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Sigma goals of heart failure management

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Abstract
The leading cause of death in India is cardiovascular disease (CVD) and its prevalence is expected to rise. A 5% prevalence of obesity in India can cause an estimated 1,80,000–3,00,000 cases of heart failure (HF) annually. Since the progression of asymptomatic left ventricular systolic dysfunction (LVSD) leads to HF, early diagnosis can help in delaying or reversing the progression. Six consensus meetings were held at the national level wherein experts from across the country discussed various factors that can hinder early diagnosis of HF and reviewed the SIGMA goals of HF management. The attitude of physicians towards HF must be reformed, and they need to be vigilant of the signs and symptoms of HF. Clinical examination with a history of past month is most crucial in screening HF. Diabetics with hypertension for >5 years must be strongly suspected. Chest radiograph can be done to rule out cardiomegaly, pulmonary venous congestion, and other differential diagnosis. Electrocardiography and echocardiography should rule out abnormal rhythm/ventricular hypertrophy/ischemic heart disease. Usually, asymptomatic patients have increased natriuretic peptides. B-type natriuretic peptide (BNP) levels help in diagnosis of HF with preserved ejection fraction (HFpEF). In the elderly, body mass index must be taken into consideration for HF assessment, and higher values of N-terminal (NT)-proBNP and BNP could predict HF diagnosis. Symptom alleviation, preventing hospitalization, and improving survival are the goals of HF therapy. HF symptom management requires meticulous diagnostic work-up as well as optimal treatment of underlying conditions. The justification for quality-of-life (QoL) inclusion can be drawn from the fact that HF not only affects patient health but also influences QoL domains, such as psychological, social, emotional, sexual, and mental well-being. Angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, and/or other cardiovascular drugs as first-line therapies that significantly reduce hospitalization risk.

Keywords: left ventricular systolic dysfunction; quality of life; ejection fraction; comorbidities; beta blockers; loop diuretics

Introduction
Heart failure (HF) is the end stage of all diseases of the heart and a major cause of morbidity and mortality [1].
Per the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) Task Force guidelines, the current definition of HF is *a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral edema* [2].
Although there are updated guidelines from European Society of Cardiology (ESC), ACCF/AHA and guidance papers from European Society of Emergency Medicine (EUSEM), European Society of Intensive Care Medicine (ESICM) for the treatment of Heart Failure (HF), physicians on the field rely on the decisions of expert opinion consensus, rather than evidence-based recommendations. This could be partly due to the paucity of evidence in the field. Rapid identification of symptoms, underlying causes, and accompanying complications is necessary for assessing the severity of condition and initiating the specific treatment course [3].

Methodology
Six national level consensus meetings were held in 2019, wherein 72 eminent experts (cardiologists) from different regions of the country attended panel meetings and discussed the importance of early diagnosis and goals of HF management. This article reviews the discussion held during these meetings and provides a consensus roadmap and a composite model for the early identification and treatment of HF.

Factors contributing to heart failure management
Morbidity and mortality of heart failure
With innovative treatment procedures, a decline in mortality is seen, but the same is not observed with respect to hospitalization rate [4].Comorbidities, congestion, and target-organ lesion are the three main factors leading to rehospitalization[5]. It is projected that 1,20,000–6,90,000 Indians could have HF due to CHD every year with a 3% prevalence in 2000, and an annual incidence of 0.4%–2.3% for patients with coronary heart disease (CHD)[6].
Obesity is an important risk factor for HF as observed in the

Framingham Heart Study, wherein the estimated increase in the annual incidence of HF due to obesity was found to be 0.3% in women and 0.5% in men after adjustment for age, hypertension, left ventricular hypertrophy, myocardial infarction, valve disease, diabetes, and cholesterol[7]. In the Indian setting, Reddy *et al* found an estimated prevalence of obesity (BMI >30 kg/m^2) from 10,970 urban Delhi and rural Haryana participants to be 6.8% [8]. Thus, a 5% prevalence of obesity in India could result in an estimated 1,80,000–3,00,000 cases of HF annually [6].

