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Under the aegis of
Cardiological Society of India

CSI Textbook of CARDIOLOGY

The Indian Perspective



Editor-in-Chief
Pradip K Deb

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The Indian Perspective

Editor-in-Chief

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CHAPTER

Scenario of Heart Failure in India: Challenges in Management

Satyendra Tewari, Deep C Raja

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INTRODUCTION

Around 26 million people worldwide[1] suffer from heart failure (HF). The data on burden of HF in India is sparse, in spite of 1.2 billion people living in our nation. India has undergone rapid epidemiological and demographic transitions in the last two decades and as a result, the burden of HF in India has increased by nearly 140% from 1990 to 2013[2] with an estimated 1.3–4.6 million people with HF in India based on risk factor models.[3]

Heart failure is presently viewed as a continuum, starting from stage A with at risk but no symptoms of HF, progressing to stage B with asymptomatic structural heart disease, stage C with structural heart disease with symptoms, and stage D with refractory symptoms and advanced disease.[4] This concept has emphasized the importance of preventing HF by treating the risk factors or even preventing the risk factors like hypertension, smoking, diabetes, etc., i.e., to intervene at the level of stage A itself. This assumes prime importance in India, as the impact of noncommunicable diseases is on the rise.

The management of chronic HF with reduced ejection fraction (HFrEF) has changed considerably over the past 30 years with the introduction of β-blockers, angiotensin converting enzyme (ACE) inhibitors, mineralocorticoid receptor antagonists (MRAs), and angiotensin receptor neprilysin inhibitors (ArNi).[5] Device therapy in form of implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) have further added to the existing armamentarium to help in reducing the mortality rates in chronic HF. Further mechanical circulatory support (MCS) and transplant exist as end-stage options for options with refractory heart failure.[4] In the year 2016, HF is becoming a preventable and treatable disease.

However, in spite of all above mentioned measures, the readmission rates and mortality in HF continue to be very high. Heart failure has become the leading cause of admissions in the United States and Europe, representing 1–2% of the total hospital admissions.[6] Heart failure is associated with significant mortality and morbidity with a 1-year mortality rate of more than 30% which is higher than many cancers.[7] Heart failure therapy consumes a major share of healthcare expenditures even in the developed world.[8] There are plenty of issues which hamper the delivery of time-tested therapies to patients with HF more so in low and middle income countries (LMIC) like India. India faces a host of other issues ranging from inadequate data, increasing risk factors for HF, inability to address the existing infective etiologies, incomplete delivery of HF therapies to the population and notwithstanding the financial burden of HF on the existing health system of the nation. The data in hand about the prevalence of HF in India suggest that the iceberg of HF is going to hit the Indian health infrastructure in a bad way. Therefore it lays the importance in recognizing and formulating solutions for each of these challenges in HF management in India.

TRENDS IN HEART FAILURE (WESTERN AND LOW AND MIDDLE INCOME COUNTRIES DATA)

The epidemiology of HF in the Western world is well-defined. The crude incidence and prevalence of HF vary from 1–5/1,000/year to 3–20/1,000 persons, respectively.[9] The lifetime risk of developing HF in adults in the US general population is 14–20%.[10] In the follow-up of the Framingham heart failure cohort, the prevalence of hypertension in HF patients was 70% in males and 78% in females, that of coronary heart disease (CAD) was 59% and 48% and that of valvular heart diseases in 22% and 31%, respectively. A changing trend in form of significant increase in the prevalence of diabetes and CAD and a reducing prevalence of hypertension and valvular heart diseases has been observed over a period of three decades.[11] In the recent Acute Decompensated Heart Failure National Registry (ADHERE) registry nonischemic cardiomyopathy is an important contributor (about 47%) for acute decompensated heart failure (ADHF) admissions.[12]

The main phenotype of the patients with HF is now a patient with a history of hypertension and a hypertrophied poorly relaxing left ventricle, that is the HF with preserved ejection fraction (HFpEF) pattern.[13] Aging and/or comorbidities may cause vascular dysfunction with increased left ventricular (LV) afterload and LV stiffness leading to HFpEF.[14] Heart failure with preserved ejection fraction, a growing fraction of the HF population, is a clinical puzzle. This entity represents more than 50% of HF cases in the United States.[15]

In the LMIC, CAD is the most commonly reported cause of HF in all regions except the Africa and the United States.[16] Both hypertension and CAD in the Americans and only hypertension in the Africans are the dominant causes of HF in this data. Cardiomyopathies cause 24% of HF cases across LMICs taken together. Peripartum, human immunodeficiency virus-associated cardiomyopathies and Chagas cardiomyopathy show regional variations in prevalence.[17, 18] Valvular heart disease is responsible for 18% of cases of HF across LMICs.[19]

