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REVIEW ARTICLE

Cardiac Imaging in Heart Failure with Comorbidities

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Abstract: Imaging modalities stand at the frontiers for progress in congestive heart failure (CHF) screening, risk stratification and monitoring. Advancements in echocardiography (ECHO) and Magnetic Resonance Imaging (MRI) have allowed for improved tissue characterizations, cardiac motion analysis, and cardiac performance analysis under stress. Common cardiac comorbidities such as hypertension, metabolic syndromes and chronic renal failure contribute to cardiac remodeling, sharing similar pathophysiological mechanisms starting with interstitial changes, structural changes and finally clinical CHF. These imaging techniques can potentially detect changes earlier. Such information could have clinical benefits for screening, planning preventive therapies and risk stratifying patients. Imaging reports have often focused on traditional measures without factoring these novel parameters. This review is aimed at providing a synopsis on how we can use this information to assess and monitor improvements for CHF with comorbidities.

Keywords: Congestive heart failure, comorbidity, echocardiography, imaging, MRI, review.

INTRODUCTION

Screening and risk stratification of congestive heart failure (CHF) are among the most established sciences for planning management pathways. Risk scores require information from clinical signs and symptoms, biomarkers, and imaging modalities. End-organ changes from causative comorbidities go through well defined stages, for example diabetes (DM), hypertension (HT) or chronic renal impairment (CRI) that leads to adverse cardiac remodeling (CR), would present with a history of poor control, subtle clinical symptoms and signs, and abnormal disease specific biomarkers before overt end organ damage [1-7]. Some of the earliest changes in tissues, e.g. endothelial dysfunction can be detected in peripheral blood vessels by techniques such as flow mediated dilatation and carotid intimal thickness. These techniques provide valuable information but are not readily available in all centers. Other investigations such electrocardiography (ECG) and brain natriuretic peptides (BNP) lack in sensitivity, specificity or reproducibility [6, 7].

Cardiac ultrasound or echocardiography (ECHO) and cardiac magnetic resonance imaging (CMR) can similarly characterize cardiac tissue with improved accuracy, adding information for risk scoring of CHF. The Framingham [8], Olmstead County [9], The Multi-Ethnic-Study of Atherosclerosis (MESA) [10], CARDIA [11], Dallas Heart [12], HyperGEN [13], Cardiovascular Health [14] and The Strong Heart Studies [15] have contributed to data that show early changes of diastolic dysfunction, left ventricular hypertrophy and regional myocardial deformation portend worse prognosis even in earliest stages [6, 8, 9, 14, 16-22]. The ability to monitor these processes, importantly, many of which are not unidirectional and thus can be delayed or reversed by treatments [6, 8, 9, 14, 16-22]. Furthermore it provides an additional avenue for clinicians to plan chronic disease care and alter the temporal profile for prevention and treatment closer to the evolution of the disease process. Accordingly some clinical and imaging guidelines have factored this in their guidelines. In this review we explore two imaging modalities that can characterize myocardial tissue and analyze myocardial mechanics providing additional information relevant for CHF care.

KEY PRINCIPLES

Pathophysiological Considerations in the Evolution of Heart Failure

All structures in the heart are subject to direct or indirect changes from comorbidities, such as the supporting connective tissues (CT), septum, valves, conduction system, blood vessels and the myocardium itself. Changes can manifest in tissue characteristics and mass, geometry, cardiac function and reserve. *Cardiac remodeling* (CR) is the term that best describes the pathophysiological process that alters molecules and genes within the cell and extracellular matrix that contributes to the clinical syndrome of CHF. There are 2 important processes affecting the anatomy and function that can be quantified [6, 23, 24]. Figure **1** highlights the evolution of this process with a clinical reference.