Symptomatic burden

Patients with HF experience a range of symptoms from physical, psychological, social, to existential distress which can escalate in the final 6 months of life. Table 1 provides the statistics of various symptoms experienced by patients with HF [9].

Table 1: Statistics of symptoms experienced by patients with heart failure

Symptom	Statistics
Pain	Up to 84% of patients from a study agreed that pain consistently contributes to their suffering
Dyspnea	More than half of patients with HF consistently report dyspnea that crescendos in the last 6 months of life
Gastrointestinal distress	Upper GI symptoms have been observed in 27% of HF patients and anorexia due to tasting/swallowing difficulties in up to half the patients. Low forward cardiac output, poor intestinal blood flow, right-sided volume overload, hepatic congestion, and gut wall edema can cause nausea and vomiting
Mood disorder	About 21%–36% of HF have a mood disorder
Fatigue	With many contributing factors beyond low cardiac output, up to 85% of HF patients suffer with fatigue

GI, gastrointestinal; HF, heart failure

Conventional diagnosis and its lacunae

The Canadian Cardiovascular Society (CCS) published an algorithm for the diagnosis of HF in the ambulatory care setting in 2017 [10].Nevertheless, poor prognosis of HF is attributed to the diagnosis of HF [11].

Moreover, lack of effective means of early detection of HF to test interventions has contributed to the limited success in slowing progression of HF severity [12].

Because asymptomatic left ventricular systolic dysfunction (LVSD) often progresses to symptomatic HF, early diagnosis of LVSD and management via interventions or pharmacotherapy can help delay or reverse the progression of adverse left ventricular remodeling [10].

Additional reasons warrant the necessity for early diagnosis of HF [13]:

1. The prognosis of a chronic progressive disease such as HF is highly dependent on the time of diagnosis (early or late in the disease trajectory), and it affects the severity of disease
2. Variation in the disease trajectory of HF is highly individualized, and the identification of palliative phase commencement is difficult. Patients generally do not exhibit a gradual downward path, but a few feel and function well before sudden death, whereas others experience an upward path after a period of poor quality of life
3. General practitioners (GPs) play a pivotal role in the diagnostic and palliative phases in determining disease trajectory, participating in co-operative care with specialist teams in the intervening period, and in preparation of transition in care for patients with HF from hospital-based care to primary care

Experts' analysis

- *Early diagnosis is very important for better outcomes of HF management*
- *In some patients, the progression is slow whereas in others it can be aggressive*
- *Associated comorbidities can have a grave impact on overall prognosis of disease*
- *Physicians should be sensitized towards high prevalence of HF. They should actively look for signs/symptoms of HF*

Thus, the current challenges in the early screening of patients with HF include the absence of uniform prognosis due to highly individualized disease trajectory and co-morbidities affecting prediction of palliative phase by healthcare teams.

Integrated Model For Cardiac Failure Management: Summating the Cardiac Care models

To be able to accurately diagnose patients suspected of HF early, a final model containing both clinical and investigative procedures had been formulated. While the clinical model included various variables such as the presentation of symptoms, medical history, past medications, and physical examinations, the working model included investigative procedures such as electrocardiogram (ECG), creatinine level, N-terminal B-type natriuretic peptide (NT-pro BNP), high-sensitivity C-reactive protein (hs-CRP), and echocardiogram (ECHO) with left ventricular ejection fraction (LVEF) as epicenter.

Although echocardiography is the prime investigation for the diagnosis of HF, its limited availability in primary care, limits its applicability in diagnosis. The conglomeration of symptoms and measurements of natriuretic peptides combined with ECG and echocardiography increases the potential of detecting HF. For detecting non-acute HF in suspected patients, the common variables [14] are:

- history of ischemic heart disease, especially prior myocardial infarction
- symptoms and/or signs of fluid retention
- laterally displaced or broadened and sustained apical beat; and
- male gender

Clinical Model: History and Clinical Findings

Rutten and Gallagher reported that the detection of any type of HF is difficult especially in the early stages due to the symptoms and signs being non-specific [13]. A key symptom of HF, breathlessness, could be easily confused with chronic obstructive pulmonary disease (COPD), obesity, or deconditioning.

