British Society of Echocardiography

A guideline protocol for the assessment of restrictive cardiomyopathy

1. Introduction

1.1 The BSE Education Committee has published a minimum dataset for a standard adult transthoracic echocardiogram, available on-line at www.bsecho.org. This document specifically states that the minimum dataset is usually only sufficient when the echocardiographic study is entirely normal. The aim of the Education Committee is to publish a series of appendices to cover specific pathologies to support this minimum dataset.

1.2 The intended benefits of such supplementary recommendations are to:

• Support cardiologists and echocardiographers to develop local protocols and quality control programs for adult transthoracic study;

• Promote quality by defining a set of descriptive terms and measurements, in conjunction with a systematic approach to performing and reporting a study in specific disease-states;

• Facilitate the accurate comparison of serial echocardiograms performed in patients at the same or different sites.

1.3 Understanding restrictive cardiomyopathy (RCM).

This document gives recommendations for the image and analysis dataset required in patients being assessed for restrictive cardiomyopathy (RCM). RCM is a functional classification that is made on the basis of adverse filling of the left ventricle and is therefore different from the structural changes that describe other forms of cardiomyopathy (such as hypertrophic or dilated). RCM can either be primary or more commonly secondary to various conditions (see table) adversely affecting the filling pattern of the left ventricle. The natural histories of conditions causing myocardial restriction exhibit a spectrum of cardiac pathophysiology from subclinical (including the early stages of diastolic dysfunction) through to severely restrictive diastolic filling patterns. Thus the operator should take care to interpret more subtle findings that may be the only manifestations of disease development, with novel deformation imaging assisting in the identification of early disease states.

The morphological and anatomical features of causative pathologies in RCM can be indicative but not specific of an underlying disease state. The majority of RCMs are secondary to systemic aetiologies, the commonest of which is amyloidosis. In contrast, idiopathic (primary) RCM is rare. The term amyloidosis describes a group of disorders caused by abnormal folding, aggregation and accumulation of certain proteins in the tissues, in an abnormal form known as amyloid deposits. This document gives recommendations for the image and analysis dataset required in patients being assessed for RCM with a particular reference to cardiac amyloidosis and the transthoracic echocardiography protocol performed at The UK National Amyloidosis Centre (NAC), with whom this guideline has been co-authored (http://www.ucl.ac.uk/medicine/amyloidosis).

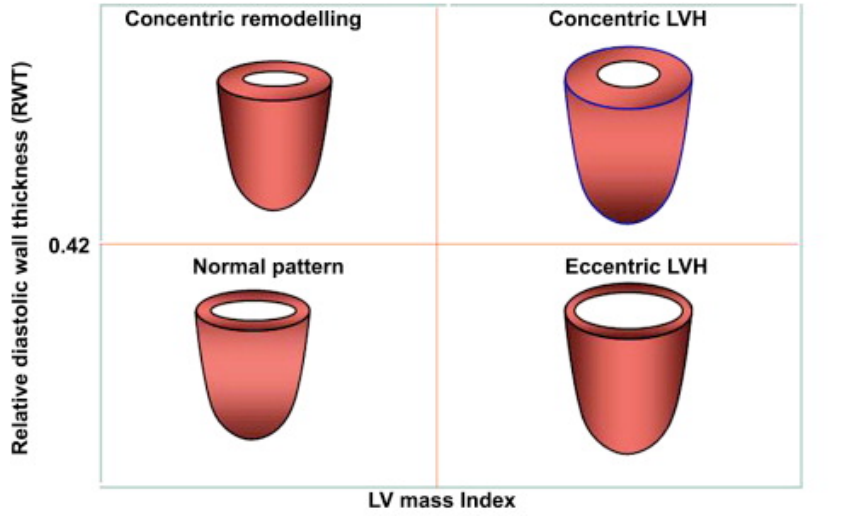
While echocardiography allows a comprehensive assessment in RCM, it is important to remember the complementary role of other imaging modalities, including cardiac MRI.