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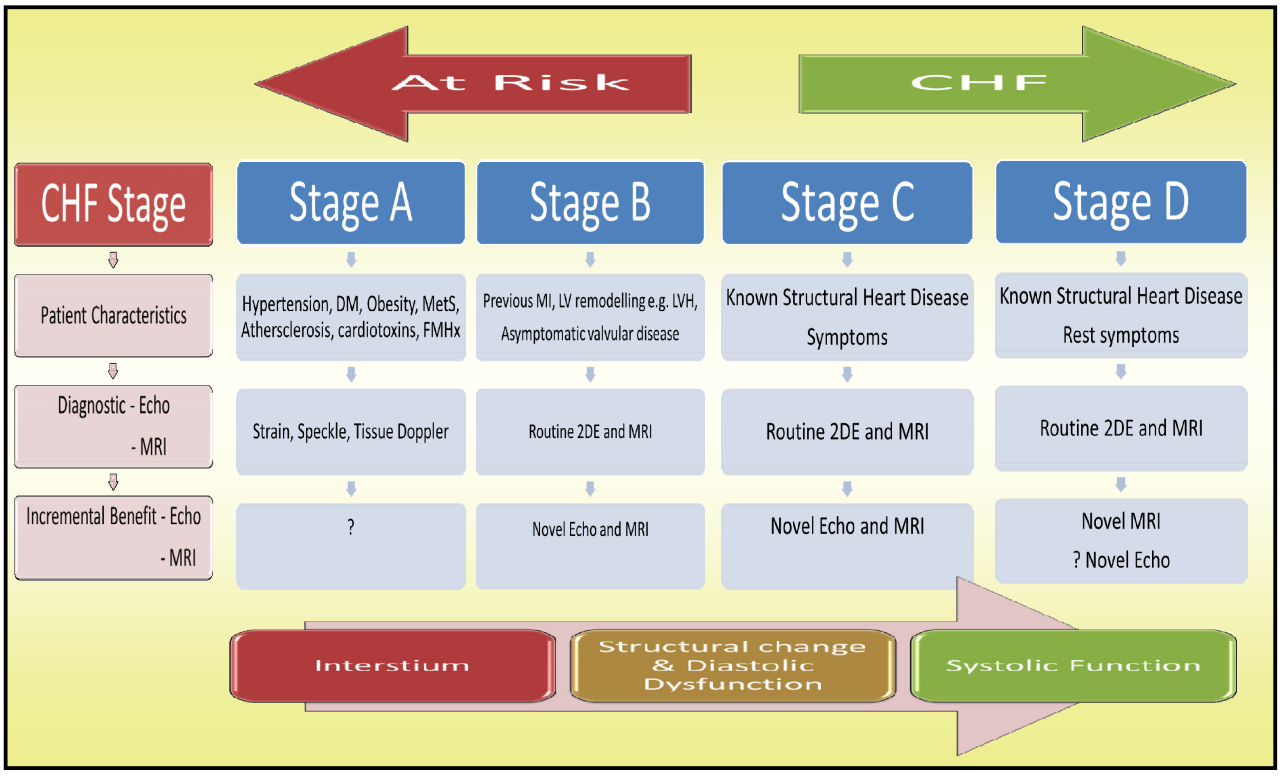

Fig. (1). Heart Failure and role of Imaging Technique. As disease progresses the risk of heart failure increases with gradual remodeling with interstitial deposition followed by structural changes. The advent of diastolic dysfunction which often precedes systolic dysfunction is perhaps the earliest stage of clinical CHF. In the at risk stages, structural changes are either undetectable in early in stage A or inferable later in stages A to B using novel MRI and echocardiographic techniques. When CHF has developed, these techniques can also be used to provide incremental information that point to a greater risk of an adverse outcome. Many of these areas are still evolving and could play important roles for clinical practice. Stages of HF: A – At high risk but without structural heart disease or symptoms; B – Structural heart disease but without symptoms; C – Structural heart disease with current or previous symptoms; D – Refractory HF requiring specialized intervention. Concepts adapted from Ref 6

1. **Cardiac and vascular anatomy:** increased cross-links of collagen and laminin fibers leading to remodeling of the extracellular matrix or '*cardiac fibrosis'*, a stage in CR. Myocardial cells also undergo structural changes including increases in cross sectional area, best described as hypertrophy or dilatation, and best studied in the left ventricle.
2. **Cardiac and vascular function:** Contraction occurs in two quantifiable phases. In ventricular systole contractionlongitudinally (base moves to apex), radially (wall thickening) and circumferentially (cavity size reduction) are coupled with rotation (base and apex moving in opposite directions) and twist where helical myocardial fibers are orientated right handed in the subendocardium to circumferential in midwall and left handed in subepicardium. Ventricular diastole is a passive energy dependent reversal of the previous process. Tissue displacement and the rate at which it occurs are quantifiable in direction and magnitude. CR increases diastolic wall stress.

