms development and adverse outcomes such as peak aortic jet velocity, severity of valve calcification, LV hypertrophy and LVEF. EE is useful to clarify the symptoms status under effort in patients with asymptomatic severe AS, and to suggest some prognostic indicators that could impact the decision of surgery, such as an increased peak aortic gradient during exercise, PH and a ≥10 mmHg fall in systolic BP at peak exercise [57], in this context, NP are pivotal for the purpose of risk stratification, reflecting the increase in their afterload, and thereby stressing the need for valve intervention [58]. Outpatient visits—including 2D-echocardiography—in patients with asymptomatic AS should be scheduled every 6 months, with a speedy evaluation of HF symptoms and NP increase.

Low-flow low-gradient (LF-LG) AS is a complex scenario, with diagnostic pitfalls and uncertainty about stenosis severity and challenges in differentiating a truly severe AS that benefits from aortic valve replacement from only moderate AS. Low-dose dobutamine stress echocardiography is indicated every year in asymptomatic patients with LF-LG AS when attempting to differentiate a truly severe AS from pseudo-severe AS and to assess contractile reserve. Moreover, in patients with suspected LF-LG AS, the calculation of the ratio of the outflow tract to aortic peak velocity and measurement of aortic valve calcium score by computed tomography would be reasonable, in order to further define the severity [59]. Although symptomatic patients with LF-LG severe AS show worse outcomes than those with high-gradient AS following aortic valve replacement, survival analyses highlight a significant benefit with intervention [60].

2.5.2 HF in mitral regurgitation

Organic and functional MR are both closely related to HF. Hemodynamically significant MR may exacerbate the hemodynamic strain on the failing LV, thus contributing to a worsening of symptoms and survival. In patients with moderate to severe MR, outpatient visit may be scheduled every 3–6 months. The onset of HF symptoms in severe MR represents the indication for mitral intervention, regardless of the LV systolic function. However, symptom onset is frequently associated with advanced MR, thus prompting the identification by 2D-echocardiography of increased LV size (LV end systolic diameter ≥40 mm) and systolic dysfunction (LVEF ≤60%), which are both prognostic echocardiographic data with an indication for surgical intervention [61]. In asymptomatic patients, the trend of NP is useful to better define the timing of valvular intervention in patients who report to be asymptomatic. In this context, EE adds essential information on the worsening of MR, the degree of PH and increased LV filling pressure under stress. The onset of LV dysfunction and PH worsen the prognosis of MR. Transesophageal echocardiography should be performed to study the mechanism of regurgitation, valve apparatus deterioration, presence of congenital valve defect and in prevision of surgical/percutaneous treatment [62]. Holter ECG may be scheduled once a year, in order to assess the arrhythmic burden (especially in mitral valve prolapse and mitral annular disjunction) and the presence of asymptomatic AF (Table 1).

Outpatient visits of secondary MR should follow the same schedule of primary MR. However, the indication for intervention in patients with chronic severe secondary MR related to LV systolic dysfunction is more questionable and should be proposed to patients with persistent HF symptoms despite optimal medical therapy for HF [63, 64]. Percutaneous valve repair is reasonable in patients with appropriate anatomy with LVEF between 20 and 50%, LV end systolic diameter ≤70 mm, and pulmonary artery systolic pressure <70 mmHg. Echocardiographic criteria for patients suitable for Mitraclip is a mitral valve area ≥4.0 cm² with central valve disease (A2/P2 scallops), normal leaflet thickness and mobility without extensive calcification, mobile length of posterior leaflet ≥10 mm or classic mitral valve prolapse. Good results are associated with a coaptation depth <11 mm and coaptation length ≥2 mm [65].

