Appropriateness criteria for cardiovascular imaging use in heart failure: report of literature review

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The Imaging Task Force appointed by the European Society of Cardiology (ESC) and the European Association of Cardiovascular Imaging (EACVI) identified the need to develop appropriateness criteria for the use of cardiovascular imaging in heart failure as a result of continuously increasing demand for imaging in diagnosis, definition of aetiology, follow-up, and treatment planning. This article presents the report of literature review performed in order to inform the process of definition of clinical indications and to aid the decisions of the appropriateness criteria voting panel. The report is structured according to identified common heart failure clinical scenarios.

Keywords
Heart failure • Appropriateness criteria • Imaging • Echocardiography • Cardiac magnetic resonance • Cardiac computed tomography • Nuclear cardiology

Introduction

In the European Society of Cardiology (ESC) Guidelines for the diagnosis and treatment of acute and chronic heart failure (HF), HF is defined as a syndrome consisting of symptoms and signs resulting from an abnormality of cardiac structure and/or function. The symptoms are non-specific and the signs can be absent in patients receiving diuretics, so the demonstration of existence of an abnormality of cardiac structure and/or function is essential for HF diagnosis. Providing information on cardiac structure and function, imaging has an important role not only in HF diagnosis, but also in definition of HF aetiology, in follow-up, and in treatment planning.

Echocardiography represents the first-line cardiovascular imaging (CVI) modality for the assessment of patients with HF. Cardiac magnetic resonance (CMR), single photon emission computed tomography (SPECT), positron emission tomography (PET), and cardiac computed tomography (CCT) complement echocardiography or represent an alternative to it in the case of suboptimal acoustic window.

The demand for CVI in HF is constantly increasing as a result of continuously evolving technology, diversification of indications, and rise in HF prevalence, partially due to better life expectancy and higher HF prevalence in the elderly. The increasing demand necessitates appropriateness criteria for CVI use in HF to assist decision-making.

A literature review was performed in order to inform the process of definition of clinical indications for CVI use in the most common HF clinical scenarios. The present report is structured according to these clinical scenarios.

HF clinical scenarios

The clinical scenarios belong to the following three categories.

Diagnosis
First diagnosis of HF
Echocardiography is recommended as the CVI modality of choice for first assessment in suspected HF because of its wide availability,
bed-side portability, accuracy, safety, and low cost together with its large evidence base in all clinical scenarios and main disadvantage only is the need for an acoustic window. Echocardiography at rest, using 2D, 3D, contrast, spectral, and colour flow Doppler and Doppler Myocardial Imaging (DMI) provides information both regarding cardiac structure (wall dimensions, cavity volumes, and geometry, structural abnormalities of valves, pericardial thickness, or effusion) and function (global and regional function of the left and right ventricle, diastolic function, valvular function, and haemodynamics). The increasing prevalence of HF with preserved left ventricular ejection fraction (LVEF) enhances the importance of echocardiography in HF diagnosis, as the main diastolic dysfunction assessment and grading modality. About 50% of patients diagnosed with HF have normal LVEF. Echocardiography can assess all diastolic function related parameters while CMR can also assess some of them. Although not often, radionuclide angiography can be used for systolic and diastolic function assessment. Furthermore, systolic and diastolic function can be assessed by gated SPECT at the time of myocardial perfusion assessment.

The initial HF diagnosis can be complemented by other imaging modalities, particularly by CMR, which provides gold standard assessment of LV/RV volumes, EF, and cardiac mass, as well as providing non-invasive in vivo myocardial tissue characterization; arrhythmias can limit the precision of CMR LV volumes/EF assessment and other disadvantages of CMR are represented by claustrophobia, overt renal failure (relative contraindications), and the presence of magnetic resonance imaging (MRI)-conditional devices, and cerebral metallic clips (absolute contraindications). Transoesophageal echocardiography (TOE) can be used for LV assessment in the case of poor transthoracic window, if CMR is not available or not applicable (ventilated patient or contraindications). TOE assessment of valves (particularly mitral or prosthetic valves) can add important information, being essential in suspected endocarditis induced valvular abnormality resulting in HF. Also, left atrial appendage thrombus exclusion by TOE may be needed in HF patients with atrial fibrillation prior to cardioversion.