Primary
Idiopathic
Secondary

Infiltrative disorders
• Amyloidosis
  • AL: cardiac involvement common.
  • Transthyretin (ATTR): familial variant, usually autosomal dominant.
  • Age-related: senile in 25% aged > 80 years (Wild Type ATTR); atrial in 90% aged > 90 years (deposits derived from atrial natriuretic peptide, ANP).
  • AA: cardiac involvement rare.
• Haemosiderosis (for example: haemochromatosis, transfusion-related iron overload)
• Sarcoidosis
Endomyocardial fibroelastosis
Scleroderma
Radiotherapy

Adapted from Nihoyannopoulos & Dawson, *European Journal of Echocardiography* (2009) 10, iii23–iii33

1.4 The distinction between concentric remodeling versus concentric hypertrophy (see figure) is an important concept that is poorly understood, but is of prognostic significance in patients with preserved left ventricular ejection fraction.



The distinction requires the calculation of relative wall thickness (RWT) and LV mass using the following formulae:

RWT = (2 x LVPWd) ÷ LVIDd

LV mass = 0.8 x {1.04 x [(LVIDd + LVPWd + IVSd)^3 - (LVIDd)^3]} + 0.6 g

Where LVIDd = left ventricular internal dimension in diastole, LVPWd = left ventricular posterior wall width in diastole, IVSd = interventricular septal width in diastole.

RWT is increased (≥ 0.42) in both concentric remodeling and hypertrophy, but in infiltrative cardiomyopathy the important distinction is the increased left ventricular mass (>95 g/m^2 in females, >115 g/m^2 in males). Conversely, the measurement of RWT in cases of increased LV mass allows the distinction between concentric (relative wall thickness ≥ 0.42) and eccentric (< 0.42) hypertrophy.

1.5 The views and measurements are focused upon RCM and are supplementary to those outlined in the minimum dataset. These are given assuming a full study will be performed in all patients.

1.6 When the condition or acoustic windows of the patient prevent the acquisition of one or more components of the supplementary Dataset, or when measurements result in misleading information (e.g. off-axis measurements) this should be stated.

1.7 This document is a guideline for echocardiography in the assessment of RCM and will be up-dated in accordance with changes directed by publications or changes in practice.

2. List of abbreviations

2.1 Views:

PLAX	parasternal long axis
PSAX	parasternal short axis
A4C	apical four chamber
A2C	apical two chamber
A5C	apical five chamber
SC	subcostal
SSN	suprasternal
ALAX	apical long axis or apical three chamber

2.2 Modality:

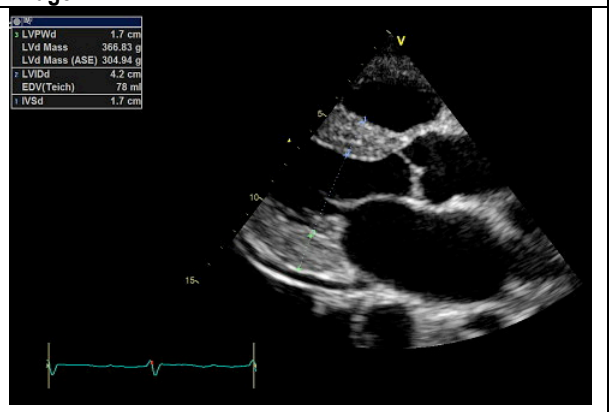
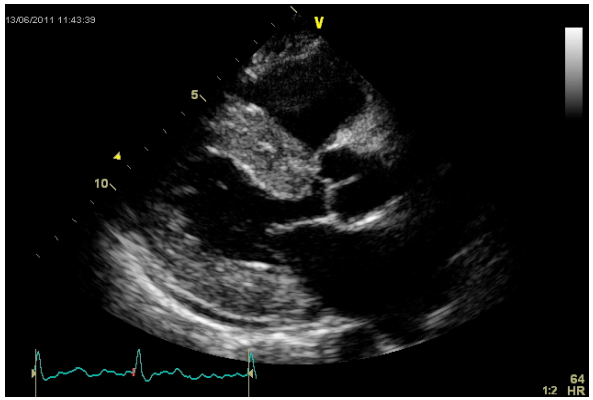
PW	pulse wave Doppler
CW	continuous wave Doppler

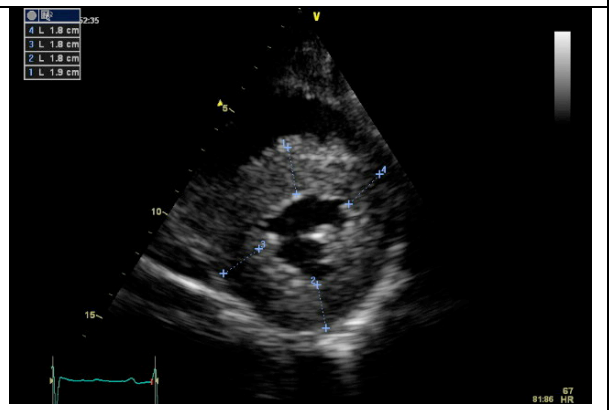
CFM	colour Doppler
TDI	tissue Doppler imaging