UNMET NEEDS IN THE INTERNATIONAL GUIDELINES AND RECOMMENDATIONS OF HEART FAILURE MANAGEMENT

High Rehospitalization and Persisting High Mortality Rates

An overall reduction in mortality and hospitalizations in HF over the years is mainly secondary to the progress made in the management of chronic HF with low ejection fraction (EF). However, the most recent European data [EURObservational Research Programme: the Heart Failure Pilot Survey (ESC-HF Pilot) study 4 shows that the 12-month all-cause mortality rates for hospitalized and stable/ambulatory HF patients were still high at 17% and 7%, respectively, and the 12-month hospitalization rates continue to be high at 44% and 32%, respectively.[4] In patients with HF (both hospitalized and ambulatory), most deaths are due to cardiovascular causes, mainly sudden death and worsening HF. All-cause mortality is generally higher in HFrEF than HFpEF. Although recent data from all United States discharge summaries of HF hospitalizations show a decline over time,[20] HF remains the major cause of referral to hospital, as shown by an analysis of hospitalizations in Sweden.[21] The 4–6 weeks following discharge is known as a "vulnerable phase", associated with high rates of mortality and rehospitalization for HF.[22] The risk of dying in the first 30 days after an index hospitalization is increased 6-fold compared with patients not hospitalized. In the Efficacy of Vasopressin Antagonism in hEart failuRE: Outcome Study With Tolvaptan (EVEREST) trial, 25% of patients were rehospitalized during the same period of time after an index hospitalization for decompensated HF.[23] In an analysis of hospital discharge summaries in the United States, HF was first as the condition for recurrent hospitalizations.[24] Because hospitalization represents approximately 70% of the cost related to the management of HF. As a result, the cost of HF management is expected to double between 2010 and 2030 in the United States.[25,26]

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The high rehospitalizations related to HF could be due to following:

- Suboptimal titration of life-saving drugs in HFrEF, which is observed in all registries (a recent survey conducted by the ESC suggests that, at best, 25–30% of patients reach the target dose of β-blockers[27]
- A changing profile of HF patients (increase in HFpEF) who are older and have often multiple comorbidities that can make the management of their condition more complex because of contraindications or intolerances and puts them at higher risk of rehospitalization due to increased frailty
- Poor follow-up and drug adherence observed in patients.

In a national survey conducted in France, only 29% of the patients had consulted a cardiologist in the first 3 months after discharge from hospital.[28]

Clinical Conundrum of Heart Failure with Preserved Ejection Fraction

Unlike what is observed for HFrEF, all attempts to reduce the mortality and morbidity rates of HFpEF have failed. The Perindopril in Elderly People with Chronic Heart Failure (PEP CHF) tested perindopril, Candesartan in heart failure with preserved ejection fraction (CHARM-Preserved) evaluated candesartan,[29] the irbesartan in heart failure with preserved systolic function (I-PRESERVE) tested irbesartan,[30] and the Treatment Of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist Trial) (TOPCAT) tested spironolactone in HFpEF. All these trials have failed to show improvements in outcomes with respect to the hard points of mortality. Possible explanations could be that the diagnosis of HFpEF is per se challenging because it requires the combination of signs and symptoms of HF, a "preserved" EF more than 50% and objective echocardiographic evidence of abnormal distensibility, LV filling or relaxation. Patients with HFpEF are usually older and have multiple comorbidities. The relative proportion of noncardiovascular death is also greater in HFpEF than in HFrEF.[30]

Drug factors may also play a role. Thus, HFpEF remains a challenging condition with imperfectly understood pathophysiology, difficult diagnosis, and heterogeneous phenotype. Hence, this explains why no progress has been made in improving such patients' outcomes.[26]

Deficiencies in Management of Acute Heart Failure

In contrast to management of chronic HF, the management of acute HF has not changed over in spite of advent of new inotropes, arginine vasopressin antagonists, adenosine receptor A1 antagonists, nesiritide, or endothelin receptor antagonists. These agents did not show any improvement in short- or mid-term outcomes. The intravenous diuretics, oxygen, opiates if needed, nitrates, or inotropes remain the mainstay in the management of acute HF.[26]

Current "Gaps in Evidence"

Gaps in existing evidence in management of heart failure have been mentioned in box 1.

BOX 1 Gaps in existing evidence in management of heart failure

Gaps in evidence

Devices and interventions

- Indications for ICDs in specific subgroups (e.g., ARVC and HFpEF)
- Optimal selection of ICD candidates
- QRS morphology or duration as a predictor of response to CRT
- CRT in patients with AF
- The role of remote monitoring strategies in HF
- Effects of novel LVADs as destination therapy and bridge to transplantation

Acute heart failure

- Prospective evaluation of the "time-to-treatment" concept in AHF
- Treatments improving mortality and morbidity
- Strategies and therapies to prevent early rehospitalization after discharge in AHF

Pharmacological therapy

- Identification of nonresponders to current guideline-based medical treatment
- Therapies for HFpEF

ICD, implantable cardioverter defibrillator; ARVC, arrhythmogenic right ventricular cardiomyopathy; AF, atrial fibrillation; HF, heart failure; AHF, acute heart failure; CRT, cardiac resynchronization therapy; LVAD, left ventricular assist device; HFpEF, heart failure with preserved ejection fraction.