3. Echocardiographic Principles

When sound waves (ultrasound) interact with cardiac tissues the resulting effect can be described by four phenomena: reflection, scattering, refraction and attenuation. Thus far the novel technology allows us to exploit the first two factors. Doppler velocity and speckle tracking can measure strain, torsion or twist, surrogates for myocardial systolic mechanics. Diastolic function can be determined by spectral doppler at mitral valve and tissue doppler at the mitral annulus. Multiarray transducers can provide 3D echocardiographic images. These appear to have increased accuracy and reproducibility for quantyfying volumes and function, as geometric assumptions are negated [24].

CMR Principles

Imaging of protons within hydrogen atoms can be done in any plane with unrestricted field of view, and without geometrical assumptions. Various MRI sequences can be used to obtain the desired information (Table **1**) [25-29]. Spin echo with dark blood provides the highest resolution for static morphology and structure. Phase contrast sequences with myocardial tagging can map myocardial mechanics as contractility, strain or twist. CMR contrast techniques with gadolinium based contrast agents that remain in the extracellular space can identify regional fibrosis or scar. Tissue mapping techniques such as TI mapping can also identify interstitial fibrosis.

Table 1. Novel Techniques and Clinical Correlates for the Left Ventricle.

Echocardiography	Modality	Methodology	Clinical Correlate/ Time	Notes
	Tissue Doppler Imaging	Velocity (cm/s) with pulsed doppler	DF	Pro: Availability Standardization Cons: (Intermediate limitation) Cost Time Reproducibility Sensitivity Specificity
	Tissue Doppler Strain	SR = $(V_2 – V_1)/D$ (s^{-1})	DF Regional SF	
	Speckle Tracking Strain	$[(L - L_0)/ L_0]$ x 100%	DF	
	Speckle Tracking motion	Rotation – long axis circular motion (d) Twist – difference in rotation base and apex (d) Torsion – gradient in rotation angle from base to apex (d/cm)	DF SF	
	Stress Testing	Tissue Doppler Strain Speckle Tracking	Cardiac Reserve	
	3D Echo	Volume and surface rendered imaging	SF Volume	
MRI	Pulse Sequence CMR	SE/FSE Dark Blood T1 FSE T2 FSE Multi-Echo SE T2	Anatomy Chamber, vasculature, pericardium, fat Cystic	Pro: Accuracy Reproducibility Sensitivity Specificity Cons: Availability Cost Standardization Time
	Cine CMR	GSE or Cine steady state free precision (SFPP) Bright Blood	Motion and volumes	
	Modifiers	FSE Saturation recover T1 weighted imaging FSE Inversion recovery - T2 fat suppression GRE Myocardial grid or line tagging/ phase contrast / DENSE GRE Phase Contrast	Improve image Edema, ischemia, infection, infiltration Intramyocardial motion (T) Flow velocity/vol	
	Contrast	GBCA GBCA T1 - LGE PSIR	Blood Flow Fibrosis	
	Perfusion imaging	Adenosine Dobutamine	Ischemia	

Novel imaging techniques are able to quantify structural (fibrosis, mass, shape) and functional changes with improved temporality. This added information could have benefit for monitoring and planning treatments. However, there remain limitations of these modalities in routine clinical practice. Echocardiographic imaging of the earliest changes is based on extrapolation of tissue-ultrasound interaction to infer subtle changes in LV structure or function, and is limited by patient characteristics. MRI is able to combine anatomical and functional data regardless of patient characteristics, in many aspects with less inference. Sensitivity, specificity and reproducibility are further areas that require attention in both these modalities. Abbreviations: cm – centimeter; d – degree; DENSE - displacement encoding with stimulated echoes; DF – diastolic function; FSE – fast spin echo; GBCA - Gadolinium based contrast agents; GRE – gradient echo; L – final length; L_0 – original length; LGE = late gadolinium enhancement; LV – left ventricular; PSIR - phase sensitive inversion recovery s – second; SF – systolic function; SR = strain rate; V – velocity.
Concepts adapted from Ref 5.