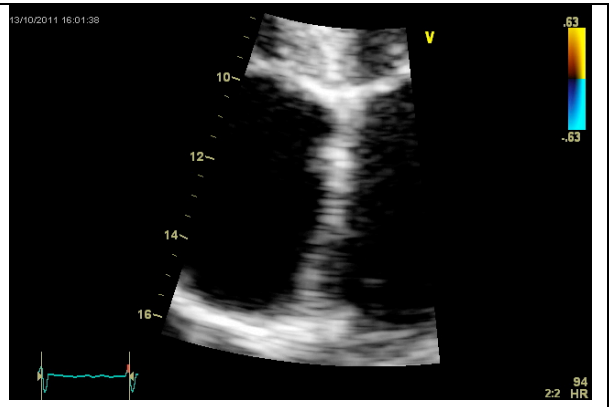
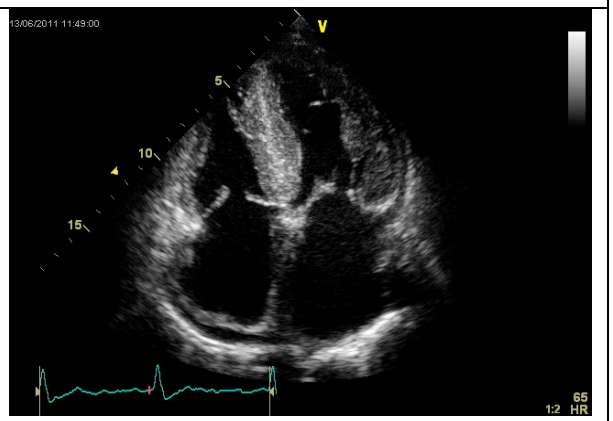
2.3 Measurement and explanatory text:

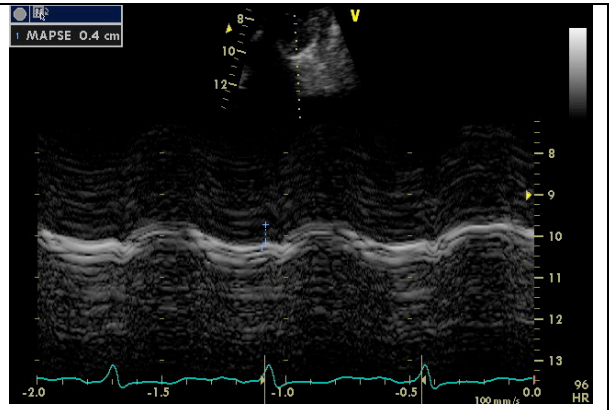
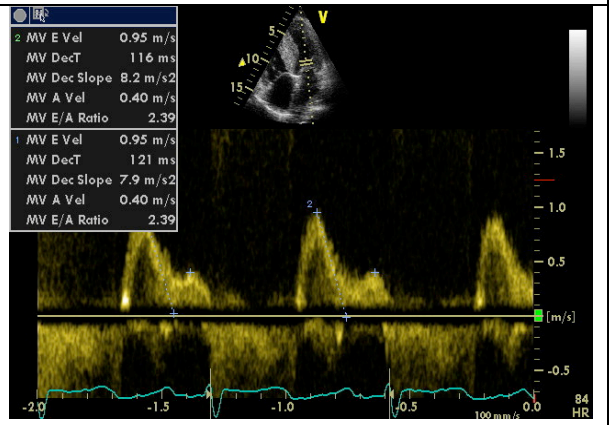
LV	left ventricle
LA	left atrium
MV	mitral valve
AV	aortic valve
Ao	aorta
LVOT	left ventricular outflow tract
RV	right ventricle
RA	right atrium
PV	pulmonary valve
RVOT	right ventricular outflow tract
L/R PA	left/right pulmonary artery
RL/RU/LL/LU PV	right lower/right upper/left lower/left upper pulmonary vein
TV	tricuspid valve
IVC	inferior vena cava
STJ	sinotubular junction
LVIDd/s	left ventricular internal dimension in diastole/systole
IVSd/s	interventricular septal width in diastole/systole
LVPWd	left ventricular posterior wall width in diastole
PHT	pressure half-time
RVd	right ventricular cavity diameter in diastole
VTI	velocity time integral
RWMA	regional wall motion abnormality
TAPSE	tricuspid annular plane systolic excursion
MAPSE	mitral annular plane systolic excursion