2.6 The importance of telemedicine in the 21st century and the COVID era

The COVID-19 outbreak has been associated with a 40–60% decrease in emergency department visits, with a nearly 3-fold increase in mortality among hospitalized patients, highlighting the need for the remote management (RM) of patients with HF [66]. The results concerning the transmission of vital signs are ambiguous: in the BEAT HF study, the combination of health coaching telephone calls and telemonitoring did not reduce the number of 180-day re-admissions for HF [67]. In the SUPPORT HF trial, the digital home monitoring with centralized specialists showed positive
| Visit, EKG, echocardiography | Exercise/stress echocardiography | Cardiopulmonary exercise CMR | Transesophageal echocardiography | Right Heart catheterization | Electrophysiological study |
|-------------------------------|---------------------------------|-------------------------------|---------------------------------|--------------------------|--------------------------|
| DCM - 1 month since hospital discharge - Every 6- 12 months based on arrhythmic burden - 1-3 months if therapy up-titration or in candidates to CRT/ICD - 6 months in stable patients and in ‘recovery’ LVEF | - At the time of first diagnosis, to evaluate functional capacity and arrhythmic burden - In patients with equivocal symptoms - HT candidates | - At the time of first diagnosis, to evaluate functional capacity and arrhythmic burden - HT candidates | - Repeat early if HF progression and worsening of LV/RV EF | - In advanced HF patients prior to mechanical circulatory support and/or HT | - EPS and eventually catheter ablation of VT refractory to medical therapy and/or HT |
| HCM - 1 year in classic phenotype - 12 months or earlier in case of suspected AF or high ventricular burden - 3-6 months in HF due to LVOT obstruction - 3-6 months in adverse remodeling and overt dysfunction phase | - At the time of first diagnosis, to evaluate functional capacity, arrhythmic burden and LVOT obstruction - In patients with equivocal symptoms - HT candidates | - At the time of first diagnosis, to evaluate functional capacity, arrhythmic burden and LVOT obstruction - In patients with equivocal symptoms - HT candidates | - Every 5 years in stable patients - Repeat early if HF progression (LV wall thickness reduction, progression of LGE) | - In patients candidate to myectomy to assess MR | - In advanced HF patients prior to mechanical circulatory support and/or HT to establish the correct diagnosis |
| CA - 1 month since hospital discharge - 12 months or months in case of suspected AF - 3-6 months in decompen-sated patients with ≥1 HF hospitalization | - At the time of first diagnosis, PH and diastolic dysfunction under stress - At the time of first diagnosis, PH and diastolic dysfunction under stress - In HT candidates | | | | - In case of advanced HF and unclear hemodynamic status despite optimal medical therapy |

Table 1. The table summarizes the outpatient planning and imaging schedule for each HF etiology.
| Visit, EKG, echocardiography | Exercise/stress echocardiography | Cardiopulmonary exercise test | Transesophageal echocardiography | Right Heart catheterization | Electrophysiological study |
|-----------------------------|---------------------------------|-------------------------------|-------------------------------|-----------------------------|--------------------------|
| **ICM**                     | - 1 month since hospital discharge | - every 12 months in the presence of high arrhythmic burden | - During follow-up to evaluate functional capacity and arrhythmic burden | - HT candidates | - During follow-up to assess biventricular function (i.e., CRT/ICD) and LGE amount for prognostic stratification | - To evaluate primary/secondary MR for HF patients prior to medical or percutaneous surgical or percutaneous circulatory support and/or HT |
|                             | - 1–3 months in HFrEF and LV remodeling to optimize therapy or candidates to CRT/ICD | - In patients who became symptomatic, to assess inducible ischemia to guide myocardial revascularization | - In patients with HF symptoms, to assess worsening of MR and PH during exercise | - In case of advanced HF and unclear hemodynamic status despite optimal medical therapy | - In case of advanced HFrEF and uncertain prognosis for CRT/ICD candidates |
|                             | - 6 months in HFpEF without LV remodeling | - In patients with equivocal symptoms or worsening of dyspnea | - Low-dose dobutamine stress in low-flow-low-gradient AS to differentiate true severe AS from pseudo-severe AS | - To assess the feasibility of percutaneous repair or surgery | - |
Fig. 4. Cross discussions between the General Practitioner and the Heart Failure specialist: check up schedule may be planned in relation to clinical stability, occurrence of other CV and non CV diseases. CKD, Chronic kidney disease; NYHA, New York Heart association; HF, Heart Failure; GPs, General practitioners; PH, Pulmonary Hypertension; CPET, Cardiopulmonary exercise test; EE, Exercise echocardiography; CMR, Cardiac magnetic resonance; CRT, Cardiac resynchronization therapy; ICD, Implantable cardioverter defibrillator.