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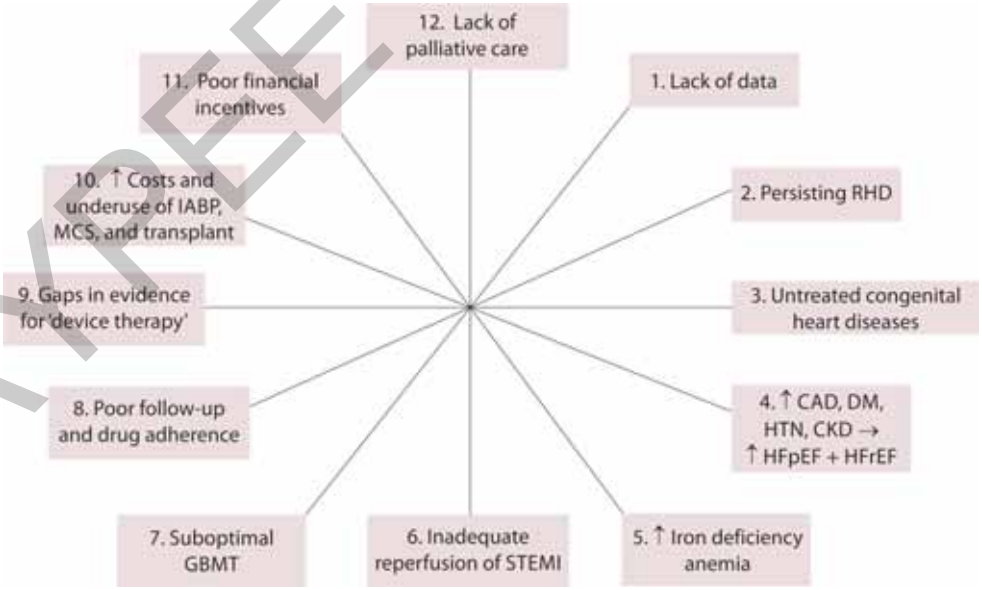
HEART FAILURE IN INDIA: THE CHALLENGES AHEAD (FIG. 1)

Dearth of Data

India is home to 16% of global population, 25% of the world's CAD burden, 120 million hypertensives, and a large number of individuals with rheumatic heart disease (RHD). The epidemiological data on HF from the developing world are very limited.[31] Data on the true incidence and prevalence of HF in India is almost nonexistent. There are few registry data available based on which crude estimates of prevalence of HF have been derived. The prevalence of HF in one particular study was 1.2/1,000.[19] The estimated prevalence of HF in India is about 1% of the population or about 8–10 million individuals. The estimates on prevalence of HF in India by projecting the rates of prevalence observed in the United Status reveal a rough estimate of 1.87% in India in 2010.[32] The prevalence of HF in India due to CAD, hypertension, obesity, diabetes, and RHD alone range from 1.3 to 4.6 million, with an annual incidence of 0.5–1.8 million.[33] Continuing prevalence of old diseases such as RHD and untreated congenital heart diseases (CHD) contributing to HF in India along with emergence of noncommunicable diseases like hypertension, diabetes mellitus (DM), chronic kidney diseases (CKD), CAD, and the aging population is likely to result in alarming numbers of HF prevalence in India. The estimated mortality attributable to HF in India is about 0.1–0.16 million individuals per year.[19]

Difficulty in Data Collection

Population based screening for undiagnosed HF or asymptomatic ventricular dysfunction is not feasible presently considering the resources that will be involved. Attempts to use serum levels of B-type natriuretic peptide for screening population 60 years and older for asymptomatic ventricular dysfunction were successful to an extent.[34] Hospital based registries from a region will help to provide data about the etiology, modified history, and practice patterns in the region. Rather than single center registries, which are likely to have referral bias, these should encompass a group of hospitals which treat HF in a region. Such registries are the call for the hour in India. Presently, the ongoing Trivandrum Heart Failure Registry (THFR) with the support of Indian Council for



RHD, rheumatic heart disease; CAD, coronary artery disease; DM, diabetes mellitus; HTN, hypertension; CKD, chronic kidney disease; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; GBMT, guideline based medical treatment; STEMI, ST-segment elevation myocardial infarction; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support.

FIG. 1: The "clock-of-challenges" in management of heart failure in India

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Medical Research (ICMR) is one such collective venture which intends to obtain data of HF.

The Scarce "Indian Data" on Heart Failure

A recent systematic review on HF care in LMICs included only one study from India (THFR) which highlights the lack of evidence.[31] The THFR was the first registry of HF from India,[7] which was funded by the ICMR. The registry enrolled 1,205 consecutive admissions (69% men) using the ESC 2012 criteria for enrollment. Mean age was 61.2 (13.7) years. The most common etiology of HF was ischemic heart disease (IHD) (72%). The HFpEF (EF ≥45%) constituted 26% of the population. Prevalence of diabetes and tobacco use was much higher compared to the Western data.[7] Patients hospitalized with HF in the THFR were younger by 10 years, more likely to be men and had a higher prevalence of CAD. The patients reported longer length of hospital stay and higher inhospital mortality compared with published data from other registries from the West.