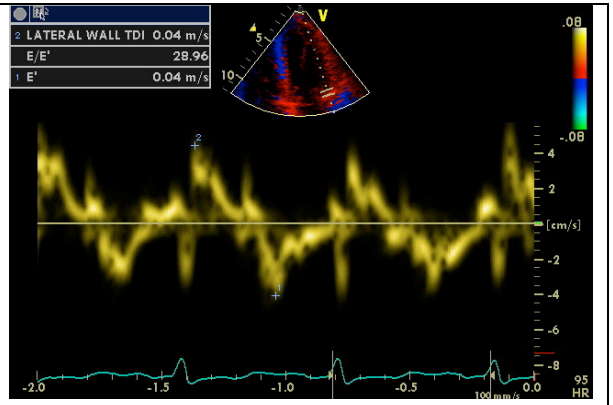
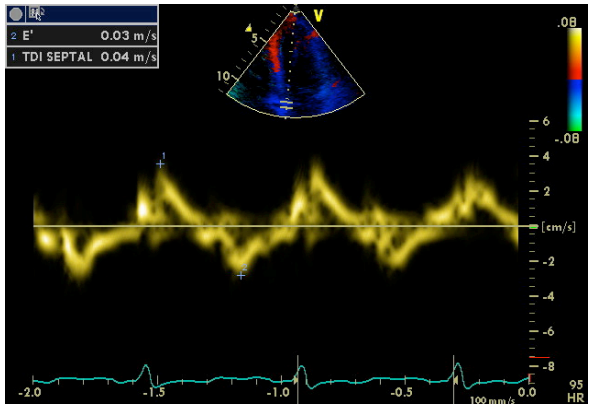
A '*' indicates that these findings, particularly when found together within an individual echo study, are strongly suggestive of cardiac amyloidosis

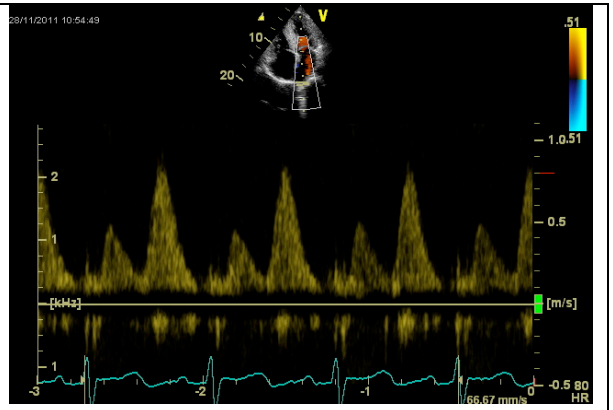
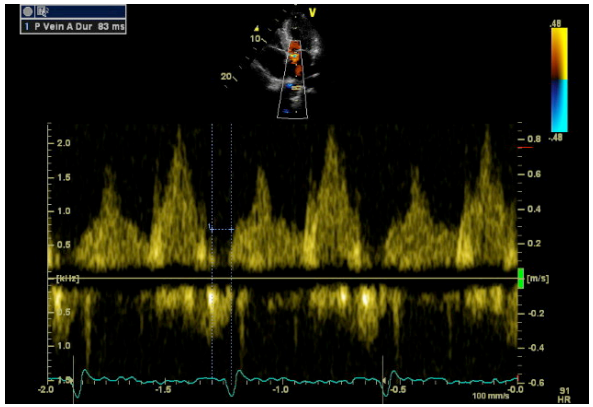
View	Modality	Measurements	Explanatory note	Image
PLAX	2D/M-mode	LV dimensions (LVIDs, LVIDd)	LV cavity size may be normal or small	
		LV wall thickness (IVSd, LVPWd)	May be normal If > 12 mm concentric thickening in the absence of other pathology (for example, hypertension, HCM or significant aortic stenosis) may suggest infiltrative disease Note: **AL** Amyloidosis particularly causes LV increased wall thickness in the mild to moderate range whereas **TTR** causes LV increased wall thickness in the moderate to severe range (although there is overlap)	
		LV mass Relative wall thickness	LV mass = 0.8 x {1.04 x [(LVIDd + LVPWd + IVSd)^3 - (LVIDd)^3]} + 0.6 g Care should be taken to ensure accurate 2D measurements, as errors are amplified by cubing when calculating LV mass Relative wall thickness = (2 x LVPWd) ÷ LVIDd In infiltrative cardiomyopathy there is concentric hypertrophy	
		*Granular or speckled appearance of myocardium	Although this feature is known to be a characteristic feature of cardiac amyloidosis, it is not a specific finding and hence should not be used in isolation	