This could lead to underdiagnosis, which was evident by the high prevalence rates of unrecognized HF (constituting up to 80% of all HF cases) in high-risk community populations such as older people with breathlessness and patients with type 2 diabetes or COPD from primary care. If this subset of population is presented to GPs with suggestive HF symptoms, these symptoms may not be recognized as causes of HF or may be confused with other diagnoses; alternatively, patients may themselves also not report them[13].

Experts' analysis

- *It should be made very clear to the physicians that HF is quite a common condition, but often misdiagnosed. All physicians should be vigilant of the signs and symptoms of HF*
- *Common differential diagnoses could be COPD, pulmonary fibrosis, pneumonia, pulmonary embolism, nephrotic syndrome, etc.*
- *Proper history and examination can easily differentiate between these conditions*

Angina pectoris is chest pain or discomfort due to CHD that occurs if the heart muscle is devoid of oxygenated blood due to ischemia (narrowing or blockage of one or more arteries)[15,16].

Atypical angina is usually associated with bloating and abdominal distress, often attributed to indigestion. Other patients suffer with dyspnea due to the sharp reversible increase in left ventricular filling pressure that often accompanies ischemia. As the ischemic symptoms require a minute or more to resolve, brief fleeting sensations rarely represent angina [17].

Nocturnal angina occurs when a dream is associated with striking changes in respiration, pulse rate, and blood pressure, and can depict recurrent left ventricular failure [17].

Angina decubitus occurs spontaneously during resting and is associated with increased heart rate and hypertension, thereby increasing oxygen demand [17].

Unstable angina has predictable characteristics and any changes should be taken seriously [17].

A Californian study reported that patients, especially women, diagnosed with both angina and impaired glucose tolerance (IGT) are at a greater risk of CHD-related mortality than those without [15].

Following age-adjusted analysis, it was found that women with diabetes and angina had 3.87 times greater risk of death from CHD when compared to women without angina ($P = 0.01$). Moreover, women with IGT and angina had a 2-fold higher risk of CHD mortality (normal glucose: hazards ratio [HR] = 1.99, $P = 0.03$; IGT: HR = 1.98, $P = 0.04$) than those without. Women with angina were significantly older and had greater waist circumferences, higher triglycerides, lower high-density lipoprotein cholesterol (HDL-C) levels, and higher rates of hypertension than women without angina ($P<0.05$)[15].

The CCS guidelines for HF (2017) recommend that apart from thorough physical examination and investigation of clinical history and initial diagnosis directed at either confirming excluding HF, investigations must be carried out to diagnose any specific systemic disorders that can alter development or progression of HF such as thyroid dysfunction [10].

The 2013 ACCF/AHA guidelines for the management of HF recommend that apart from physical examination and clinical history including response to older pharmacological agents, investigations should be carried out for onset of first symptomatic attack or date of discovery of atrial fibrillation (AF), frequency, duration, precipitating factors, and modes of termination of AF and any underlying heart disease or other reversible conditions (e.g., hyperthyroidism or alcohol consumption) if any[2].

Experts' analysis

- *Clinical examination and history are the most important investigations in the screening of heart failure*
- *History of past one month is very important*
- *For patients with a medical history of hypertension and diabetes mellitus for more than five years, HF should be strongly suspected and investigations listed in Table 2 should be mandated*
- *While screening for HF, medication part could be kept in last*