Assessing Cardiac Remodeling

Echo and CMR could benefit ACC stage A and B patients by detecting subclinical components of geometry and deformation (function) of early HF (Fig. **1**). Comorbidities such as diabetes [1, 31-33], hypertension [2, 34-36], obesity [21, 37-41] and renal impairment [3, 42-44] can all contribute to cardiac remodeling individually, together or idiosyncratically. Myocardial hypertrophy is an early feature of CR and warrants further discussion. Morphologically the left ventricle can be classified as having: normal geometry [normal left ventricular mass (LVM) and relative wall thickness (RWT)]; concentric remodeling (normal LVM, ↑ RWT); concentric hypertrophy (↑ LVM, ↑ RWT); or eccentric hypertrophy (↑LVM, normal RWT). Cardiac remodeling is defined by M-mode echo as LVM >115g/m^2 in men and >95g/m^2 in women or RWT >0.42. Subclinical alteration in systolic function is also a feature of CR, but has been less well studied and described. Risk scores are the easiest to use non-invasive surrogates. However, they are inconsistently used as they do not consistently assist daily clinical decisions [45, 46]. Examples include the Framingham, Health ABC and Atherosclerotic Risk In Communities (ARIC) HF risk scores, which predict 10-year risk of CHF [47-49]. Adding N-terminal pro-B-type natriuretic peptides (NT-proBNP) increases risk prediction [47]. Biomarkers and ECG on their

own lack accuracy and reproducibility, while cardiac CT exposes individuals to unacceptable radiation [6, 50, 51].

COMORBIDITY ASSESSMENT WITH ECHOCARDIOGRAPHY

Disease Specific Considerations

There are no contraindications to echocardiography. In the majority of cases echocardiography provides qualitative and quantitative information with good sensitivity, specificity and reproducibility at rest and under stress. Operator and observer training contribute largely to any temporal variations. Client related factors such as chronic lung disease and obesity can interfere with optimal image quality.

Cardiac Geometry with Echocardiography

2DE is the gold standard for assessing and is also the only guideline-approved modality for monitoring volumes and mass, which also has prognostic correlates. In this assessment we have to make an assumption of the LV shape as ellipsoid. In addition the formula for mass requires a cubing of the linear measurements, with the potential to magnify errors. Many of the earlier studies used M-Mode to generate and report data [52-57]. This is one reason this important prognostic marker, is not used more readily in clinical decision-making. Armstrong *et al*. and Gjesdal *et al*. have presented the findings in chronological detail. Essentially the findings support good reproducibility and reliability when one method is used. M-Mode is however the least accurate. Large hypertensive trials and population studies have been the main source for data. Variations in ethnicity and sex can be standardized by body surface area [6, 54, 57]. Several points are worth considering: less standardization have been done for non-hypertensive comorbidities; and despite positive reproducibility, many clinicians use the geometric findings but not the LVM in routine clinical decisions.

3DE, with increased spatial resolution, provides greater accuracy than 2DE for volumes and LVM. The early studies showed comparable results with CMR, with better interobserver variability compared to 2DE [58-64]. Increasingly comparisons are being done with younger participants, obese subjects, dialysis, post myocardial infarction, dyssynchrony and with novel techniques such as 3D strain dispersion, with promising findings [65-71]. 3DE is limited by lower temporal resolution than 2DE. Acquisition still requires good windows and image quality. Patients need to comply with breath holds to acquire images over several heartbeats. Cardiac arrhythmias can be a problem. Finally post-processing is required. Thus 2DE remains the gold standard cardiac investigation for all cases where feasible. 3DE echo is likely to fill the space where MRI level accuracy and reproducibility are needed, such as volumes and LVM.

Cardiac Function with Echocardiography

Tissue Doppler imaging (TDI) assessing diastolic function, is now validated and in the guidelines. TDI and speckle tracking can be used to quantify myocardial strain and strain rate. The latter, that is angle independent, has also been increasingly used to assess torsion. Such subtle changes can be seen when the ventricular structure is altered, the connective tissues is fibrosed, wall stress is increased or a reduction in blood supply at rest or exercise. Many of the earlier studies went on to study these techniques in normal subjects and athletes [72-82], while validating the technique with other modalities including over time [83-87], which allowed factoring in guidelines [88]. Clinical correlations have highlighted predictive capacity for exercise capacity in HF [89], prognosis [90], valve assessment [91-93], chemotherapy cardiotoxicity [94] and ischemia evaluation [95-99]. The data suggest that, like TDI this technique is user friendly and can answer important clinical questions. The important points are addressing subclinical changes reproducibly. The data from oncology patients and valve assessment is an example where this technique can alter practice. What is needed are prospective studies where actual clinical decisions are made in comparison to CMR derived data.