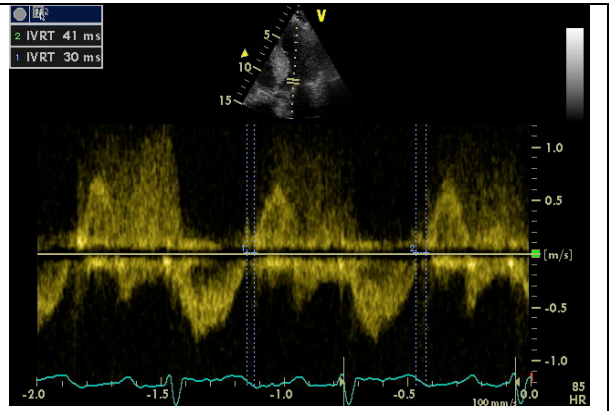
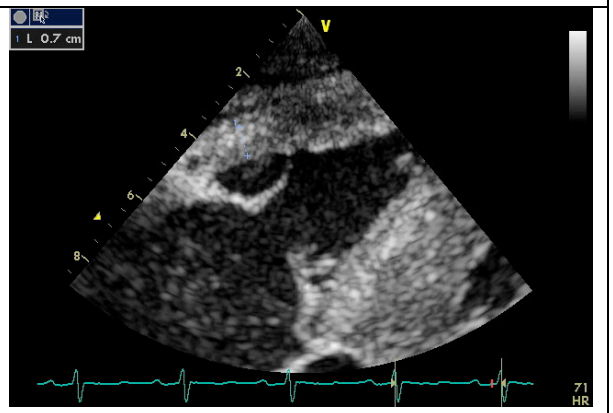
			Note: Low dynamic range, low grey scale compression and harmonic imaging can mimic this appearance. Turning off 'harmonic' settings may help to reduce over diagnosis	
		*Aortic and mitral valve leaflet thickening	Homogenous thickening of leaflets of all valves often seen in amyloidosis Note: Caution should be taken in this qualitative assessment when using harmonic imaging, which may give rise to the appearance of valve leaflet thickening (see note above)	
		*Pericardial and pleural effusions	Frequently, trace or small pericardial and pleural effusions are seen	
PSAX	2D	LV wall thickness at 4 points using clock face as reference (12, 3, 6, 9)	2D frozen image at mid LV level at end diastole to demonstrate concentric increased wall thickness Note: Avoid inclusion of papillary muscles when measuring LV wall thickness by 2D caliper	
Apical 4CH	2D	EF (Simpson's Biplane)	Reduced in end stages, but may be normal or mildly reduced in early disease	