The THFR suggests that the phenotype of HF in India may be different as participants are relatively younger in comparison to other HF registries in the US and the Europe.[2] This is consistent with the demographic findings of the Practice Innovation And Clinical Excellence (PINNACLE) India Quality Improvement Program (PIQIP) registry of outpatients with HFrEF in India where the mean age was 56 years.[2] Both Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry,[35] and INTERnational Congestive Heart Failure Study (INTER-CHF)[36] report a mean age of 60 years in Asian patients. More than two-third of cases report ischemic etiology and this is not surprising as it reflects the "changing trends in the etiology of heart failure in India" with more ischemic cardiac events.[37]

There are no major reports on the causes of HF in India. As early as in 1949, Vakil et al. reported that the primary causes of HF in 1,281 patients hospitalized due to HF were represented by hypertension/coronary in 31%, RHD in 29%, syphilis in 12%, and pulmonary diseases in 9%.[38] This "epidemiological transition" is being observed in India also. Data from the Kerala Heart failure registry and AII India Institute of Medical Sciences (AIIMS) suggest that CAD and RHD are the top two responsible conditions. The contributions of either conditions to HF reflects the propensity of chronic RHD to result in HF. Rheumatic heart disease is mentioned as the commonest cause of HF at the AIIMS, New Delhi as well.[39]

Chaturvedi et al. had attempted to estimate the burden of HF in rural India.[40] The prevalence of HF in this rural community was estimated to be 1.2/1,000. In this community study, two-thirds of the patients had HFpEF and all of them had uncontrolled hypertension. In the inhospital group of the same study, RHD (52%) was the most common cause followed by ischemic and/or hypertensive heart disease (27%).[41]

In a study comparing presentations of HF in migrant Indians and South Asians versus the rest of ethnicities, south Asian HF patients tended to be younger, had higher prevalence of CAD, diabetes and had higher readmissions when compared to Whites. They had lesser prevalence of atrial fibrillation and lower age-adjusted mortality.[42] In addition to RHD and CAD, certain other diseases do contribute significantly to the burden of HF in India, like anemia, infective endocarditis, grown up CHFs, etc. Endomyocardial fibrosis is a condition, which is more often encountered in certain pockets of the country like south Kerala and significantly impacts the health system of those areas.[43]

Pulmonary hypertension and cor pulmonale is a common cause of HF in India. This is secondary to valvular heart diseases and chronic obstructive airway diseases [chronic obstructive pulmonary disease (COPD)] in the community. The high prevalence of COPD due to biomass fuel use in India also contributes to the HF burden.[7]

Increasing Burden of Heart Failure in India due to Noncommunicable Diseases

As a whole, cardiovascular diseases will be the leading cause of morbidity and mortality in India by 2020.[44, 45] The prevalence of hypertension using lower thresholds of 140/90 mmHg is in the range of 25–40% in urban areas and 10–15% in rural areas.[46] It has been estimated that the overall burden of hypertension in India is about 118.2 million.[47] The prevalence of diabetes in urban Indians is in the range of 8–15% among adults while that in rural areas is approximately 2–4%.[48] The prevalence of HFpEF is also set to increase in India due to the increasing

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prevalence of CAD, DM, hypertension, and CKDs. There are data to show that prevalence of vascular diseases is rising in the developing world also. In the THFR, one out of four (26%) participants had HFpEF.[7]

Increasing Burden of Heart Failure in India due to Rheumatic Heart Disease and Congenital Heart Disease

The total prevalence of RHD in India was approximately 1.4 million in 2001 (or about 0.09% of total population) with projections of about 5,00,000 new cases added each year.[49] According to estimates by the WHO, approximately 25% of all RHD worldwide had HF, a large proportion of which eventually require cardiac valve surgery.[50] These numbers are proof to the facts that we have failed to address the healthcare facilities at the suburban and rural level, thus leading to continuing cases of rheumatic fever and RHD.

Congenital heart disease complicates about 0.8% of all live births and HF of significant severity is present in about 20% of these and thus with an assumed birth rate of 27/1,000, 54,000 children have HF due to congenital heart disease every year in India.[51] The overall prevalence is expected to be about 0.3–0.5 million children. A large proportion of CHD remain to be underdiagnosed in India and with an increasing burden of CHD to the surgical community, offering a timely repair of these defects has remained a challenge. As a result we are facing a trend of growing number of cases of adult CHD in HF.