Moving on, this point than becomes relevant in assessing and monitoring for cardiac changes from comorbidities. In obesity the multiethnic CARDIA study tracked 3,265 particpants aged 18-30 years from the mid 1980's. After 25 years the authors noted associations between impaired stress echocardiography (STE) systolic and diastolic parameters with duration of obesity. A comparison of STE at baseline was however not possible [100]. These changes appear to occur quite early [101]. In 172 diabetics followed for 3 years, baseline decrease in longitudinal systolic strain was associated with greater wall thickness and volumes that failed to decrease over time [102]. This appears to correlate with the severity of diabetes. Supporting this finding, in 1,065 type 1 diabetics decrease strain was largely noted in participants with albuminuria [103]. Furthermore in the Valsartan trial of heart failure with preserved ejection fraction, in 219 subjects and 50 hypertensive and normal controls lower strain rates identified systolic impairments, not detected by routine 2DE [104]. Interestingly these studies appear to paint a picture consistent with the chronology and pathophysiology. Hypertensives appear to have changes later and starting with the basal segments with radial and circumferential segments altered later. As LVM and wall thickness correlates with strain impairment, this would imply that strain may not be as beneficial in HT, or alternatively the added information could point to other contributors to CR [105, 106]. Finally in CRI, where hypertension and diabetes are potential contributors, strain rate imaging similarly confirms the ability to detect subclinical systolic changes [107, 108]. A learning curve still exists for use in dynamic loading conditions [109].

COMORBIDITY ASSESSMENT WITH CMR

Disease Specific Considerations

Excluding the routine contraindications and patients preference CMR has no limitations for major comorbidities if safety guidelines are adhered [110]. Nephrogenic systemic fibrosis, a very rare but serious multisystem disease has been associated with the use of gadolinium contrast agents. The greatest risks are in renal impairment (glomerular filtration rate $<30ml/min/1.73m^2$) and these patients are typically excluded from contrast administration unless the information obtained is likely to outweigh the risks [28]. We believe

however that in many patients with severe renal impairment, CR is usually advanced and other modalities can provide similar information.

CMR for Cardiac Geometry

CMR is the gold standard for ventricular geometry assessment [57, 111-113], with validation in an ex-vivo canine model [30]. Direct comparison with 2D echocardiography (2DE) has shown superior accuracy and reproducibility [114-116]. Accurate and reproducible imaging of chamber size, wall thickness and mass are among the most important surrogates in ACC stage A/B HF risk prediction [6, 7]. The Multi-Ethnic-Study of Atherosclerosis (MESA) study, with 4,309 participants provides much of the data on CMR and LVM [117]. In a review by Armstrong et.al, four studies from MESA and a fifth with 2194 participants referred for known or suspected coronary artery disease, showed correlations with development of HF and adverse clinical outcomes with follow-up from 2.5 to 5.8 years [57, 118-122]. Higher systolic blood pressures were associated with increased LVM and volume [41], while participants diagnosed with diabetes had 1.5 fold increased risk of LVH, increased LVM, lower stroke volumes and ejection fractions [41, 123, 124]. Similarly in the Dallas Heart Study with 2, 548 healthy participants increasing cystatin C levels correlated with higher LVM, concentricity and wall thickness [125]. CMR offers an opportunity for diagnosis and monitoring accurately and reliably. However, several ongoing issues need to be addressed: measurement techniques can influence LVM estimates. Papillary muscle exclusion appears to have greater reproducibility [126] but may not be as physiologically accurate; imaging protocols with cine bright blood have differences when GRE or SSFP sequences are used, although SSFP sequences are now the standard of practice. The latter has a shorter acquisition time and improved signal and contrast-to-noise ratios, with lower LVM estimates, although reproducibility with either technique is still good [57, 127-129]. Finally interobserver variation is greatest for LVM estimates highlighting need for greater standardization and consensus before this technique is factored into guidelines [57, 130-132].

CMR for Cardiac Fibrosis

CMR is the gold standard for imaging myocardial fibrosis. With accurate measures of relaxation properties of tissues, changes in content of various components can be estimated and monitored over time to determine fluctuations between inflammation or fibrosis from many groups [133-147]. Myocardial fibrosis is a significant cause and consequence for HF. We are now learning that the pattern and degree of fibrosis are important factors. In ischemic cardiomyopathies LGE-CMR can assess viability or reversibility of injured myocardium following acute or chronic infarcts [148-152], without stressing patients [28, 153, 154], the transmural extent (even small subendocardial infarcts) [144] and localize no reflow segments [28, 155]. Combining T2-weighted imaging high signal from edema differentiates acute from chronic injury and size of ischemic zone following reperfusion [28, 156-159]. In non-ischemic cardiomyopathies LGE-CMR and more recently T1 mapping, can identify the foci of regional or diffuse scarring [133, 134]. These patterns vary with different etiologies for HF. The differences in the techniques are the tissue characterization with or without contrast replacement in the scar. TI mapping has the added advantage of detecting diffuse interstitial fibrosis, thus severity, where LGE is less sensitive [133, 160].