Symptomatic patient
Echocardiography is recommended as the first CVI modality of choice in patients with symptoms suggestive of HF.

In symptomatic patients with emergency presentation, echocardiography is recommended immediately in the case of haemodynamic compromise and early during hospitalization in the other cases. TOE may be necessary in suspected endocarditis or if the transthoracic window is poor, particularly in mechanically ventilated patients.

In symptomatic patients with elective presentation, in the absence of cardiac history, echocardiography is recommended in the case of elevated natriuretic peptide.

Asymptomatic (screening)
Screening first-degree relatives of cardiomyopathy patients, we can identify individuals with cardiomyopathy and subclinical or clinical HF. Echocardiography is usually the only imaging modality used for screening. CMR may be necessary, for example, to exclude or confirm arrhythmogenic right ventricular cardiomyopathy or to identify infiltration. Serial testing is necessary in the absence of genetic exclusion of disease or in genotype-positive but phenotype-negative individuals. The screening timing and follow-up intervals have been described by the ESC Working Group on Myocardial and Pericardial Diseases.

Patients on cardiotoxic chemotherapy often undergo periodic LV systolic function screening, despite lack of HF symptoms or signs. The same CVI modality should be used at follow-up to ensure comparability. A baseline echocardiogram is performed before commencing treatment to assess LV systolic and diastolic function, the valves and unexpected abnormalities. Echocardiography, with standardized image acquisition and analysis, provides reliable, reproducible, and cost-effective follow-up of systolic function in the majority of patients. Endocardial border delineation can be improved with contrast administration when needed. 3D echocardiography improves accuracy and DMI and speckle tracking increase sensitivity for subclinical cardiotoxicity detection. Radionuclide LV angiography with multi-gated acquisition (MUGA) provides accurate and reproducible LV function assessment at the cost of ionizing radiation exposure. CMR provides a radiation-free alternative but the high cost makes it difficult to justify CMR follow-up for patients on cardiotoxic drugs, considering the current low incidence of LV systolic dysfunction as a result of practice changes in oncology. Following gadolinium-contrast administration though, CMR can identify myocardial fibrosis in cancer survivors.

The high incidence of HF in patients with diabetes justifies screening for asymptomatic LV systolic dysfunction in this population with or without BNP screening first, particularly in the case of associated risk factors for CAD, advanced age, hypertension, proteinuria, and retinopathy. Echocardiography is again the CVI modality of choice for screening, but an alternative modality can be used in the case of poor acoustic window or need for additional information.

Asymptomatic patients in whom a murmur has been detected or with ECG abnormalities suggesting a primary or secondary underlying cardiomyopathy that could lead to HF should also be investigated.

Patient with cardiac history
(i) History of myocardial infarction.
(ii) History of structural heart disease.

Echocardiography is recommended in patients with a cardiac history of myocardial infarction or structural heart disease without prior natriuretic peptide check in the case of elective presentation with symptoms suggestive of HF.

Diagnosis of HF aetiology
Diagnosis of aetiology begins with echocardiography, which may suffice for this purpose (echocardiography at rest with or without stress echocardiography). Other CVI modalities may complement echocardiography, depending on their availability, affordability, diagnostic profile, contraindications, and associated risk.

Diagnosis of ischaemic aetiology
Echocardiography may suffice for HF ischaemic aetiology diagnosis in the case of existence of regional wall motion abnormalities with thinned and highly echogenic (old, calcified) scar of myocardial infarction. Systolic dyssynchrony may mislead, giving false appearance of regional wall motion abnormality. Furthermore, a severely dilated LV with severely reduced global LV systolic function may have...
apparent regional distribution of systolic dysfunction due to more pronounced hypokinesia without or with thinning in some areas.