results in terms of efficacy, but no improvements in the use of evidence-based treatments have been found in digital home monitoring alone [68]. Favorable results come from a selected group of patients with HF (New York Heart Association [NYHA] class II–III, LVEF <45% or—if higher than 45%—in therapy with oral diuretics) who have been randomized to a web-based system plus usual care or to usual care only [69]. The CHAMPION-HF trial shows an adequate adjustment of the medical therapy and a reduction in HF hospitalizations using the CardioMEMS monitor (a real time sensor of pulmonary pressure percutaneously implanted in the pulmonary artery) [70]. The remote assessment of lung congestion by measuring thoracic impedance shows a benefit in reducing early HF hospitalization [71]. In patients with the CRT/ICD device, the HeartLogic multisensor index and algorithm provides a highly sensitive and timely predictor of impending HF decompensation [72]. A few studies on a small cohort confirm that during the pandemic the use of RM is likely to substantially reduce HF hospitalization [73]. Smart watches and smartphones can measure the heart rate (HR) and heart rhythm through a single lead electrocardiography (ECG) or photoplethysmography by calculating beat-to-beat time intervals. ECG sensors are available in various forms, and are the gold standard for HR and heart rhythm measurement, since in HF patients heart rate variability provides independent information on the clinical status and the prognosis [74, 75]. D-Heart® is a portable device that enables the acquisition of the ECG on multiple leads, which is then streamed via Bluetooth to any smartphone [76]. Despite these opportunities, the impact of mHealth interventions on cardiovascular mortality, HF hospitalizations, NYHA class, quality of life and LVEF are inconsistent; however, further research is necessary, and these results should be contextualized during the pandemic [77].

The arrangement of a “virtual visit” should include: (1) a reimbursement by the Italian ministry of health; (2) an easily downloadable PC program for video-calls; (3) digital medical systems able to record HF parameters; (4) dedicated slots for HF visit. The first step is to identify patients who live alone or with family members or caregivers able to connect by remote modality and exclude vulnerable patients at risk of decompensation or with advanced HF [78]. The aim is to identify any symptom variation, transmit the vital signs or the hemodynamic data (only in patients with a device), up titrate the therapy and identify earlier patients at risk of decompensation. At the end of the visit, the clinician should write a brief report with instructions regarding laboratory testing and drug adjustments, schedule imaging/laboratory testing and organize the next follow-up (specifying if in person or virtual). In this context, a multidisciplinary link between the HF specialist and the general practitioner (GP) is crucial, with a pivotal role for the latter to recognize the early symptoms of congestion and monitor any potential side effects of the HF medication. A self-monitoring evaluation—mediated by a specialized nurse—would also be useful, and patients could gain confidence with their daily physical activity,
diuresis and body weight measurement. The identification of patients at risk for HF readmission may be accomplished by using clinical and laboratory parameters, easily assessed by the GP [79] (Fig. 4).

The various models proposed over the last years, during the pandemic, may become an opportunity for a novel practical HF approach, and may prevent the need for many redundant visits and outpatient accesses. Accordingly, the above experiences could lead to a lower burden for the Health System, together with quality-of-life improvement in stable patients who do not require repetitive check-ups. Program goals can be tailored according to the geography and location: especially for patients who live in geographic areas with difficult access to HF medication-assisted treatment. In this context, the GP needs dedicated outpatient HF program and a simple laboratory (NP measurement) and imaging ultrasound instruments to measure the inferior vena cava and detect lung ultrasound to assess pulmonary congestion by imaging B-lines. Several telemedicine programs have proven their feasibility and effectiveness in the HF populations, mostly in frequently overloaded Health Systems [80]. This approach could be suggested in situations in which physical consultation is difficult, due to logistical constraints. Several National Programs suggest a specific algorithm to distinguish from low to high risk mortality or re-hospitalization and to identify those patients that may benefit from a closer monitoring and an aggressive evidence-based treatment [81]. Ongoing experience will evaluate the availability and usefulness of different models, recognizing the more practicable ones in relation to the health resources and the local opportunities.