In hypertensives and diabetics with preclinical HF, CMR detected fibrosis predicts the risk of diastolic dysfunction [138,139, 161] and future HF [162-164]. When comparing to a younger cohort with mean duration diabetes 4.7 years, aortic distensibility and diabetes duration correlated with diastolic dysfunction, which was significantly associated with lower peak systolic strain. In regards to prognosis, one study of 187 diabetic subjects showed one in three patients had LGE-CMR evidence of a silent prior myocardial infarction (MI). The subsequent 17 months of follow-up revealed there were four and seven fold increased risk of cardiovascular event and all-cause mortality, similarly noted in a larger study with 300 patients [165, 166], and even in those with just impaired fasting glucose [33, 167]. This highlights again that across the spectrum of the comorbid disease serial CMR can predict and monitor progression with therapies as early as ACC stage 1, or recommend those who require more aggressive treatment [168, 169]. There have also been benefits reported for predicting clinical response to resynchronization therapies [141, 142, 145-147] and electrophysiological procedures [140, 146].

Tissue mapping may also allow for prediction of which comorbid condition is contributing greater to the disease burden. The premise here is that disease duration, severity or poor control should show signs specific to that disease with a temporal profile. For example diabetic cardiomyopathy may be associated with cardiac steatosis, which precedes fibrous deposition [33, 164, 170]. Hypertensives would show cardiac geometrical changes earlier [6, 34-36]. CRI could show a combination as both the previous etiologies contribute and with areas of increased calcification. The prevalence and distribution of fibrosis has been well summarized by Mewton *et al*., describing: in diabetics, a nonspecific or ischemic pattern; in hypertensives, patchy, nonspecific or ischemic pattern; and CRI, ischemic pattern, diffuse and mid wall-focal [160]. In time we should gain better insights into the temporal profiles of tissue changes and how this correlates with more advanced risk such as sudden cardiac death.

CMR Functional Imaging

Myocardial tagging has been used to show impairment in myocardial mechanics with carotid intimal thickness and higher calcium scores in asymptomatic participants [171-174]. Phase contrast imaging and myocardial tissue tagging can provide diastolic measurements that match or better 2DE: In the former similar parameters as Doppler echocardiography are used; in the latter diastolic torsion and strain recovery rates are extended with diastolic dysfunction [175, 176]. Stress Myocardial Perfusion Imaging by CMR provides greater accuracy than SPECT and is among the strongest predictors of major cardiovascular outcomes [177-184]. For real world clinical use three issues stand out: firstly, myocardial tagging requires extensive user involvement and are laborious and time consuming - the ability of new software to “feature track” myocardial MRI images without the

need for dedicated tracking sequences may address some of these issues; secondly, standardizations of values need further study; finally, sensitivity and specificity issues with any one modality. Increasingly combinations of parameters are being used to provide incremental benefits and negate this point. Specifically for comorbidities, studies have explored such combinations [185-190].

Among diabetics and obese subjects: in a study of 19 diabetics, 30 pre-diabetics and 16 controls who underwent comprehensive CMR, LVM and LV torsion, were increased while myocardial perfusion reserve (MPR) was decreased. There was significant correlation between MPR and early diastolic strain rate and LV torsion [191]; Ernande et al, showed in 37 diabetics without known heart disease circumferential, radial and longitudinal strain were decreased compared with 23 age matched controls, reproducibly between operators [192]; in obese subjects with poor echocardiographic windows, longitudinal systolic strain, and peak radial and longitudinal diastolic strain were lower in the 59 obese compared to 40 controls [193]. Among hypertensives, CMR offer good correlations for LVM, LVH and MPR which provide prognostic information [194]. There is less data on TI mapping and LGE in HDD [195, 196]. Nearly half of hypertensives with LVH have detectable fibrosis which correlates with diastolic abnormalities [197, 198]. Available data also suggests that the benefits in screening can be increased by recognizing aortopathy and atrial myopathies in HDD [199]. In the MESA study with 1184 participants peak systolic circumferential strain was inversely correlated with diastolic BP [200]. Small vessel ischemia can be a feature of LVH and HHD and is detected accurately by CMR [201-204]. CMR can similarly detail CR in CRI. As there are other determinants of LVH beyond hypertension including calcium-phosphate balance, this method can inform the adequacy for RRT [205-213]. Impairment in strain rates from all fibers, which go onto correlates with outcomes, is noted in early CRI and hemodialysis [210, 211]. Edwards et al, has summarized all the findings and associations with CRI and CMR and proposes strong arguments for increased use across all stages [208].