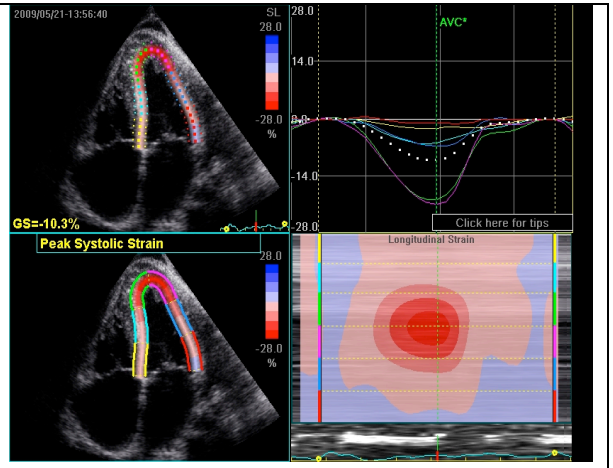
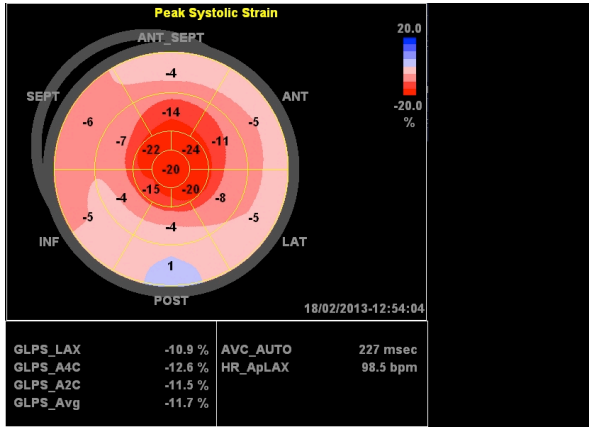
		*IAS thickening	Visual assessment	
		*Mitral and tricuspid valve leaflet thickening	Visual assessment: homogenous thickening	
Apical 4CH and 2 CH	2D	RA and LA volumes and areas	Measured at end ventricular systole and BSA indexed Biatrial dilatation: RA area> 19cm², LA volume>28ml/m²	

Apical 4CH	M-mode	MAPSE	MAPSE<10mm Reduced longitudinal function may be seen before deterioration in global function assessed by EF	
Apical 4CH	PW Doppler	MV inflow pattern: E/A ratio	Severe diastolic dysfunction is more suggestive of an underlying restrictive cardiomyopathy. Earlier in the natural history of restrictive disease, abnormalities of LV filling by PW Doppler of mitral inflow may be in the mild or moderate categories of diastolic dysfunction. Please refer to the BSE diastolic function assessment guidelines	
		E deceleration time	Short deceleration time. Note: normal diastolic filling is extremely rare in cardiac amyloidosis	

Apical 4CH	PW TDI	Mitral annulus: e' e'/ a' E/e' Sept and Lat s'	In restrictive filling: Restrictive filling pattern with low e' e'/ a' << 1 E/e' (average of septal and lateral mitral annulus) > 13 Earlier in the natural history of restrictive disease, abnormalities of mitral annular PW TDI may be in the mild or moderate categories of diastolic dysfunction. Please refer to the BSE diastolic function assessment guidelines Reduced systolic velocity. Reductions in TDI systolic and diastolic indices typically occur earlier in the natural history of the amyloid disease process than traditional echocardiographic measures, and may be a subclinical marker when this condition is suspected	 

Apical 4CH	PW Doppler	PV flow: PVs/PVd PV_a a_{dur} - A_{dur}	In restrictive filling: PV_s << PV_d ≥ 0.35 m/s ≥ 20 ms	 

Apical 5CH	PW or CW Doppler	IVRT	Short IVRT (<50ms) is in keeping with severe restrictive filling, but in earlier stages of the disease process may be prolonged or pseudonormal. Please refer to the BSE diastolic function assessment guidelines IVRT is quantified as the time interval between the end of LVOT ejection and the onset of mitral inflow. This can be quantified by PW or CW Doppler to record both mitral inflow and LVOT outflow velocity profiles: - PW Doppler: position the sample volume within the LVOT, but in close proximity to the anterior mitral valve leaflet - CW Doppler: position the Doppler beam in a hybrid position that captures mitral inflow and LVOT outflow	
Subcostal	2D M-mode	RV free wall thickness	M-mode or 2D frozen image with zoom at end-diastole at the level of the tricuspid valve chordae tendinae ≥ 5 mm RV free wall thickening is abnormal and is frequently seen in cardiac amyloidosis The administration of intravenous agitated saline may assist in situations where endocardial definition is poor	

Apical 4CH and 2Ch	Deformation imaging	Global and peak longitudinal systolic strain (optional but extremely useful)	Reduced with relative apical sparing, giving rise to a characteristic 'bull's eye' appearance on speckle tracking software* Ensure high quality, optimized views for speckle tracking post-processing. This should result in a frame rate that is commensurate with optimal speckle tracking (at least > 80 fps) Reductions in strain indices typically occur earlier in the natural history of the amyloid disease process than traditional echocardiographic measures, and may be a subclinical marker when this condition is suspected Due to inter-vendor variability, 'cut-off' values are not currently advised, but must be interpreted relative to normative data for individual speckle tracking packages	 

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Further reading about cardiac amyloidosis and evidence for novel techniques for assessing myocardial function

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