Table 2: Check-list for the clinical model

Symptoms (Yes/No)	Medical history (tick whichever appropriate)	Medications used (tick whichever appropriate)	Physical examination (enter/tick the relevant findings)
Increasing Breathlessness – Y/N	Hypertension	Diuretics	BMI
PND/orthopnea – Y/N	Diabetes mellitus	ARBs	Heart rate
Peripheral edema/nocturia- Y/N	Ischemic heart disease	ACEis	Blood pressure
Angina pectoris - Y/N	Prior MI	Statins	Pedal edema
Claudication pain - Y/N	Asthma	OHA	Displaced apical impulse
	COPD	Insulin	Murmur
	TIA/stroke		Pulmonary crepitations
	Post PCI/CABG		Elevated JVP
	Atrial fibrillation		Hepatomegaly

ACEi, angiotensin converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; JVP, jugular venous pulse; MI, myocardial infarction; OHA, oral hypoglycemic agent; PCI, percutaneous coronary intervention; PND, paroxysmal nocturnal dyspnea; TIA, transient ischemic attack

Working Model [Diagnostic Workup]

In the patients suspected with HF, 2-dimensional echocardiography and Doppler transthoracic echocardiography are the initial imaging modalities for assessment of systolic and diastolic ventricular function, wall thickness, chamber sizes, and valvular function along with pericardial disease. For patients with poorly developed echocardiographic images, contrast

echocardiography or radionuclide angiography can be utilized [11].With increased applicability in recent studies, echocardiography is recommended as the most practical way for assessing cardiac function [18].

Unlike ECG, which is necessary to detect possible causes and consequences of HF, e.g. AF, chest X-ray may not be very helpful, unless there is clear fluid overload, in which case, signs and symptoms generally already point in the same direction [13].

According to the recommendations of the 2017 CCS guidelines, a 12-lead ECG should be performed- for determining heart rhythm, heart rate, QRS duration, morphology as well as for detecting possible etiologies [10].

The three natriuretic peptides are important mediators of cardiac function. Atrial natriuretic peptide (ANP) is released from the atria in response to stretch and causes natriuresis and vasodilatation. Brain/B-type natriuretic peptide (BNP) has similar actions as ANP but is predominantly released from the ventricles. C type natriuretic peptide is released from the vascular endothelium and central nervous system and has limited effects on natriuresis and vasodilatation [19].

ANP and BNP, which act as physiological antagonists to the effects of angiotensin II on vascular tone, aldosterone secretion, and renal-tubule sodium reabsorption, are released following volume expansion and pressure overload of the heart [19].

The diagnostic, prognostic, and therapeutic potential of these peptides are of high interest because their concentrations are elevated in patients with HF and since the development of non-peptide agonists of ANP and BNP receptors and agents inhibiting neutral endopeptidase, the enzyme that metabolizes ANP [19].

If a patient is suspected with HF on the basis of medical history and signs and symptoms, additional investigations are required for differential diagnosis. The updated European Society of Cardiology (ESC) guidelines on HF recommend low exclusionary cut-off values for natriuretic peptide levels in primary care and low likelihood of HF if values are below the cutoff point (<125 pg/mL and <35 pg/mL for NTproBNP and BNP, respectively) [20]. In the primary care setting, a cut-off value of 125 pg/mL for NTproBNP has a negative predictive value of >99% vis-à-vis multiple echocardiograms [19]. Patients with HF with a preserved ejection fraction (HFpEF) will constitute the missed cases. Thus, utilization of low cut-off points helps identify HF patients with mild disease severity and non-acute breathlessness patients. Nevertheless, other factors such as AF, age over 75 years, renal impairment, and LV hypertrophy, could underlie elevated NTproBNP levels in patients with non-acute breathlessness [20].

In patients with natriuretic peptide levels above the cut-off values, echocardiography is indicated as the next diagnostic step to differentiate HF with reduced EF (HFrEF) from HFpEF and HF with mid-range EF (HFmrEF) [20].

During differential diagnosis, blood tests other than BNP are indicated to rule out precipitating factors such as thyroid disease or anemia to measure modifiable cardiovascular risk factors such as cholesterol and to assess baseline liver and renal function before treatment initiation [20]. C-reactive protein (CRP) may be a prognostic marker for patients at intermediate CV risk given that its levels are elevated in atherosclerosis as a result of inflammation within the vessel walls [21]. Nevertheless, in patients at low CV risk (those without a history of high cholesterol levels, diabetes, hypertension, smoking, etc.) or in those independently identified at high risk, its prognostic value may be limited.