NOVEL IMAGING AND CLINICAL TRIALS

Clinical trials in HF can cost billions, and take and average of 7 years. Only 3 in 10 drugs recuperate investment costs and there is a high attrition rate for novel drugs. Innovations of heart failure therapeutics for many areas are lacking and the impetus for this is likely to decline, as the business case remains uncompetitive. It is thus vital that measures to reduce cost are explored. Imaging with novel techniques can reduce follow-up times. Presently surrogate endpoints for HF outcomes are unreliable or lacking [214]. Novel surrogates of CR will take time to secure a front line role in clinical trials. Routine electrocardiography and echocardiography will also remain a modality for the majority of information. An important area where CMR and 3DE should be used with the current evidence is the assessment of LVH and LVM [215, 216], and to guide protocol driven clinical decisions [217]. CMR is able to accurately obtain and reproduce these values that are also independent of loading conditions tested in all comorbidities mentioned in the review, thus potentially leading to reduced sample sizes [218-221]. LGE and strain rate imaging are alos important parameters that will require more studies to understand the incidences, chronology and reversibility with therapies for the various comorbidities. Health systems should invest in researching novel imaging devices and techniques to deliver improvements in detection, initiating preventive therapies and/or improving clinical trial conduct.

CONCLUSION

Cardiac remodeling occurs chronologically in all the common comorbid contributors to CHF. In many of these cases cardiac fibrosis and hypertrophy can be identified early and accurately with echo and CMR. These tools are however not used frequently enough for this indication. There are still research translational gaps in the more novel non-invasive tools. However their promise for a 'one stop shop' from screening and risk stratification, to diagnosis, to monitoring and planning long term cardiovascular care will more than likely advance. It is important that knowledge of these techniques be disseminated to general practitioners, and specialists such that the experience can be built within health clusters. On the research front there are important gaps that need to be addressed. Feasibility of use particularly of acquisition times and offline processing in busy clinical units are areas manufactures need to factor. Clinician scientists need to generate data for normal values that can be standardized for clinical use for each modality and across modalities and factor these into guidelines. Cardiologists should increasingly factor these advancements for their patients.

DISCLOSURES

All co-authors have won independent and governmental research funding. None pose a conflict of interest for this review.

ABBREVIATIONS AND SYNONYMS

2DE	=	two dimensional echocardiography
ACH	=	All Cause Hospitalization
ACM	=	All Cause Mortality
AHF	=	Acute Heart Failure
CDMP	=	Chronic Disease Management Programs
CHF	=	Congestive Heart Failure
CM	=	cardiomyopathy
CMR	=	cardiac magnetic resonance
CRI	=	chronic renal insufficiency
CRT	=	cardiac resynchronization therapy
CT	=	connective tissues
DENSE	=	displacement encoding with simulated echoes
DM	=	diabetes mellitus
ECG	=	electrocardiography
ECHO	=	echocardiography
EF	=	ejection fraction

FSE = fast spin echo

GE = gradient echo

HDD = hypertensive heart disease

HFDMP = Heart Failure Disease Management Programs

HFH = Heart Failure Hospitalization

HT = hypertension

LAP = left atrial pressure

LGE = late gadolinium enhancement

LVEDD = left ventricular end diastolic diameter

LVM = left ventricular mass

MACE = major adverse cardiovascular event

MPR = myocardial perfusion reserve (MPR),

MRI = magnetic resonance imaging

PWT = posterior wall thickness

QOL = quality of life

RCT = randomized controlled trials

RRT = renal replacement therapies

RWM = relative wall mass

RWT = relative wall thickness = (2x PWT/LVEDD)

RF = radio frequency

SE = spin echo

STE = speckle tracking echocardiography

SSFP = steady state free precession

TDI = tissue Doppler imaging

TSE = turbo spin echo

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Declared none.

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