3. Conclusions

The HF clinic is becoming an important tool in the decision-making process aimed at avoiding the excessive rates of re-hospitalization and adverse event during the early and late post-discharge phases. At this point, there is no universal HF algorithm codifying for primitive diseases, etiology, evolution and severity. New outpatient clinic models should be organized following these criteria, in order to focus the efforts towards a significant reduction in the re-hospitalization and mortality rates. New, non-invasive telematic processes monitoring vital parameter, congestion and ECG criteria may be promoted, especially during this pandemic, in order to minimize hospital access among stable patients and to optimize treatment in those with recurrent worsening episodes.

Author contributions

MB and AP conceived the idea presented, wrote the manuscript and supervised the work. SB and MM collected figures and tables and performed the literature research. All authors contributed to the editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Acknowledgment

The authors would like to thank all the peer reviewers for their opinions and suggestions.

Funding

This research received no external funding.

Conflict of interest

The authors declare no conflict of interest.

References

[1] Khazanie P, Liang L, Qualls LG, Curtis LH, Fonarow GC, Hammill BG, et al. Outcomes of Medicare Beneficiaries with Heart Failure and Atrial Fibrillation. JACC. Heart Failure. 2014; 2: 41–48.
[2] Adams KF, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). American Heart Journal. 2005; 149: 209–216.
[3] O’Connor CM, Abraham WT, Albert NM, Clare R, Gattis Stough W, Gheorghiade M, et al. Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). American Heart Journal. 2008; 156: 662–673.
[4] Chun S, Tu JV, Wijeysundera HC, Austin PC, Wang X, Levy D, et al. Lifetime analysis of hospitalizations and survival of patients newly admitted with heart failure. Circulation. Heart Failure. 2012; 5: 414–421.
[5] O’Connor CM, Miller AB, Blair JEA, Konstam MA, Wedge P, Bahit MC, et al. Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduced left ventricular ejection fraction: results from Efficacy of Vasopressin Antagonism in Heart Failure Outcomes (EVEREST) program. American Heart Journal. 2010; 159: 841–849.
[6] Ross JS, Mulvey GK, Stauffer B, Patlolla V, Bernheim SM, Keenan PS, et al. Statistical models and patient predictors of readmission for heart failure: a systematic review. Archives of Internal Medicine. 2008; 168: 1371–1386.
[7] Maggioni AP, Otro F, Calabria B, Rossi E, Cinconze E, Baldasseroni S, et al. The real-world evidence of heart failure: findings from 41 413 patients of the ARNO database. European Journal of Heart Failure. 2016; 18: 402–410.
[8] Stauffer BD, Fullerton C, Fleming N, Ogola G, Herrin J, Stafford PM, et al. Effectiveness and cost of a transitional care program for heart failure: a prospective study with concurrent controls. Archives of Internal Medicine. 2011; 171: 1238–1243.
[9] Holland R, Batterbye J, Harvey I, Lenaghan E, Smith J, Hay L. Systematic review of multidisciplinary interventions in heart failure. Heart. 2005; 91: 899–906.
[10] Buck HG, Stromberg A, Chung ML, Donovan KA, Harkness K, Howard AM, et al. A systematic review of heart failure dyadic self-care interventions focusing on intervention components, contexts, and outcomes. International Journal of Nursing Studies. 2018; 77: 232–242.
[11] Palazzuoli A, Evangelista I, Ruocco G, Lombardi C, Giovannini V, Nuti R, et al. Early readmission for heart failure: an avoidable or ineluctable debacle? International Journal of Cardiology. 2019; 277: 186–195.
Gustafsson F, Arnold JMO. Heart failure clinics and outpatient management: review of the evidence and call for quality assurance. European Heart Journal. 2004; 25: 1596–1604.

Pinto YM, Elliott PM, Arbusinstein E, Adler Y, Anastasakis A, Böhm M, et al. Proposal for a revised definition of dilated cardiomyopathy, hypokinetic non-dilated cardiomyopathy, and its implications for clinical practice: a position statement of the ESC working group on myocardial and pericardial diseases. European Heart Journal. 2016; 37: 1850–1858.