Increasing Burden of Heart Failure in the "Elderly Indian"

Age is one of the most important risk factors for development of HF of any type. In a study from the United Kingdom, about 20% of the community surveyed was above 65 years of age. However, 80% of incident HF was in this age group.[52] Similarly, in the US, the population above 65 years of age is about 12%. In India, the prevalence of old age more than 65 years is about 5.5% or about 70 million individuals.[53] The number of people above 60 years of age in India is projected to increase from 105 million in 2011 (8.4% of total population) to 376 million in 2051 (21.6%).[54]

Heart failure management and self-care behavior are complicated by aging, comorbid conditions, cognitive impairment, frailty, and limited social support. Heart failure is also a leading cause of hospital admission in the older adult, where it is associated with increased hospital length of stay and risk of mortality. Frailty is common in older adults with HF, with a recent study suggesting it may be present in 70% of patients with HF and above 80 years of age.[4] Apart from the comorbidities, the access to good healthcare has been a problem for the aging population in India.

Anemia: A Perennial Problem in India

In India, 62.9% of females below 50 years and 23.3% of males below 50 years have been reported in various surveys to be anemic.[55] Poor vitamin B12 availability in food, lack of iron and folic acid supplementation, and lack of natural sources of iron in a vegetarian diet are possible causes for anemia in India. Anemia in HF is predominantly due to anemia of chronic disease or iron deficiency. In a study of 150 patients of HF in northern India, iron deficiency was present in 76% patients and iron deficiency anemia was detected in 51.3% patients. In another study involving 50 patients, anemia was detected in 35% patients and iron deficiency anemia in 20% of the patients. In Europe, prevalence rates of iron deficiency range from 37 to 50%.[56] Unfortunately, such trials involving larger number of patients and the effect of iron therapy in such patients are lacking in the Indian subtext. Many studies have shown that iron deficiency is associated with advanced symptoms and contribute to greater morbidity in HF.[57,58]

Evidence of High Mortality in Heart Failure in India

In the THFR, the cumulative all-cause mortality at 1-year was 30.8% (n = 371) but the greatest risk of mortality was in the first 3 months (18.1%). It is important to note that majority of deaths (61%) occurred in patients younger than 70 years. Despite the relatively younger age of participants in THFR, all-cause mortality at 1-year was 30.8%. In the European ESC-HF-LT and American

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ADHERE registries, the all-cause mortality at 1-year for acute HF was 23.6% and 38.3%, respectively.[19]

Lack of Concept of Prevention

An important component of the latest classification scheme of HF into stages A-D is to identify patients at stage A, i.e., those with risk factors for developing HF, and therefore, prevent the development of HF in such population. However, majority of the healthcare providers including physicians are sensitive to the problem only once symptoms of pulmonary venous congestion set in. To have a meaningful impact in the population, this concept of prevention has to be incorporated both at the population level as well as the healthcare provider level.

Lack of Guideline Based Medical Treatment

Angiotensin converting enzyme inhibitors, β-blockers, angiotensin receptor blockers (ARBs), aldosterone antagonists, and ArNi are now standard therapies with "additive-mortality benefits" for chronic HFrEF.[5] Ivabradine can be used for better heart rate control as an addition to β-blockers and are implicated in further improvement of the quality of life.[5] These medications are available in LMICs, including India.

Failure to meet guideline based medical treatment (GBMT) is omnipresent in the LMIC. In a meta-analysis of HF treatments in LMICs, the most commonly prescribed treatments were loop and/or thiazide diuretics (69%). Benefit-proven drugs were grossly under prescribed. The ACE inhibitors are being used only in 57%, β-blockers in 34% and mineralocorticoid receptor antagonists in 32% patients of HF.[16]

Except for ArNi and ivabradine, all other drugs are available as more affordable generic formulations. Despite the availability of these generic formulations, their use remains limited. This can be blamed for the poorer outcomes in the Indian population with respect to high mortality as well as readmission rates.[59] The PIQIP of outpatients with HFrEF in India showed that only 30% of patients received both ACE inhibitor/ARB and β-blockers.[60] Despite compelling scientific evidence that ACE inhibitor/ARB, β-blockers, and MRAs reduce hospitalizations and mortality in HF patients,[2] these therapies continue to be underutilized in India.

The adoption of GBMT was recorded to be sub-optimal (25% in the Kerala Heart Failure registry) in India. The reasons could be many. Lack of awareness among the physicians on the latest developments is one of the reasons. This is of paramount importance because of the higher prevalence of heart failure patients in the rural and suburban India where the doctors continue with age old practices and are unaware of the guidelines. There has been hesitance amongst the physicians in initiation of newer drugs which have proven mortality benefit. Lack of Indian data cannot be counted as reason for not initiating such drug therapies. Inability to reach optimal dosages of the drugs could be due to fear of side-effects among the physicians, intolerance among the Indian patients, and most importantly, the poor follow-up of clinical as well as investigations among the Indian patients. Reasons for poor follow-up could again be due to lack of facilities in the periphery and financial costs involved in frequent travels and investigations.

The THFR illustrates that hospital readmission occurs in nearly one of every three patients over the course of 1 year. One out of every three (30.2%) patients was readmitted at least once over 1 year. The majority of these readmissions are attributable to HF exacerbation. Importantly, the propensity for hospital readmission over 1 year was 30% higher in individuals who did not receive optimal guideline based medical therapy. This implies that prescription of guideline-directed medical therapy at discharge from the index HF hospitalization is of paramount importance and significantly affects patient outcomes.