In symptomatic patients with emergency presentation, initial existence of systolic dysfunction, usually with coronary artery territory distribution, with subsequent normalization, suggests ischaemic HF aetiology. This transient systolic dysfunction is due to myocardial stunning following an episode of acute ischaemia,13 phenomenon which can persist for a few hours. Myocardial stunning may occur in both symptomatic and silent ischaemia and it can provoke ischaemic mitral regurgitation of similar transient nature. When performed late, echocardiography may miss these transient abnormalities. Strain assessment with echocardiography may detect ischaemia induced abnormal regional myocardial deformation in HF due to a non-ST-elevation acute coronary syndrome.37

Echocardiography at rest can be complemented by stress echocardiography, CMR and perfusion CMR, SPECT, CT coronary angiography or PET.

Stress echocardiography can be used to reveal inducible ischaemia as reason for an episode of unexplained acute pulmonary oedema. It can be also used detect viability,13 by demonstrating existence of inotropic reserve with an increase in regional (in a coronary artery territory) and global LV systolic function. A low dose dobutamine infusion protocol with prolonged (5 min) stages is used for this purpose. Inotropic reserve is recruited in the case the systolic dysfunction is due to myocardial hibernation,38–41 a phenomenon due to chronic post-ischaemic dysfunction resulting from cumulative stunning.36 Inotropic reserve is also recruited in the case the systolic dysfunction is due to non-transmural infarct. Continuous improvement in systolic function throughout the test is observed in the case of non-ischaemic aetiology of systolic dysfunction. A bi-phasic response can be observed in the case of existence of flow limiting coronary disease, with drop in regional systolic function after an initial increase. Only in the case of bi-phasic response demonstration does stress echocardiography add information regarding ischaemic aetiology to the information provided by rest echocardiography.

Depending on availability and local expertise, CMR can be used for coronary artery disease (CAD) diagnosis in HF patients and for viability assessment.40–44 Since regional wall motion abnormalities can also be found in non-ischaemic cardiomyopathies, the specificity of cine-imaging alone for CAD detection is limited.45 Late gadolinium enhancement (LGE) assessment post contrast injection may help the differential diagnosis based on the distinct distribution patterns of contrast in ischaemic and non-ischaemic cardiomyopathies.46 Subendocardial or transmural LGE is present in most ischaemic HF patients (sensitivity 86%).47 CMR has good performance in CAD diagnosis.48,49 It can predict reversibility of wall thinning due to myocardial hibernation rather than necrosis.50 LGE CMR predicts systolic function recovery following revascularisation.50,51 T1 mapping is a recently developed CMR technique, which allows the detection of interstitial myocardial fibrosis, an early marker of disease that has an evolving role in HF.52 CMR can be used for detection of inducible ischaemia, either by detecting inducible regional wall motion abnormalities or by assessing myocardial perfusion. Inducible regional wall motion abnormalities assessed with dobutamine stress CMR, similarly to dobutamine stress echocardiography, carries an increased risk in HF patients with severely reduced LV systolic function and high likelihood of proximal coronary disease. Myocardial perfusion assessment is performed with vasodilator stress (usually adenosine)13 so it is safe for use even in suspected acute coronary syndromes.53

SPECT can be used to detect ischaemia and viability, providing diagnostic and prognostic information.1,55–58 Thallium-201 (201TI) and technetium-99m (99mTc) labelled tracers (sestamibi and tetrofosmin) are commonly used. Exposure to ionizing radiation, relatively low spatial resolution and attenuation artefacts are disadvantages of SPECT.36 Nevertheless, there is extensive evidence that SPECT can predict global and regional systolic function improvement after revascularisation.36 The CAD diagnosis relies on existence of flow heterogeneity and as such, SPECT should be used with caution for diagnosis of HF aetiology because of the likelihood of falsely negative results in balanced ischaemia with uniform radioisotope uptake encountered in 5–10% of patients with three vessels coronary disease.59