Becker MAJ, Cornell JH, van de Ven PM, van Rossum AC, Al-laart CP, Germans T. The Prognostic Value of Late Gadolinium-Enhanced Cardiac Magnetic Resonance Imaging in Nonischemic Dilated Cardiomyopathy: a Review and Meta-Analysis. JACC: Cardiovascular Imaging. 2018; 11: 1274–1284.

Halliday BP, Baksi AJ, Gulati A, Ali A, Newsome S, Igi C, et al. Outcome in Dilated Cardiomyopathy Related to the Extent, Location, and Pattern of Late Gadolinium Enhancement. JACC: Cardiovascular Imaging. 2019; 12: 1645–1655.

Mehra MR, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. Journal of Heart and Lung Transplantation. 2016; 35: 1–23.

Sinagra G, Iorio A, Merlo M, Cannata A, Stolfo D, Zambon E, et al. Prognostic value of cardiopulmonary exercise testing in Idiopathic Dilated Cardiomyopathy. International Journal of Cardiology. 2016; 223: 596–603.

Marrow BA, Cook SA, Prasad SK, McCann GP. Emerging Techniques for Risk Stratification in Nonischemic Dilated Cardiomyopathy. JACC Review Topic of the Week. Journal of the American College of Cardiology. 2020; 75: 1196–1207.

Hirashiki A, Kondo T, Okumura T, Kamimura Y, Nakano Y, Fukaya K, et al. Cardiopulmonary Exercise Testing as a Tool for Diagnosing Pulmonary Hypertension in Patients with Dilated Cardiomyopathy. Annals of Noninvasive Electrocardiology. 2016; 21: 263–271.

Merlio M, Pyxaras SA, Pinamonti B, Barbati G, Di Lenarda A, Sinagra G. Prevalence and prognostic significance of left ventricular reverse remodeling in dilated cardiomyopathy receiving tailored medical treatment. Journal of the American College of Cardiology. 2011; 57: 1468–1476.

McNamara DM, Starling RC, Cooper LT, Boehmer JP, Mather PJ, Janosko KM, et al. Clinical and demographic predictors of outcomes in recent onset dilated cardiomyopathy: results of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy) 2 study. Journal of the American College of Cardiology. 2011; 58: 1112–1118.

Finocchiaro G, Merlo M, Sheikin N, De Angelis G, Papadakis M, Olivotto I, et al. The electrocardiogram in the diagnosis and management of patients with dilated cardiomyopathy. European Journal of Heart Failure. 2020; 22: 1097–1107.

Guaeni A, D’Aloia A, Gentilini A, Pagani M, Giordano A, Faggiano P. Effects of maximally tolerated oral therapy on the six-minute walking test in patients with chronic congestive heart failure secondary to either ischemic or idiopathic dilated cardiomyopathy. American Journal of Cardiology. 1998; 81: 1370–1372.

Rowin EJ, Hausvater A, Link MS, Apt B, Gionfriddo W, Wang W, et al. Clinical Profile and Consequences of Atrial Fibrillation in Hypertrophic Cardiomyopathy. Circulation. 2017; 136: 2420–2436.

Cabati M, Funagalli C, Beltrami M, Vignini E, Martinesi L, Tomberli A, et al. Prevalence, causes and predictors of cardiovascular hospitalization in patients with hypertrophic cardiomyopathy. International Journal of Cardiology. 2020; 318: 94–100.

Olivotto I, Orezia A, Barrales-Villa R, Abraham TP, Masri A, Garcia-Pavia P, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2020; 396: 759–769.

Elliott P, Anastasakis A, Borger M, Borggreve MF, Cecchi F, Char-ron P, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy. The Task Force for the Diagnos-sis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology. European Heart Journal. 2014; 35: 2733–2779.