Experts' analysis

- *Many asymptomatic patients have increased levels of natriuretic peptides*
- *BNP should be tested at the non-specialist level in all suspected cases. Also, periodic measurement of BNP should be done. BNP levels help in diagnosis of HFpEF*
- *Chest radiograph should always be done in a patient suspected of HF to rule out differential diagnosis such as cardiomegaly and pulmonary venous congestion*
- *ECG and echocardiography must be done for all patients to detect any abnormal findings/to rule out abnormal rhythm/ventricular hypertrophy/ischemic heart disease (Table 3)*
- *Biomarkers also play an important role because symptoms could often be missed*

Table 3: Checklist for Working Model

Abnormal ECG (tick whichever relevant)	Creatinine level	NTproBNP	hs-CRP	ECHO with LVEF as epicenter
Abnormal Q waves	mg/dL	>450 pg/mL for patients <50years	Not so important??	(……%)
ST-T waves	eGFR preferred in elderly	>900 pg/mL for patients >50 years		
Tachycardia				
Bradycardia				
Partial or complete LBBB or RBBB				
LVH				
AF				
Other ECG changes				

AF, atrial fibrillation; ECG, electrocardiogram; ECHO, echocardiography; eGFR, estimated glomerular filtration rate; hs-CRP, high sensitivity C-reactive protein; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; NT pro BNP, N-terminal pro-B-type natriuretic peptide; RBBB, right bundle branch block

The final integrated model obtained with the analysis of both the clinical model and the working model can be utilized as a composite screening tool for the early diagnosis among HF suspects.

Screening approach for detection of HF risk in the elderly

HF is highly prevalent among the elderly, can remain unrecognized especially in those with comorbidities and cause premature death and disability. Early diagnosis can facilitate prompt treatment initiation to delay or prevent further progression of HF; it can also improve quality of life and reduce mortality risk [22].

Kievit *et al* investigated individual patient data from 4 primary care screening studies and concluded that [22]:

- BMI must be taken into consideration when assessing the probability of HF
- Laterally displaced or broadened/sustained apex beat has a high predictive value (mean odds ratio ~2.50 [95% confidence interval: 1.73–3.62]),consistent with its inclusion in the recommendations of the ESC guidelines
- NTproBNP had an independent predictive value (c-statistic: 0.76–0.89).
- Higher values of NTproBNP could predict the diagnosis of HF

SIGMA - Goals for the Management of Heart Failure

Management of HF has considerably evolved with the understanding of its pathophysiology and the development of new drugs [23].

QOL assessments including psychological, social, emotional, and mental well-being are an important aspect of HF management because they can predict HF severity and mortality [24].

Thus, goals of HF therapy are aimed at improving survival, reducing morbidity such as hospitalizations and symptoms, and enhancing functional capacity and QoL [10, 24].

SIGMA goals were thus devised for the Indian setting based on the above guiding principles:-

- **S**ymptomatic relief
- **I**mprovement in QoL
- Disease modification
- Decrease recurrent hospitalization (**G**uard against recurrent hospitalization)
- **M**ortality Reduction
- Preventing **A**dverse ventricular remodeling

GOAL 1: Symptomatic relief

Symptom management is marked as top priority by the patients with severe chronic illness, including those with HF. Symptoms can negatively impact QoL there by dwindling the will to live. Comprehensive symptom assessment and knowledge of available approaches to relieve the physical, emotional, social, and spiritual aspects of symptoms are the two key components of symptom management [9].

