in the Name of GOD
Echocardiography in cardiac amyloidosis

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CA is a common cause of restrictive cardiomyopathy and should be considered in patients with heart failure with preserved ejection fraction, a progressive disorder and usually has a poor prognosis.

Endomyocardial biopsy has traditionally been the gold standard for diagnosis of CA, but its invasive nature has curtailed its use, leading to more dependence on Cardiac imaging.
CMR is a reference standard for the diagnosis of cardiac amyloidosis and, in addition, is an excellent tool for risk stratification and disease tracking. But it is often not available or feasible because of movement artifacts due to cardiac arrhythmias or the presence of implantable device non-MR compatible. Furthermore, it requires an interpretation by highly trained physicians.

Additionally, technetium 99m-pyrophosphate (Tc99m-PYP) is a single-photon emission CT (SPECT) agent that is highly sensitive and specific for the diagnosis of ATTR amyloidosis.
By contrast, **Echocardiography remains the first-line imaging technique for patients presenting with heart failure**

- Echocardiologist remains on the “front line” for raising the possibility of the diagnosis in early cases
- Early diagnosis is critical and once suspected: amyloidosis should be reported in the differential diagnosis on the echocardiographic report, thereby prompting the ordering clinician to pursue the diagnosis.

- Echocardiographic findings that have been proposed for diagnosis of CA range from conventional LV remodeling parameters to those evaluating diastolic function and deformation
The most frequent types of systemic amyloidosis are as follows:

1. **Light chain (AL)** amyloidosis, in which the precursors of amyloid fibrils are immunoglobulin light chain produced in high concentration due to plasma cellular dyscrasia.

2. Mutant transthyretin-related form (**ATTRm**), caused by more than 100 mutations in the gene codifying for transthyretin, a transport protein synthesized in the liver.

3. Wild-type transthyretin-related form (**ATTRwt**), which differs from the latter because it is not hereditary and affects mainly elderly people also known as senile systemic amyloidosis (SSA).
The development of CA varies with the type of amyloidosis:

- it is frequent in some forms of transthyretin amyloidosis and SSA, whereas in AL form, its development is variable and ranges from absent to severe

- **Secondary** Amyloidosis (consequence of chronic inflammatory conditions) almost **never** affects the heart
Cardiac Amyloidosis

- the most frequent diagnosed, AL amyloidosis, has an annual incidence of 6 to 10 cases per million population in the UK and USA

- The features of cardiac involvement differ according to the stages of diseases. The first phase begins with a subclinical stage characterized by mild and unspecific cardiac symptoms.

- In this phase, amyloid deposition can involve atria (LA enlargement), atrioventricular valves, mild left ventricular (LV) wall thickness (<15 mm and >12 mm), mild diastolic dysfunction, and mild impaired LV longitudinal strain.
The typical clinical scenario (‘hypertrophic’ stage), in the fully developed disease, is characterized by a marked thickening of the LV wall (> 15mm) and congestive heart failure with preserved ejection fraction (EF) with a restrictive diastolic pattern with nonspecific symptoms including weakness, fatigue, weight loss or weight gain, and shortness of breath.

Progressively, in the advanced phase of the disease, biventricular systolic function deteriorates, and symptoms of heart failure (The features of rightsided heart failure almost always predominate) become refractory to medical therapy (end-stage phase). In most cases, death occurs for electromechanical dissociation or arrhythmia.
Irrespective of the subtype of systemic amyloidosis, cardiac involvement worsens the prognosis and reduces the survival.

AL amyloidosis is associated with a more rapid progression of heart failure than transthyretin-related form (TTR-related) amyloidosis with a median survival of approximately 6 months in untreated AL amyloidosis with heart failure (HF) compared with 6 years in ATTRwt.

However, the myocardial involvement is more extensive in ATTRwt than in AL amyloidosis.
we should consider that cardiac amyloidosis is much more common than we would normally think.

Left ventricular wall thickening is sometimes due to multiple factors.

Several studies have shown recently that ATTR CA is frequent in common cardiac diseases that exhibit IWT.

