

**Table ii:** Summary table for Executive statements for CMR endpoints. LV – left ventricle. RV – right ventricle. PV – pressure-volume. LGE – late gadolinium enhancement. AAR – area at risk. PWV – pulse wave velocity. \*Only studies reporting interstudy variability are included.

		Number of studies	Total number of subjects
<b>Ventricular volumes and function</b>			
CMR is the reference standard for quantification of LV and RV volumes, function and mass. CMR should be considered as the first line technique in clinical trials requiring one of these parameters for in- or exclusion or as an endpoint. <b>The evidence for the use of quantification of cardiac function and volumes is favourable.</b>			
<i>Analytical validation</i>	Excellent validation of LV mass and volumes	7	121
<i>Precision</i>	Large body of evidence on interstudy, inter- and intraobserver reproducibility	2*	32
<i>Normal values</i>	Available for various field strengths, imaging sequences, post-processing approaches, age-, sex- and ethnicity groups	9	6895
<i>Qualification/Utilisation</i>	The original evidence base by transthoracic echocardiography has been revalidated and expanded upon by CMR	7	14711
<b>Regional wall motion, deformation and dyssynchrony</b>			
CMR-based strain-imaging techniques seem similarly suited as echocardiographic techniques for assessing longitudinal motion and strain. <b>The evidence for the use of CMR-based strain imaging techniques is promising.</b>			
<i>Analytical validation</i>	CMR tagging techniques have been well validated. Other MR based strain imaging techniques have been either directly compared with tagging or indirectly against a technique originally compared to tagging.	11	600
<i>Precision</i>	Limited data on inter-study reproducibility	9	168
<i>Normal values</i>	Normal values are available, but show considerable regional variation as well as variation between different studies	11	3191
<i>Qualification/Utilisation</i>	Outcome data suggest utility in addition to standard measures of care in clinical management.	5	2462
<b>Diastolic function</b>			
CMR may have advantages over other techniques by direct assessment of myocardial tissue. <b>The evidence for the use of CMR-based assessment of diastolic function is promising.</b>			
<i>Analytical validation</i>	Reasonably well validated versus PV loops and echocardiography for diastolic filling, atrial volumes and function and transmitral and pulmonary venous flow	4	212
<b>Late gadolinium enhancement</b>			
CMR based LGE should be used as the first line technique in clinical trials requiring the assessment of regional scar or fibrosis for inclusion or exclusion or as an endpoint. CMR should also be employed for optimal risk-classification of trial subjects with ischemic or non-ischemic cardiomyopathies.			

**The evidence for the use of LGE imaging for visual detection of regional myocardial fibrosis and quantification of ischaemic scar is favourable. The quantification of non-ischaemic scar remains promising.**

<i>Analytical validation</i>	Extensively validated as a marker of irreversible damage post myocardial infarction in animals as well as versus biopsies, in explanted hearts and versus other imaging techniques	8	406
<i>Precision</i>	Strong data on inter-study reproducibility	7	200
<i>Qualification/Utilisation</i>	Strong parameter to predict outcome, superior to volumes and function.	37	12562

## **T2-weighted imaging**

Due to the availability of many different sequences no generally accepted standard has been defined. For clinical trials, it is important to use a validated and standardized approach amongst different centres and vendors and use normal values and effect sizes specifically for these sequences.

**The evidence for the use of T2W imaging of AAR is promising.**

<i>Analytical validation</i>	Well validated in animals, phantoms and humans	15	817
<i>Precision</i>	Scarce data on inter-study reproducibility in acute myocardial infarction. Lack of reproducibility data and outcome studies for T2W-oedema imaging in inflammatory cardiac conditions	4	234
<i>Qualification/Utilisation</i>	Small number of outcome studies using AAR	17	1509

## **T1 mapping**

Due to the availability of many different sequences, no generally accepted standard has been defined. To employ T1 mapping in clinical trials, the use of validated (well understood sequence) and standardized approach amongst different centres and vendors is mandatory, due to the different normal values and effect sizes between various sequences.

CMR T1-mapping may be considered as a standard for adequate risk-assessment of patients with non-ischemic dilated cardiomyopathy in clinical trials.

**The evidence for the use of T1 mapping is promising.**

<i>Analytical validation</i>	Well validated in phantoms, animal models, human biopsies and explanted hearts.	15	267
<i>Precision</i>	Evidence on interstudy, inter- and intraobserver variability	10	270
<i>Normal values</i>	Sequence-specific normal values available	4	1735
<i>Qualification/Utilisation</i>	Strong predictors of outcome in non-ischaemic dilated cardiomyopathies, superior to volumes, function and LGE.	37	6153

## **T2 mapping**

Due to the availability of many different sequences no generally accepted standard has been defined. The use a validated and standardized approaches amongst different centres and vendors is mandatory for the use in clinical trials, due to the different normal values and effect sizes specifically for these sequences. The timing of imaging after an acute event must be highly standardized.

**The evidence for the use of T2 mapping is promising.**

<i>Analytical validation</i>	Well validated against phantoms, animal models, human biopsies and other imaging biomarkers	11	340
<i>Precision</i>	Evidence on interstudy, inter- and intraobserver variability	1*	73
<i>Normal values</i>	Sequence-specific normal values available	3	205
<i>Qualification/Utilisation</i>	Useful in detecting myocardial oedema and inflammation	12	680

## T2\* mapping

T2\* can be regarded as the clinical reference standard in thalassemia and provide superior outcome data if used for therapy guidance.

T2\* measurements during or shortly after an acute coronary or vascular event provides important prognostic information in terms of short-term LV remodelling.

**The evidence for the use of T2\* mapping is favourable.**

<i>Analytical validation</i>	Excellent validated and standardized in iron-overload	17	1728
<i>Precision</i>	Evidence on interscanner, intercenter, interstudy, inter- and intraobserver variability	4*	59
<i>Normal values</i>	Normal values and established clinically relevant cut-offs available	5	100
<i>Qualification/Utilisation</i>	Outcome data in thalassaemia major. Prognostic information after a coronary event	19	1778

## Stress myocardial perfusion

Perfusion imaging should be considered as a first line technique for assessing the presence, extent and localization of inducible ischemia.

Its use for full quantification requires locally validated and standardized sequences with specific normal values.

**The evidence for the use of myocardial perfusion imaging for visual detection of ischaemia is favourable. The quantification remains promising.**

<i>Analytical validation</i>	Well-validated against animal models and alternative techniques	63	10916
<i>Precision</i>	Limited evidence on interstudy, inter- and intraobserver reproducibility due to need of stress and contrast injection	5*	73
<i>Normal values</i>	Limited data on normal values due to lack of standardization of image acquisition and post-processing	3	42
<i>Qualification/Utilisation</i>	Large body of evidence showing significant predictive association for the presence/severity of myocardial ischemia with outcome	14	26494

## Vascular

CMR vascular imaging is well suited to assess vascular anatomy and function.

Aortic and carotid vessel wall imaging, are robust markers of atherosclerotic burden in these vessels and can be used in clinical trials.

<i>Analytical validation</i>	Validation of PWV against alternative techniques and T2 mapping against histology	7	237
<i>Precision</i>	Limited evidence on interstudy reproducibility of anatomical and tissue measurements. Excellent evidence for PWV	6	95
<i>Normal values</i>	Available for different anatomical and functional measurements	7	4112
<i>Qualification/Utilisation</i>	Aortic wall imaging and PWV serve robust biomarkers of cardiovascular risk	2	5797