Financial Burden

Heart failure poses a huge burden to the health expenditure, accounting for about 2% of the total health-care budget in developed countries.[61] The treatment of HF is resource intensive and a major burden on the healthcare system. In a country like India where 90% of patients with CHD meet the expenses of treatment on their own, the impact of HF at the population level is huge. Aspects of management of patients in stage C and D account for the third challenge. Many of such

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patients require hospitalization, frequent interactions with healthcare providers, and periodic counseling. Establishment of dedicated HF programs with clinics and rehabilitation programs will help to provide focused care on such patients. This would also ensure in adherence to the available guidelines and improve clinical outcomes including readmissions.[62] Poor financial incentives and lack of insurance cover for these patients has been one of the main reasons behind poor drug-adherence in the Indian patients.

Deficiencies in "Acute Heart Failure" Management

Acute heart failure remains a major challenge for HF treatment not only in India but also in the developed world.[63] It is associated with an increased mortality, persisting also in the long-term.[64] Similar to HFpEF, no drug has improved outcomes in AHF and the lack of success may be, at least partially, caused by the extreme heterogeneity of this condition, further heightened by geographical differences.[65] Delayed times-to-presentation, inadequate infrastructure, lack of widespread availability of LV assist devices including intra-aortic balloon pump (IABP) have contributed to very high mortality rates in acute HF. In a recent study from North India in patients with ADHF, inhospital mortality was 30.8%. Cumulative 1- and 3-month mortality rates of discharged patients were 15.8% and 26.3, respectively.[66] As with any other acute illnesses in India, the time-to-presentation is often delayed. This has a significant impact on the out-of-hospital deaths as well as long-term morbidities.

Poor Management of Acute Coronary Syndromes in India

It is estimated that the burden of CAD in India is approximately 29.8 million with approximate prevalence being 10% in urban areas and 4–5% in rural areas.[67] The burden of ACS is estimated to be about 3.7 million annually. An acute coronary syndrome (ACS) event can lead to acute as well as chronic deterioration in the heart functions. The delayed times in presentation and lack of proper infrastructure in dealing with ACS have therefore contributed to the increasing HF incidences. The CREATE and the KERALA-ACS registries have been pivotal in recording data in ACS and have noticed suboptimal delivery of reperfusion therapy to these patients of ACS. The CREATE registry[68] of ST-segment elevation myocardial infarction (STEMI) patients from India suggest that only 58.5% received reperfusion and the time-to-first medical contact is around 300 minutes and the KERALA-ACS registry suggests that 41.2% of STEMI had a presentation time more than or equal to 6 hours.[69]

Device Therapy: Do Indians Need to Be Addressed Differently?

Device-based therapies used in patients with HF are the ICD and CRT. Implantation of these devices is currently recommended for patients with a low EF (i.e., 30% after myocardial infarction, irrespective of the severity of symptoms, or 35% in other patients).

Indian patients are different when it comes to applying these guidelines. First, we are treating a younger population that is not represented in clinical trials. Second, devices are expensive and implementing Multicenter Automatic Defibrillator Implantation Trial-II (MADIT-II) criteria, are associated with a significant cost burden to budgets that are under pressure. Also, the benefits of ICD therapy could have been overestimated in trials by the use of toxic antiarrhythmics.

Proposed recommendations for treatment options with CRT for people with HF who have LV dysfunction with an left ventricular ejection fraction (LVEF) of 35% or less [according to New York Heart Association (NYHA) class, QRS duration, and presence of left bundle-branch block (LBBB)], and on optimal medical therapy. These guidelines are written after considering the economic constraints so that it is suggested that ICDs and CRT are implanted in a population likely to benefit the most from these devices.

Recommendations for primary prevention featuring in the Western guidelines are difficult to apply for a country like India, where device therapy should be individualized keeping in mind the financial resources of the patient. In clinical practice, not all patients in this subset are getting ICD implants.

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Underuse of Cardiac Transplantation and Left Ventricular Assist Devices in India

We have not been able to improve upon this arena of HF management. In addition to the sparse availability of left ventricular assist devices and MCS as a means to tide over the acute crisis of refractory heart failure, these devices continue to impose extraordinary treatment costs and therefore have remained out-of-reach to most of the tertiary healthcare centers. Apart from the shortage of donor hearts, the main challenges in transplantation are the consequences of the limited effectiveness and complications of immunosuppressive therapy in the long term (i.e., antibody-mediated rejection, infection, hypertension, renal failure, malignancy, and coronary artery vasculopathy).

Cardiogenic shock requires either continuous intravenous inotropic support or MCS with an IABP counter pulsation device or MCS. The MCS is also applicable to patients with persistent NYHA class IV chronic HF symptoms refractory to maximal medical therapy (LVEF <20%) and other alternative therapy including CRT. These are often patients with ischemic or dilated cardiomyopathy. Congenital heart disease, either primary uncorrectable or failed palliated congenital in HF may also be offered MCS.