PET or PET–CT can be used for assessment of both ischaemia and viability.1 PET has superior spatial resolution compared with SPECT. Ischaemia can be evaluated using perfusion tracers like Rubidium-82, Nitrogen-13 ammonia, or Oxygen-15 water. For viability detection, F-18-fluorodeoxyglucose (FDG) is most commonly used. Among viability imaging modalities, FDG PET has the highest sensitivity and is regarded as the gold standard.60,61 PET can predict improvement in HF symptoms, functional status, quality of life12,62,63 global, and regional systolic function post revascularisation.36 Limitations are the need for a cyclotron on site64 when very short half-life tracers are used, the high cost and the exposure to radiation.1

CT calcium scoring and CT coronary angiography can be used in HF patients, mainly for CAD diagnosis, having the advantage of their non-invasive nature. The absence of coronary calcium on CT virtually excludes CAD as cause of HF. CT coronary angiography can reliably rule out CAD, being most effective in patients with a relative low probability of ischaemic HF aetiology.45,64 Disadvantages are the exposure to radiation and the potential contrast nephrotoxicity of CT coronary angiography often relevant in patients with renal impairment at the time of HF diagnosis. Limited data and current practical challenges prevent recommendation of late-enhancement CT for viability detection.67

Diagnosis of non-ischaemic aetiology

Echocardiography is the first test of choice and often sufficient for non-ischaemic HF aetiology diagnosis (valve disease, cardiac tumours, pericardial disease, congenital heart disease, non-ischaemic LV systolic dysfunction, or LV diastolic dysfunction).

Valve disease can be identified on the initial echocardiogram performed to investigate HF symptoms and signs. The degree of valvular abnormality may be enough to explain HF (e.g. severe mitral regurgitation or moderate mixed aortic and mitral valve disease). Further assessment with stress echocardiography is needed if the degree of valvular abnormality at rest does not justify HF. Stress echocardiography with supine bicycle exercise is needed in moderate mitral regurgitation to detect a dynamic component (increase in regurgitation severity on exertion). Changes in pulmonary artery pressure during exercise have prognostic and therapeutic importance. For assessment of mitral stenosis, both supine bicycle exercise and dobutamine stress echo can be appropriate. With exercise, increase in mean transvalvular gradient to >15 mmHg and increase in systolic pulmonary artery pressure (SPAP) to >60 mmHg suggest severe mitral stenosis. With dobutamine, increase in mean gradient to >18 mmHg suggests severe
mitral stenosis; SPAP changes are not interpretable. In the case of suspected severe paradoxical low flow aortic stenosis, both supine bicycle exercise echo and low dose dobutamine stress echo can be appropriate. In low flow low gradient aortic stenosis with reduced LV EF, low dose dobutamine stress echo is the classical investigation of choice, for assessment of both flow reserve and valve compliance to flow. Nevertheless, usually patients can exercise enough to trigger sufficient myocardial recruitment and flow increase at low workload for severity of disease diagnosis. When existence of flow reserve and significant exertion induced rise in transvalvular gradient with or without concomitant increase in functional valve area are demonstrated, supine bicycle exercise echocardiography can be diagnostic. In the case of a negative result for existence of flow reserve or in the case of suboptimal exercise, low dose dobutamine stress echo should be performed. CMR is the second line imaging modality in valve disease, and sometimes it can complement echocardiography. CMR provides information regarding the surrounding anatomy (great vessels), accurate quantification of ventricular volumes and regurgitations, as well as assessment of myocardial fibrosis, which carries prognostic information. Diagnosis of cardiac tumours or of cardiac involvement by tumour as reason for HF can be made by echocardiography. CMR may complement the echocardiography diagnosis. The diagnosis of pericardial disease as reason for HF can be made by echocardiography. Cardiac CT or CMR can complement the diagnosis. Even if echocardiography can provide a first diagnosis of congenital heart disease and can usually suffice for a complete comprehensive evaluation, CMR is the CVI modality of choice in complex congenital heart disease. Non-ischaemic LV systolic dysfunction is diagnosed by exclusion of CAD, described in the ‘Diagnosis of ischaemic aetiology’ section. Diastolic dysfunction is diagnosed as reason for HF in the absence of LV systolic dysfunction, valvular abnormality or pulmonary hypertension which explain the HF symptoms and signs. Diastolic dysfunction is usually diagnosed by echocardiography. Morphologic correlates of diastolic dysfunction (LV hypertrophy and left atrial dilatation) can be diagnosed by echocardiography or CMR. Serial studies of morphologic correlates (cardiac mass, left atrial volume) for follow-up of disease progression or regression can be performed more accurately with CMR. Furthermore, CMR provides tissue characterization, detecting infiltration, or inflammation. Functional correlates of diastolic dysfunction—left atrial function and pulmonary artery systolic and diastolic pressure—can be diagnosed by echocardiography or invasive cardiac catheterization. LV relaxation, filling, diastolic distensibility, and diastolic stiffness are assessed with cardiac catheterisation. Echocardiography can provide a comprehensive complete diastolic function study. In the case of inconclusive diastolic parameters at rest and no other diagnostic structural cardiac abnormality, exercise echocardiography, ideally with a supine bicycle, can be used for diagnosis. CMR can provide many filling parameters similar to echocardiography, but it is not used routinely due to the need for specific image acquisition and lengthy analysis. Radionuclide angiography can assess all parameters of diastolic function, but its use is limited nowadays. Diastolic function can also be assessed by myocardial perfusion gated SPECT. Cardiomyopathies can be first diagnosed as a result of presentation with HF symptoms and signs. Usually, echocardiography alone makes the diagnosis. CMR may be needed, for example to diagnose arrhythmogenic right ventricular cardiomyopathy or to confirm an echocardiographic diagnosis by identifying inflammation or infiltration with tissue characterisation. Myocardial inflammation and oedema are diagnosed with T2 weighted CMR imaging, whereas myocardial infiltration and fibrosis are diagnosed with T1 weighted CMR imaging post contrast (LGE). Non-ischaemic LGE patterns include mid-wall, epicardial, and patchy. For example, mid-wall LGE can be detected in dilated cardiomyopathy (DCM) albeit it cannot indicate the underlying aetiology (idiopathic DCM vs. DCM secondary to myocarditis). Amyloidosis can have a characteristic diffuse LGE, or a zebra pattern LGE coupled with a typical dark myocardial cavity due to very abnormal contrast kinetics.