Re F, Zachara E, Avella A, Baratta P, di Mauro M, Uggiosi M, et al. Dissecting functional impairment in hypertrophic cardiomy-opathy by dynamic assessment of diastolic reserve and outflow obstruc-tion: a combined cardiopulmonary-echocardiographic study. International Journal of Cardiology. 2017; 227: 743–750.

Lazzaroni E, Picano E, Dodi C, Morozzi L, Chiriatti GP, Lu C, et al. Dipyridamole echocardiography for diagnosis of coexistent coronary artery disease in hypertrophic cardiomyopathy. American Journal of Cardiology. 1995; 75: 810–813.

Cortigiani L, Rigo F, Gherardi, Calderesi M, Sicari R, Picano E. Prognostic implications of coronary flow reserve in left ante-rior descending coronary artery in hypertrophic cardiomyopathy. American Journal of Cardiology. 2008; 102: 926–932.

Quarta G, Aqward GD, Pedrotti P, Pontone G, Dellegrottaglie S, Iacovoni A, et al. Cardiovascular magnetic resonance imaging in hypertrophic cardiomyopathy: the importance of clinical context. European Heart Journal: Cardiovascular Imaging. 2018; 19: 601–610.

Olivotto I, Cecchi F, Poggesi C, Yacoub MH. Pattern of disease progression in hypertrophic cardiomyopathy: an individualized approach to clinical staging. Circulation: Heart Failure. 2012; 5: 535–546.

Salerno M, Sharif B, Arheden H, Kumar A, Axel L, Li D, et al. Recent Advances in Cardiac Magnetic Resonance. Circulation: Cardiovascular Imaging. 2017; 10: e003951.

Levine J, Collins JD, Ogele E, Murtagh G, Carr JC, Bonow RO, et al. Relation of Late Gadolinium Enhancement and Extracellu-lar Volume Fraction to Ventricular Arrhythmias in Hypertrophic Cardiomyopathy. American Journal of Cardiology. 2020; 131: 104–108.

Raiker N, Vallaganti S, Collins JD, Allen BD, Choudhury L. Myocardial tissue characterization by gadolinium-enhanced cardiac magnetic resonance imaging for risk stratification of adverse events in hypertrophic cardiomyopathy. International Journal of Cardiovascular Imaging. 2020; 36: 1147–1156.

Coats CJ, Rantell K, Bartnik A, Patel A, Mist B, McKenna WJ, et al. Cardiopulmonary Exercise Testing and Prognosis in Hypertrophic Cardiomyopathy. Circulation. Heart Failure. 2015; 8: 1022–1031.

Ho CY, Day SM, Ashley EA, Michels M, Pereira AC, Jacoby D, et al. Genotype and Lifetime Burden of Disease in Hypertrophic Cardiomyopathy: Insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). Circulation. 2018; 138: 1387–1398.

Gonzalez-Lopez E, Gallego-Delgado M, Guzzo-Merello G, de Haro-del Moral FJ, Cobo-Marcos M, Robles C, et al. Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction. European Heart Journal. 2015; 36: 2585–2594.

Maurer MS, Schwartz JH, Dundapaneni B, Elliott PM, Merliini G, Waddington-Cruz M, et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. New England Journal of Medicine. 2018; 379: 1007–1016.

Pan JA, Kerwin MJ, Salerno M. Native T1 Mapping, Extracellu-lar Volume Mapping, and Late Gadolinium Enhancement in Car-diac Amyloidosis. JACC: Cardiovascular Imaging. 2020; 13: 1299–1310.

Garcia-Pavia P, Rapezzi C, Adler Y, Arad M, Basso C, Brucato A, et al. Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. European Journal of Heart Failure. 2021; 42: 1554–1568.

Briceno N, Schuster A, Lumley M, Perera D. Ischaemic cardiomy-opathy: pathophysiology, assessment and the role of revasculari-sation. Heart. 2016; 102: 397–406.
Felker GM, Shaw LK, O’Connor CM. A standardized definition of ischemic cardiomyopathy for use in clinical research. Journal of the American College of Cardiology. 2002; 39: 210–218.

Sutton MGJS, Sharpe N. Left Ventricular Remodeling after Myocardial Infarction. Circulation. 2000; 101; 2981–2988.

Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2020; 42: 1289–1367.

Perry AS, Mann DL, Brown DL. Improvement of ejection fraction and mortality in ischaemic heart failure. Heart. 2021; 107: 326–331.

de Waha S, Patel MR, Granger CB, Ohman EM, Maehara A, Eitel I, et al. Relationship between primary percutaneous coronary intervention and ST-segment elevation myocardial infarction: an individual patient data pooled analysis from seven randomized trials. European Heart Journal. 2017; 38: 3502–3510.

Palazzuoli A, Beltrami M, Gennari L, Dastidar AG, Nuti R, McAlindon E, et al. The impact of infarct size on regional and global left ventricular systolic function: a cardiac magnetic resonance imaging study. International Journal of Cardiovascular Imaging. 2015; 31: 1037–1044.

Hombach V, Merkle N, Bernhard P, Rasche V, Rottbauer W. Prognostic significance of cardiac magnetic resonance imaging: Update 2010. Cardiology Journal. 2010; 17: 549–557.

Bello D, Fieno DS, Kim RJ, Perelles PS, Pasmann R, Song G, et al. Infarct morphometry identifies patients with substrate for sustained ventricular tachycardia. Journal of the American College of Cardiology. 2005; 45: 1104–1108.

Roes SD, Kelle S, Kaandorp TAM, Kokocinski T, Poldermans D, Lamb HJ, et al. Comparison of myocardial infarct size assessed with contrast-enhanced magnetic resonance imaging and left ventricular myocardial function and volumes to predict mortality in patients with healed myocardial infarction. American Journal of Cardiology. 2007; 100: 930–936.

Kinnel M, Sanguinetti F, Pazel T, Unterseeh T, Hovasse T, Toupin S, et al. Prognostic value of vasodilator stress perfusion CMR in patients with previous coronary artery bypass graft. European Heart Journal-Cardiiovascular Imaging. 2020; 13: jea316.

Frank S, Johnson A, Ross J. Natural history of valvular aortic stenosis. British Heart Journal. 1973; 35: 41–46.

Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. New England Journal of Medicine. 2010; 363: 1597–1607.

Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. New England Journal of Medicine. 2017; 376: 1321–1331.

Thyregod HGH, Steinbrüchel DA, Ihlemann N, Nissen H, Kjeldsen SJ, Petursson P, et al. Transcatheter Versus Surgical Aortic Valve Replacement in Patients with Severe Aortic Valve Stenosis: 1-Year Results from the all-Comers NOTION Randomized Clinical Trial. Journal of the American College of Cardiology. 2015; 65: 2184–2194.

Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: a Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021; 143: e72–e227.

Elbaz-Greener G, Ghanim D, Kusniec F, Rabin A, Sudarsky D, Carasso S, et al. Pre- and Post-Transcatheter Aortic Valve Replacement Serum Brain Natriuretic Peptide Levels and all-Cause Mortality. Cardiology. 2020; 145; 813–821.

Clavel M, Magne J, Pibarot P. Low-gradient aortic stenosis. European Heart Journal. 2016; 37: 2645–2657.

Anjan VY, Herrmann HC, Pibarot P, Stewart WJ, Kapadia S, Tuzcu EM, et al. Evaluation of flow after transcatheter aortic valve replacement in patients with low-flow aortic stenosis: a secondary analysis of the PARTNER randomized clinical trial. JAMA Cardiology. 2016; 1: 584.

Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. European Heart Journal. 2017; 38: 2739–2791.

Namazi F, Vo NM, Delgado V. Imaging of the mitral valve: role of echocardiography, cardiac magnetic resonance, and cardiac computed tomography. Current Opinion in Cardiology. 2020; 35: 435–444.

Obadia J, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, et al. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. New England Journal of Medicine. 2018; 379: 2297–2306.

Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, et al. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. New England Journal of Medicine. 2018; 379: 2307–2318.

Katz WE, Conrad Smith AJ, Crock FW, Cavalcante JL. Echocardiographic evaluation and guidance for MitraClip procedure. Cardiovascular Diagnosis and Therapy. 2017; 7: 616–632.