Lack of Palliative and End-of-life Care

Palliative care approaches include a focus on symptom management, emotional support and communication between the patient and his/her family. Ideally, this should be introduced early in the disease trajectory and increased as the disease progresses. A decision to alter the focus of care from modifying disease progression to optimizing quality of life should be made in discussion with the patient, cardiologist, nurse, and general practitioner. The patient's family should be involved in such discussions if requested by the patient.

PROPOSED FUTURE DIRECTIONS

The projected burden of 1% prevalence of HF in India is most likely an underestimate of the problem. There are many implications of the data which have emerged from India on HF. Patients with HF in India are younger, sicker and have a much higher morbidity and mortality as compared to their western counterparts. They also do not tolerate the high level of medications recommended in western guidelines. Similarly, devices and other advanced therapies are often too costly and out of reach of many of our sickest patients. We know that treatment of HF is resource sensitive and majority of the people cannot afford such costly treatment.

Since Indian patients with HF are different and respond differently to therapy, it is necessary to create guidelines in HF therapy which are specific to Indian patients. In the following discussion, we have attempted to list the most important arenas where there is an immense scope for improvement in India. The younger population with more risk factors will demand longer duration and more intensive treatment regimen.

Recognition of Risk Factors

Prevention of HF is the way forward is to reduce the burden of HF in India. This can be achieved through control of risk factors such as hypertension, diabetes, tobacco use, and early and timely initiation of evidence-based therapy. This only can reduce the enormous burden of HF in India. Primary prevention efforts to control the incidence of ischemic events, better secondary care facilities for all high risk patients and efficient transportation to hospitals in case of acute events may help to reduce the number of patients with HF at the population level.

Detection and Correction of Iron Deficiency

Iron deficiency is an easily correctable factor in HF. Oral supplementation is easy to provide and safe intravenous supplementation are now also available. Various studies with beneficial effect of iron supplementation in HF have been published including two open, non-controlled trials[56] and four randomized, placebo-controlled trials.[56] Apart from NYHA class and walking distance, iron supplementation has also been shown to improve echocardiographic parameters of myocardial performance.[56]

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Improving Outcomes in Rheumatic Heart Disease

Keeping in mind the growing number of cases of RHD in HF, efforts should be directed to improvement in the primary healthcare infrastructure. This will enable curtailing the incidences of acute rheumatic fever, detection and prompt referral of RHD patients to tertiary care centers. Timely surgeries should be delivered to these patients so as to improve surgical outcomes and reduce morbidity in such patients.

Establishment of Registries

Government (ICMR)-sponsored and independent registries will help in understanding the "Indian" phenotype of HF patients. With more support from the government, this will also help in recognizing the lacunae involved in the present health infrastructure in both rural as well as urban India. These registries can thus help in policy making.

Getting-along-with-guidelines

The physicians in public health sectors and those in rural India are exposed to the maximal burden of HF in India. Education of all doctors, especially those in the primary healthcare, regarding the latest developments in HF therapy and the need-to-initiate drugs with mortality benefit, will help in reducing the readmission rates as well as mortality.

Improving Patient Follow-up

Protocol-driven postdischarge transitional care at the primary care level has been shown to reduce hospital readmissions. The lack of comprehensive postdischarge transitional care in India may be one reason for the high readmission rates for HF in this population. The impact of the measurements of natriuretic peptides levels in clinical practice remains uncertain, particularly in some large subgroups of patients, such as elderly patients or those with HFpEF where frequently comorbidities play a major role.[70, 71] In a resource sensitive nation like India, it makes more sense to follow-up patients with necessary investigations like serum electrolytes, blood counts, and renal function tests.

Reducing the Financial Burden

Availability of low-cost generic medicines to everyone may improve adherence to guideline-directed therapy. Improvement of the public health infrastructure in rural India will help in avoiding unnecessary costs involved in investigations and travel. This will also ensure better follow-up of the patients which is of utmost importance to improve drug adherence.

Improving Acute Heart Failure Outcomes

We have to improve patient education schemes so that every HF patient is aware of the symptoms of decompensation, side effects of drugs, and dietary requirements. We also have to ensure the timely delivery of healthcare by improving the transport facilities and increasing tertiary care establishments.

Improving Outcomes in Acute Coronary Syndromes

The Tamil Nadu-STEMI model-of-care[72] has noticed significant improvement in timely delivery of reperfusion therapies either by means of primary percutaneous coronary intervention or by pharmacoinvasive means. Tamil Nadu-STEMI network is a hub-and-spoke model-of-care in South India which has improved STEMI care through greater use of percutaneous coronary intervention and has shown improvement in 1-year mortality. This model may serve as an example for developing STEMI systems of care in other LMICs.