With regard to symptom management in HF, meticulous diagnostic work-up to understand the etiology of the syndrome and optimal treatment of the underlying condition are necessary [24].By presence and severity of symptoms, following treatment options are recommended for patients with HF caused by left ventricular systolic dysfunction [25]:

- Asymptomatic patients (in the context of postmyocardial infarction, hypertension, and, nonischemic dilated cardiomyopathy) may be treated with ACE inhibitors and □-blockers
- Symptomatic patients may also be treated with ACE inhibitors and □-blockers if they do not exhibit physical signs of congestion; diuretics are recommended for edema and congestion. Digoxin is recommended if symptoms persist
- Symptomatic patients with a recent history of dyspnea at rest may be treated with diuretics, ACE inhibitors, spironolactone, □-blockers, and digoxin. All five medications should be continued with symptom improvement, but diuretic dose should be modified according to the magnitude of congestion
- Patients who are symptomatic with dyspnea at rest should not be started on □-blockers; however, patients who develop dyspnea at rest during □-blocker therapy may respond to increased diuretic therapy without requiring □-blocker withdrawal

GOAL 2: Improve quality of life

In a study evaluating QoL of 20 patients with HF using semi-structured, audio-taped interviews, Heo *et al* found that patients' definition of QoL composed of three features: 1) The ability to perform physical and social activities, 2) psychological and 3) social wellbeing [26]. We used other commonly used QoL questionnaires for patients with heart disease or HF, such as the specific activity questionnaire (SAQ) [27], left ventricular dysfunction questionnaire (LVD 36) [28], and the Minnesota living with heart failure® questionnaire [29] to formulate a consolidated version relevant to the Indian setting under SIGMA. The proposed SIGMA QOL questionnaire for patients with heart failure, listed in Table 4, focusses on different aspects of patient's life with heart failure and helps in assessing the quality of life. The six questions emphasize on social, psychological, physical and personal well-being of the patient. It accounts for a patient's daily life activities, dependency on others in performing basic actions through the day, psychological well- being and awareness of disease control, thus, giving us an overview of the Quality of Life in patients with Heart failure.

Table 4: SIGMA QoL questionnaire for patients with heart failure

Q1	**How much is the disease interfering with your daily life activity at home or at workplace?**		
	Very Much	Not so much	Not at all
Q2	How much your disease has made your walking about or climbing stairs difficult?		
	Very Much	Not so much	Not at all
Q3	Is your disease making you feel dependent on others (Family members/ Caretakers)?		
	Very Much	Not so much	Not at all
Q4	Because of your disease, how much has your sleep pattern changed?		

	Very Much	Not so much	Not at all
Q5	Is your disease making you feel depressed?		
	Very Much	Not so much	Not at all
Q6	How fast are you gaining weight recently?		
	Very Much	Not so much	Not at all

Goal 3: Disease modification

Apart from symptoms and QoL, concurrent morbidities such as COPD, renal dysfunction, psychological disorders, and stroke contribute significantly to the clinical and economic burden of HF while increasing the risk of hospitalization [30].

In a historical-prospective cohort study to assess usefulness of disease-modifying therapy in Medicaid patients with HF, Shaya *et al* found that ACEi/ARBs, □-blockers, and/or other cardiovascular drugs such as nitrates or hydralazine alone as first-line therapies significantly reduced the hospitalization risk. However, aldosterone receptor antagonists or combinations of nitrates with hydralazine did not elicit a significant effect on hospitalization risk [30].

The CCS guidelines recommend following management strategies [10]:

- Loop diuretics should be used to control symptoms of congestion and peripheral edema; ACEi/ARBs and □□blockers should be initiated or continued in patients with HF receiving chronic dialysis
- Nonsteroidal anti-inflammatory drugs (NSAIDs) as well as cyclooxygenase-2 inhibitors should not be used in patients with HFrEF given that NSAIDs have been shown to increase the risk of HF including new-onset HF and HF-related hospitalization and mortality risk
- Morphine not to be used routinely in acute heart failure (AHF) patients
- Chronic □-blocker therapy with AHF can be continued unless the patient is symptomatic from hypotension or bradycardia

Experts' Analysis

- Many medications such as NSAIDs could precipitate HF
- Diuretics provide fast symptomatic relief in HF
- □-blockers are used as first-line drugs when heart rate is above 70 bpm

Goal 4: Decrease recurrent hospitalization

Earlier studies have identified several factors serving as precipitants of rehospitalization (Figure 1) [4, 31]. In addition, non-clinical factors such as social, cultural, and economic factors can also influence readmission rates [4, 31].