For example, 13.3% of elderly patients admitted with heart failure with preserved ejection fraction, 16% of patients with aortic stenosis treated with TAVR, and 5% of outpatients with IWT of >=15 mm have been reported to have CA.
Echocardiographic features of amyloid infiltration of the heart

1. Increased LV wall thickness in the absence of secondary causes.
2. “Mismatch” between echocardiographic and electrocardiographic findings.
3. “Granular sparkling” appearance of myocardial walls in the nonharmonic imaging.
4. Biatrial dilatation and normal or reduced LV cavity dimensions
5. Valve thickening and atrial septal thickening
6. LV Longitudinal dysfunction and diastolic dysfunction are common findings but not specific signs of CA.
7. Increased RV wall thickness (>7mm), PH, RV dysfunction, PE in advanced disease
6. Apical sparing is easily recognizable and a specific sign in predicting CA over more traditional parameters.
Echocardiography is the First-Line Screening Tool for Cardiac Amyloidosis

- The most important echocardiographic feature predictive, although not specific, of cardiac amyloidosis is the **concentric left ventricular hypertrophy**.

- Concentric hypertrophy was diagnosed in patients with relative wall thickness >0.42 and LV mass index >115 g/m2.

- <5% of cases, is an appearance mimicking classical hypertrophic cardiomyopathy, with **asymmetric septal hypertrophy** and even left ventricular outflow tract obstruction.

- The latter increase the stiffness of the ventricular wall.

- Besides, amyloid deposits produce, in fundamental (nonharmonic) imaging, a pathognomonic hyperreflective appearance, defined as “**granular sparkling,**” of the thickened ventricular myocardium. (*poor sensitivity: seen only in 26% cases)*

- In advanced stages, and also seen in HCM, myocarditis with severe fibrosis, other infiltrative
In addition, harmonic 2D imaging often gives a **speckled appearance** to the myocardium, which is suggestive of cardiac amyloidosis.

The most common areas with granular sparkling are the ventricular septum or the posterior wall, whereas the apex does not show indirect sign of **amyloidotic presence**.

In the advanced stages of cardiac amyloidosis and, sometimes, in the early stage, even **papillary muscles are thickened**.
Left ventricular (LV) thickening (most common) in the absence of hypertension is highly suggestive of an infiltrative heart disease (such as amyloidosis, sarcoidosis, hemochromatosis, and glycogen storage diseases).

Three of the leading causes of RCM are cardiac amyloidosis, cardiac sarcoidosis, and cardiac hemochromatosis.
The low voltage on an ECG is an important marker of suspected cardiac amyloidosis if integrated with the echocardiographic evidence of LV hypertrophy.

Such a dissociation between echocardiographic and electrocardiographic findings reflects the difference between the amyloidosis and the rest of all the hypertrophic cardiomyopathies. Amyloidosis can be considered a "pseudo-hypertrophic cardiomyopathy."
The diastolic dysfunction begins from the atria: the reduced atrial compliance, due to amyloid infiltration, increases the diastolic atrial pressure.

As consequence, the transmitral blood flow is rapid. The latter, in association with the high atrial pressure, gives the false impression of a diastolic “restrictive pattern.”

average $E/e'$ ratio becomes abnormal in early stages of amyloidosis.

In contrast, advanced cardiac amyloidosis (with a wall thickness equal to 15 mm or more) showed a short deceleration time and an increasing $E/A$ ratio, which are consistent with restrictive physiology.

Pulmonary vein flow is abnormal in the advanced CA
E’ velocity: 5.7 cm/sec
Elevated LV filling pressure could lead to **left atrial enlargement** and also to post-capillary pulmonary hypertension with consequent right ventricular cavity enlargement.

Most of the ventricular filling occurs in the first part of the diastole and is due to the ventricular suction. The latter is influenced by the stored energy generated by the previous systolic contraction.

Therefore, diastolic function depends on the myocardial long-axis systolic function.

**In conclusion, diastolic impairment and longitudinal systolic dysfunction are the signs of cardiac amyloidosis in the earlier stage**
Cardiac amyloidosis is also called “heart stiff syndrome” because it causes myocardial relaxation abnormalities in early stage and systolic dysfunction in advanced stages. Global LV systolic function assessed by ejection fraction is normal or nearly normal until the late stages of disease.

Longitudinal contractile dysfunction (measured by mitral annular displacement) can be observed in the early stages.

Therefore, a global evaluation of the cardiac performance in amyloidosis can be useful. Myocardial performance index (MPI) or Tei index combines diastolic and systolic time intervals.

That isovolumetric relaxation time (IVRT) is prolonged both in early and advanced stage of cardiac amyloidosis, especially in patients with left ventricular wall more than 15 mm. As a consequence, the preejection time is prolonged, whereas the ejection time is shortened.
The shortening of the ejection time is associated with a decreased left ventricular stroke volume. Hence, in advanced amyloidosis, when the stroke volume starts to decrease, Tei index is high.