Better Palliative Care

Specific therapies and actions may provide palliation of symptoms and improve quality of life but have a limited evidence base: Morphine (with an antiemetic when high doses are needed), increasing the inspired oxygen concentration, diuretic management, reduction of HF drugs that reduce blood pressure to maintain sufficient oxygenation and reduce the risk of falls. These therapies should be delivered in the patient's home. In the majority of cases, the whole family should receive social support.[4]

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Excerpts from "Indian Consensus Statement on Heart Failure" 2015

In note to the above areas for amendment, an assignment was carried out wherein experts from AIIMS, Ram Manohar Lohia, Safdarjung Hospital, Govind Ballabh Pant, Postgraduate Institute of Medical Education and Research Chandigarh, and Care Hospitals got together to create a "consensus statement". Excerpts from this paper are as below:[73]

- Biomarkers B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) are only useful if there is a diagnostic doubt. These investigations are not available in many places and the usefulness of BNP or NT-proBNP-guided therapy for acutely decompensated HF is not confirmed
- Ivabradine may be used in stable chronic HF with systolic dysfunction (EF <35%) in combination with standard therapy or when β-blocker therapy is contraindicated or not tolerated
- The ArNi in place of an ACE inhibitor/ARB in patients who have HF with a reduced EF has recently been approved by the Food and Drug Administration
- Trimetazidine is a cytoprotective drug that has been shown to reduce HF hospitalizations
- Oral or intravenous iron supplements should be initiated to improve functional capacity in established iron deficiency. Testing for ferritin levels and transferrin saturation will quantify iron deficiency. Erythropoiesis stimulating agents (ESAs) need not be routinely used to treat anemia in HF. The iron supplement recommendation was derived mostly from the experience of clinicians, small clinical trials, and two large randomized controlled trials (RCTs). The recommendations against the use of ESAs were derived from robust data from RCTs
- In acute HF, diuretics (class I), vasodilators if systolic blood pressure more than 90 mmHg (class IIa) along with advanced respiratory support like positive airway ventilation from the predominant mode of management[73]
- Apart from the conventional indications for an IABP for specific acute mechanical problems (e.g., acute mitral regurgitation, interventricular septal rupture), acute severe myocarditis and in selected patients with acute myocardial ischemia or infarction before, during and after percutaneous or surgical revascularization. There is no good evidence that an IABP is of benefit in other causes of cardiogenic shock[4]
- Device therapy with an ICD is recommended in patients with a life expectancy of more than 2 years and with a history of hemodynamically significant sustained ventricular arrhythmia (VA) in the absence of a reversible medical cause (secondary prevention). The ICD therapy is suggested for primary prevention of sudden cardiac death to reduce total mortality in selected patients with nonischemic dilated cardiomyopathy or ischemic heart disease at least 40 days post-myocardial infarction, with LVEF of 35% or less and NYHA class II or III symptoms, or less than 30% with NYHA class I with one additional risk factor such as frequent ventricular premature complexes or nonsustained ventricular tachycardia on Holter, wide QRS on surface electrocardiogram, or history of syncope. A single chamber ICD (as opposed to a dual chamber ICD) should be preferred for prevention of sudden cardiac death. This is relevant to Indian populations as the cost of dual chamber ICD is more than that of single chamber ICD
- Clinical benefit in patients in class I and ambulatory class IV and with QRS 120–130 ms is likely to be less. One should emphasize on optimal medical therapy, lifestyle changes, and address the comorbid conditions. An ICD need not be implanted in NYHA class IV HF patients who are not expected to improve with any further therapy and who are not candidates for cardiac transplant or mechanical circulatory support
- When CRT is implanted in younger patients, without comorbid illnesses, CRT-D should be considered when there is high risk of ventricular arrhythmias
- Cardiac transplant is considered for advanced HF-EF less than 20% on optimal medical treatment. Ventricular assist device may also be considered for these patients as a "destination therapy" if not suitable for transplant or as a "bridge-to-transplant". Younger patients with lesser comorbidities and a prolonged expected survival are to be preferred for transplant. Enormous financial implications on the patient should be discussed well before hand in order to adhere to therapy. These patients waiting for transplant should be motivated, well-informed, and

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BOX 2 Improving heart failure management in India: the "ten commandments" for better heart failure-care in India

1. Recognition and treatment of risk factors (acute rheumatic fever, coronary artery disease, diabetes mellitus, hypertension, chronic kidney disease)
2. Detection and treatment of iron deficiency anemia in heart failure
3. Targeting rheumatic heart disease and untreated congenital heart diseases
4. Establishing registries for data collection
5. Getting-along-with-guidelines
6. Increase in financial-aid through government incentives and insurance covers
7. Timely reperfusion in ST-segment elevation myocardial infarction
8. Timely delivery of acute heart failure therapy
9. Better palliative care especially for the elderly
10. Designing guidelines/consensus applicable for the Indian population

emotionally stable and capable of complying with the intensive treatment required postoperatively.

"TEN COMMANDMENTS" FOR BETTER HEART FAILURE-CARE IN INDIA

The "ten commandments" for better heart failure-care in India are mentioned in box 2.

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