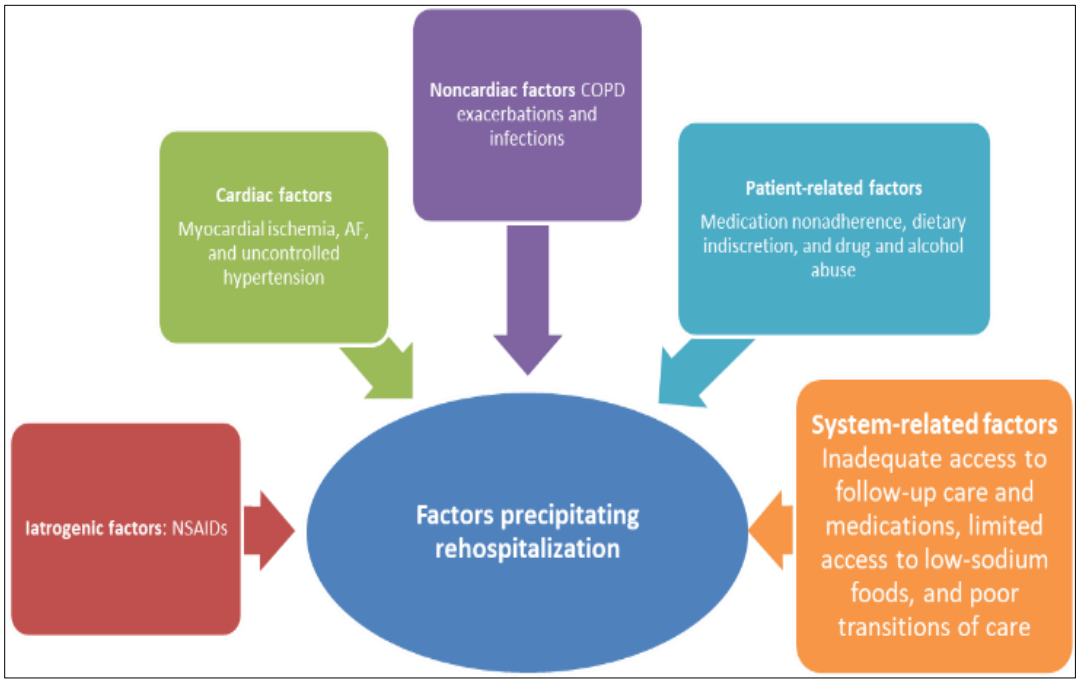

Fig 1: Factors precipitating rehospitalization

AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; NSAIDs, nonsteroidal anti-inflammatory drugs

Assessment of rehospitalization in patients with heart failure

Chioncel *et al* [32] utilized the 6-axis model comprising factors such as clinical severity, de novo or chronic HF, blood pressure, comorbidities, precipitant, and heart rate/rhythm [33] to assess long-term prognostic value of its components and determine post-discharge mortality in patients hospitalized for acute HF. Severity of congestion and multi-organ injury were identified as determinants of in-hospital and post-discharge course.

After patients have been stabilized, it is suggested that cardiac structure and function be evaluated using Doppler echocardiography to assess LV function, left atrial size, presence

and severity of mitral regurgitation, pulmonary arterial pressures, and wall motion abnormalities; the extent and severity of CAD may be assessed using invasive and noninvasive testing[31].