### Treatment planning

Imaging plays a central role in HF treatment planning, being used for risk stratification and to predict treatment benefit.

#### Revascularization

Coronary revascularization may improve LV systolic function in ischaemic HF, by reversing systolic dysfunction due to hibernation rather than infarction. The benefit depends not only on the existence of regional viability, but also on the existence of appropriate revascularization targets in the respective coronary arteries and on the degree of LV remodelling.

**HF and angina symptoms**

Based on evidence, revascularization is recommended in patients with angina and HF due to ischaemic LV systolic dysfunction. In the case of severe proximal CAD, the ESC recommends surgical revascularization regardless of any other considerations. Concomitant surgical ventricular reconstruction may be necessary when the LV end-systolic volume index is >60 mL/m² and there is transmural scar in the LAD (left anterior descending artery) territory. Percutaneous coronary intervention may replace CABG in the case of suitable coronary anatomy and existence of viability in the respective territory of distribution. Evidently, treatment planning implies imaging based assessment of end-systolic volume and viability. As detailed in the ‘Diagnosis of ischaemic aetiology’, echocardiography can provide this assessment, and so does CMR. SPECT or PET can be used to detect viability. In the case of angina symptoms, HF patients will have invasive coronary angiography performed for CAD diagnosis, making usually unnecessary the detection of inducible ischaemia and consequently reducing the risk of a dobutamine stress echocardiography viability test.

**HF without angina symptoms**

In the absence of angina, revascularization planning is strictly based on existence of viability, increasing further the significance of the above discussed considerations. The Surgical Treatment for Ischaemic Heart Failure (STICH) Trial found lower rates of death from cardiovascular causes and of hospitalization for cardiovascular causes in HF patients treated with CABG revascularization. Nevertheless, a sub-study of the STICH Trial, despite finding greater likelihood of survival in patients with viability, found no differential survival benefit of revascularization based on diagnosed viability. However, many criticisms accompanied this sub-study, including the fact that...
viability imaging was offered at the physicians’ discretion, rather than randomization.