In patients with CA, the isovolumetric contraction time (IVCT) is abnormally prolonged, even when the systolic function is not compromised.

Therefore, **in cardiac amyloidosis, IVCT is a more sensible and earlier marker of systolic dysfunction than ejection fraction.**
Considering the limits of standard 2D echocardiography and the not always easy availability of advanced diagnostic methods, new imaging techniques, such as two-dimensional speckle tracking echocardiography (2D-STE), can play a big part in CA assessment.
New echocardiographic techniques such as tissue Doppler strain rate imaging, speckle tracking based, and three dimensional echocardiographic LV analysis have been shown to allow the detection of cardiac amyloid at a subclinical stage when other echocardiographic measurements are normal.

In particular, 2D-STE has been found more sensitive and more reproducible than Doppler imaging and has shown promise for the early diagnosis of CA.
TDI measures the longitudinal function of the myocardium through the evaluation of the annular displacement toward the ventricular apex in systole and away from the same in diastole.

The myocardial profiles of the systolic and diastolic curves of velocity recorded from septal or lateral mitral annulus in amyloidosis patients are significantly reduced because the amyloidotic infiltration decreases myocyte longitudinal motion.

The velocities measured by TDI in one myocardial segment can be influenced by the translation motion driven by the adjacent segments.

TDI is also affected by translational and tethering movements of the heart. On the contrary, Speckle Tracking Echocardiography (STE) has a high special and temporal resolution.
Speckle tracking echocardiography is a novel non-Doppler-based method for the angle independent and objective quantification of myocardial deformation from standard bidimensional datasets.

STE (Speckle Tracking Echocardiography) has been shown to allow the detection of cardiac amyloid at a subclinical stage when other echocardiographic parameters are normal.

Speckles are groups of myocardial pixels with particular gray-scale characteristics. A speckle is defined as the spatial distribution of gray values.
2D-STE

- In CA strain and strain rate values are reduced compared with healthy people, even with a completely normal ejection fraction. Cardiac amyloid profoundly alters all left ventricular strain parameters (longitudinal, radial, circumferential).

- Patients with different diseases, all characterized by LVH, in different stages of progression, may have reduced global strain in the same range, so it is difficult to differentiate left ventricular hypertrophies from one another solely on the basis of global strain impairment.

- Sun et al. showed that standard deviation of time to peak strain was significantly higher in the groups with hypertrophic cardiomyopathy and amyloidosis compared with the control group, indicating the asynchronized contraction pattern that underlies the pathology of these patients.
However, in patients with CA, myocardial deformation is not only globally reduced, but it is **impaired mostly in the basal segments, whereas the apical contractility is preserved.**

Cardiac amyloidosis was predicted by **basal longitudinal strain of -11.3% or below** (63.3% sensitivity, 100% specificity) and an E/e' of 12.3 or greater (69.7% sensitivity, 83.3% specificity).

Using Doppler-derived strain in AL amyloidosis **Mean basal strain was a strong predictor of survival, with a cutoff of <=12 % representing a significantly worse prognosis than in those>12 %**

**This expected “apical sparing” is clearly observed on longitudinal speckle tracking**

**An LV apical ratio > 1 was found to be the best cutoff value for the diagnosis of CA**
A bull's eye plot showing a relative “apical sparing” pattern of LS, suggestive of cardiac amyloidosis.
Global longitudinal strain (GLS)

“Cherry on top”
The apico-basal gradient of longitudinal strain or apical sparing is typically described in patients with advanced cardiac amyloidosis, the finding is also clinically useful for detecting CA in less advanced patients with a borderline or mildly thickened LV wall (≤ 14 mm).

**RapLS = mean apical LS / mean basal LS + mean mid LS**

Apical ratio > 1 was found to be the best cutoff value for the diagnosis of CA. Relative apical longitudinal strain (LS) of 1.0, defined using this equation, was sensitive (93%) and specific (82%) in differentiating CA patients from controls (area under the curve 0.94).
- Patients with TTR CA were found to have significantly lower average apical LS than those with AL amyloidosis.

- Relative apical sparing is distinct, easily recognizable, and specific.

- In fact, among patients with increased left ventricular wall thickness, *RapLSI has incremental value in predicting CA over more traditional parameters.*
EF:GLS ratio of more than 4.1 had 89.7% sensitivity and 91.7% of specificity to diagnose CA and distinguish it from other causes of LVH.