Colivicchi F, Di Fusco S, Magnani M, Cipriani M, Imperoli G. The impact of the COVID-19 pandemic and Italian lockdown measures on clinical presentation and management of acute heart failure. Journal of Cardiac Failure. 2020; 26: 464–465.

Ong MK, Romano PS, Edgington S, Arowon HU, Auerbach AD, Black JT, et al. Effectiveness of Remote Patient Monitoring after Discharge of Hospitalized Patients with Heart Failure: the Better Effectiveness after Transition – Heart Failure (BEAT-HF) Randomized Clinical Trial. JAMA Internal Medicine. 2016; 176: 310–318.

Rahimi K, Nazarzadeh M, Pinho GA. Home monitoring with technology-supported management in chronic heart failure: a randomized trial. Heart. 2020; 106: 1573–1578.

Mohabadi D, Kittleson MM. Remote monitoring in heart failure: current and emerging technologies in the context of the pandemic. Heart. 2021; 107: 366–372.

Abraham WT, Adamson PB, Bourge RC, Aaron MF, Costanzo MR, Stevenson LW, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet. 2011; 377: 658–666.

Lala A, Barghash MH, Giustino G, Alvarez-Garcia J, Konje S, Parikh A, et al. Early use of remote dielectric sensing after hospitalization to reduce heart failure readmissions. ESC Heart Failure. 2021; 8: 1047–1054.

Boehmer JP, Hariharan R, Devecchi FG, Smith AL, Molon G, Capucci A, et al. A Multisensor Algorithm Predicts Heart Failure Events in Patients with Implanted Devices: Results from the MultiSENSE Study. JACC: Heart Failure. 2017; 5: 216–225.

Almufleh A, Ahluwalia M, Givertz MM, Weintraub J, Young M, Cooper J, et al. Short-term Outcomes in Ambulatory Heart Failure during the COVID-19 Pandemic: Insights from Pulmonary Artery Pressure Monitoring. Journal of Cardiac Failure. 2020; 26: 633–634.

Bayomy K, Gaber M, Elshafeey A, Mhaimed O, Dineen EH, Marvel FA, et al. Smart wearable devices in cardiovascular care: where we are and how to move forward. Nature Reviews Cardiology. 2021; 18: 581–599.

Oseran AS, Afari ME, Barrett CD, Lewis GD, Thomas SS. Beyond the stethoscope: managing ambulatory heart failure during the COVID-19 pandemic. ESC Heart Failure. 2021; 8: 999–1006.

Maurizi N, Faragli A, Imberti J, Briante N, Targetti M, Baldini K, et al. Cardiovascular screening in low-income settings using a novel 4-lead smartphone-based electrocardiograph (D-Heart®). International Journal of Cardiology. 2017; 236: 249–252.

Sattic S, Iyngkar P, Andrew S, Patil A, Bidargaddi N, Battersby M, et al. Rethinking heart failure care and health technologies from early COVID-19 experiences - a narrative review. Reviews in Cardiovascular Medicine. 2021; 22: 105.
[78] Koehler F, Koehler K, Deckwarte O, Prescher S, Wegscheider K, Kirwan B, et al. Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial. Lancet. 2018; 392: 1047–1057.

[79] Verhestraeten C, Weijers G, Debleu D, Ciarka A, Goethals M, Droogmans S, et al. Diagnosis, treatment, and follow-up of heart failure patients by general practitioners: A Delphi consensus statement. PLoS ONE. 2020; 15: e0244485.

[80] Afonso Nogueira M, Ferreira F, Raposo AF, Mónica L, Simões Dias S, Vasconcellos R, et al. Impact of telemedicine on the management of heart failure patients during coronavirus disease 2019 pandemic. ESC Heart Failure. 2021; 8: 1150–1155.

[81] Bonow RO, Bennett S, Casey DE Jr, Ganiats TG, Hlatky MA, Konstam MA, et al. ACC/AHA Clinical Performance Measures for Adults with Chronic Heart Failure: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to Develop Heart Failure Clinical Performance Measures): endorsed by the Heart Failure Society of America. Circulation. 2005; 112: 1853–1887.