LV aneurysmectomy is recommended at the time of surgical revascularisation and in this regard, the definition of the transition zone in between the scarred and not scarred myocardium is of major significance. LGE CMR or transthoracic echocardiography can be performed before the procedure while TOE can be performed intraoperatively. Echocardiography has the advantage of concomitantly assessing the mitral valve for need of repair, based on assessment at rest or during exercise. CMR has the advantage of accurate assessment of volumes and better definition of the transition zone and it represents the gold standard for patient selection for aneurysmectomy.

Contrast echocardiography, CMR or CCT can all assess the existence of mural thrombus prior to surgery.

No symptoms
In the absence of symptoms, detection of inducible ischaemia should complement the above discussed investigations. Considerations discussed in the ‘Diagnosis of ischaemic aetiology’ are appropriate in this regard.

Device therapy
Accurate assessment of LV EF is essential for deciding on device therapy. Echocardiography is the first CVI modality of choice for LV EF assessment. 2D echocardiography can be used to assess LV EF with the bi-plane method, with or without the help of contrast to improve endocardial delineation. 3D echocardiography provides accurate and reproducible LV EF assessment. CMR provides gold standard assessment of LV EF and can be used in patients with poor acoustic window. Gated SPECT can be also used in patients with poor acoustic window and CMR contraindications.

Implantable cardioverter defibrillator planning
LV EF assessment with or without assessment of existence of ischaemic aetiology of HF are necessary for implantable cardioverter defibrillator (ICD) implantation planning. Echocardiography is the first CVI modality. Accurate LV EF assessment is essential for decision-making. CMR, MUGA, or gated SPECT can be used for LV EF assessment in patients with poor acoustic window. Considerations extensively presented in the ‘Diagnosis of ischaemic aetiology’ are relevant for aetiology assessment. There is emerging evidence that LGE CMR can predict ventricular arrhythmic events in ischaemic cardiomyopathy.

Cardiac resynchronization therapy (CRT) planning
A complete echocardiographic assessment is recommended before considering CRT. As for ICD planning, accurate EF assessment is essential and can be performed with echocardiography, CMR, MUGA, or gated SPECT. Viability assessment may be needed in the case of myocardial infarct involving potential LV lead placement areas (basal infero-lateral or lateral wall). CMR has been used to guide LV lead placement avoiding areas of transmural infarct and to predict clinical outcome in CRT patients based on assessment of the right ventricle. Cardiac CT can visualize the coronary veins non-invasively if pre-procedural planning of LV lead placement is needed.

There is a wealth of echocardiography research performed in the field of dyssynchrony, using DMI derived techniques, speckle tracking, 3D regional volume curves analysis, and even M-mode. Nevertheless, based on currently existent evidence, echocardiographic dyssynchrony assessment should not be used to exclude patients from CRT. Similarly, gated SPECT phase analysis, gated PET/CT, and CMR techniques have been studied for the assessment of dyssynchrony. In the absence of relevant randomized control trials though, no CVI assessment of dyssynchrony should be used for clinical decision-making.

LV assist device
A complete echocardiographic assessment is needed before considering an LV assist device. Accurate assessment of LV EF is essential for device treatment timing.

Follow-up
Planned follow-up
HF follow-up
Echocardiography is the first imaging modality of choice for follow-up of HF progression or regression on medical treatment or in patients treated with CRT. CMR can be used for follow-up when acoustic window is suboptimal and in the absence of an implanted non-MRI-conditional device (which prohibits the use of CMR).

CRT follow-up
Based on current evidence, echocardiography follow-up for assessment of LV volumes and EF together with assessment of functional mitral regurgitation and pulmonary hypertension is recommended. Echocardiography based CRT optimization may be useful but it is not strongly recommended based on current evidence.

New symptoms
A complete echocardiogram is necessary in the case new symptoms develop. Findings may justify involvement of an alternative CVI modality, mirroring already described scenarios.

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