Reducing readmissions

Gheorghiade *et al* suggested following steps to reduce the rates of readmission [31]:

Step 1: Managing congestion

- Manage fluids via sodium restriction
- Use loop diuretics as they remain the mainstay of congestion management
- Reduce intravascular volume by considering mechanism and region (intravascular/extravascular) of fluid removal and composition of fluid removed
- Continue aggressive fluid management while considering that diuretic therapy may cause transient worsening of renal function and may not represent kidney injury
- Consider supine and orthostatic blood pressure measurements and renal function to determine initial and maintenance diuretic dosing strategies
- Consider use of metolazone in patients unresponsive to initial therapies; for patients with hyponatremia, hypotension, and/or impaired renal function, consider use of the vasopressin antagonist tolvaptan

Step 2: Use of Nondiuretic therapies

- Consider using recommended doses of ACEi/ARBs, □-blockers, and mineralocorticoid receptor antagonists (MRAs) for patients with HFrEF
- Monitor serum potassium and renal function in patients receiving MRAs
- Though not recommended, digoxin in combination with diuretics and ACEis has shown to decrease hospitalization without adverse effects on survival in patients with chronic HF in sinus rhythm

Step 3: Adopting a mechanistic approach to identify cardiac abnormalities contributing to heart failure

Myocardium:

- Identify potentially viable but dysfunctional myocardium in patients with and without CAD
- Adopt a multidimensional practice-specific treatment approach with various tools to optimize adherence to improve LVEF

Coronary arteries

- Consider 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors, antiplatelet/antithrombotic agents, and revascularization procedures for patients with CAD given their susceptibility to high risk of mortality and rehospitalization vis-à-vis those without CAD

Electrical system

- Consider receiving anticoagulation and rate control with □-blockers and digoxin for patients with AF
- Consider cardiac resynchronization therapy in patients with HFrEF after hospital discharge

Apart from the above-mentioned recommendations, consideration must be given to identify abnormalities in heart valves and pericardium. Additionally, management of systemic hypertension and pulmonary hypertension, noncardiac comorbidities such as COPD, diabetes obstructive sleep apnea, and renal impairment, and HFpEF is critical. Strategies to cope with transition from hospital-based care to primary care and to manage post-discharge care should be adopted [31].

Goal 5: Mortality reduction

Age, gender, race, and LVEF have been identified as factors contributing to mortality in patients with HF [34]. Several studies have shown that advancing age causes progressive increase in mortality rates [35-38], whereas conflicting evidence exists about gender differences and mortality risk, with some studies reporting females at lower risk of HF compared with men and others indicating no gender-related differences [39-41].

With regard to LVEF, several cohort studies have shown lower CV death rates in patients with HFrEF versus those with HFrEF. Among patients with HFpEF, non-CV deaths are more common in the presence of diastolic dysfunction [34].

A recent review by Wright and Thomas indicates that current pharmacological agents are incapable of reducing morbidity or mortality in patients with HFpEF; therefore, management of HFpEF is currently limited to managing underlying comorbidities such as hypertension, ischemic heart disease, and diabetes and using diuretics to manage fluid overload [42].

Goal 6: Preventing adverse ventricular remodeling

Ventricular remodeling is known to deteriorate ventricular function. Pathophysiological mechanisms underlying this phenomenon include myocyte death via apoptosis, necrosis or autophagy, altered energy metabolism via decreased fatty acid oxidation (leading to triglyceride accumulation, lipotoxicity, mitochondrial atrophy and altered mitochondrial function) and increased glucose oxidation, increased oxidative stress, inflammation, and others [43].

- To decrease remodeling, ACEi, ARBs, □-blockers, and aldosterone antagonists are currently indicated for patients with ejection fraction of <40% [43]
- CCS guidelines recommend management of anemia in patients with HFrEF given its association with more advanced HF and active ventricular remodeling [10].

Conclusions

In conclusion, the expert panel recognized that the earlier the diagnosis of HF, the higher are the chances of treating patients without or with minimal adverse effects. A composite model had been proposed to assist primary care physicians in identifying HF. Improvement of survival and reducing morbidity such as hospitalizations and symptoms, while enhancing functional capacity and quality of life, have been summarized as the goals of HF therapy.

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