- HCM is characterized by a marked reduction in longitudinal strain at the septum with normal/super-normal strain values in the resting segments
- patchy reduction in longitudinal strain in left ventricular hypertrophy related to aortic stenosis
- Systolic dysfunction occurs only in the advanced stage of CA, is based on studies that do not consider the myocardial longitudinal function.
- The latter is given by the motion of the subendocardial fibers.
Strain patterns in different types of left ventricular hypertrophy

<table>
<thead>
<tr>
<th>Type of left ventricular hypertrophy</th>
<th>Strain pattern</th>
<th>Typical impairment on STE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Athlete’s heart</td>
<td>Normal GLS</td>
<td>None</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Reduced GLS</td>
<td>IVS</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>Normal/Reduced GLS</td>
<td>IVS</td>
</tr>
<tr>
<td>Cardiac amyloidosis</td>
<td>Reduced GLS</td>
<td>Apical sparing</td>
</tr>
<tr>
<td>Fabry disease</td>
<td>Reduced GLS</td>
<td>Basal posterior-lateral</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>Reduced GLS and GRS</td>
<td>Basal LV segments/patchy</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>Reduced GLS</td>
<td>Diffused</td>
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<tr>
<td>Mitral regurgitation</td>
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<tr>
<td>Initial disease</td>
<td>Normal/supranormal GLS</td>
<td>None</td>
</tr>
<tr>
<td>Advanced disease</td>
<td>Reduced GLS</td>
<td>Basal segments, lateral wall</td>
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</tbody>
</table>
Atrial function

- Atrial function is very often significantly impaired in cardiac amyloidosis, due to infiltration with amyloid protein. LA function was more impaired in ATTRwt compared to AL.

- **Left atrial thrombi may occur in cardiac amyloidosis even in sinus rhythm.**
- In this context, the study of LA function, also with STE, could represent a useful clinical tool to identify CA patients with higher thromboembolic risk.
- Based on these evidences, the assessment of LA function in CA should be performed routinely in the clinical practice.

- Left atrial enlargement, biatrial enlargement (late): Left atrial size is an independent predictor of overall survival in patients with primary systemic amyloidosis; the extent of left atrial LGE on CMRI is highly predictive for cardiac amyloidosis.
The atrial strain is severely impaired, with a mean peak strain of 8%, normal being >25%. The source of the stroke was thromboembolism from the left atrium despite sinus rhythm.
3D Echocardiography is a recent advance in the volumetric assessment of left ventricular function and software allows the quantification of the dispersion of timing to peak systole among the different ventricular regions, a measure of intraventricular dyssynchrony.

Early studies demonstrate that dyssynchrony measured by the dispersion of systolic timing among the 16 segments is associated with systolic Dysfunction.

Intraventricular segmental dyssynchrony is recently demonstrated in light chain amyloidosis subjects compared to healthy controls with higher temporal pattern of dispersion of regional volume systolic change on 3D echocardiography.

Further, using 3D-STE–derived measurements, there are evidences of significant alterations in segmental LV rotation in CA including near absence of left ventricular twist.
Dyssynchrony between volume curves of LV by 3D echo
Right ventricular hypertrophy (RVH), RV dilatation (a marker of poor prognosis):

- RV dysfunction is common in cardiac amyloidosis, and a tricuspid annular plane systolic excursion (TAPSE) below 14 mm is an independent predictor of adverse cardiac events.

- Independent determinants of TAPSE below 14 mm are:
  LVEF, E/E', N-terminal pro b-type natriuretic peptide (NT-proBNP) levels, and pulmonary artery pressure, but not RV late gadolinium-enhancement (LGE) on cardiac magnetic resonance imaging (CMRI).
Role of Right Ventricular Strain Measured by Two-Dimensional Echocardiography in the Diagnosis of Cardiac Amyloidosis

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Background: Cardiac amyloidosis (CA) causes restrictive cardiomyopathy usually associated with a poor prognosis. Two subtypes predominate: systemic light-chain CA (ALCA) and transthyretin-derived CA (either wild type transthyretin amyloidosis [TTRwt] or mutant transthyretin amyloidosis). Left ventricular (LV) apical sparing has been extensively studied using speckle-tracking echocardiography for diagnosis, but the right ventricular (RV) deformation pattern has not been described. The aims of this study were to characterize RV involvement in patients with CA and to identify parameters that may help in the differential diagnosis between ALCA and transthyretin-derived CA subtypes.

Methods: Seventy-eight patients with CA (47 with ALCA, 20 with TTRwt, and 11 with TTRm) and 24 healthy control subjects were included. Global longitudinal strain (GLS) was analyzed in 16 LV and six RV segments. LV and RV apical ratios (ARs) were obtained. GLS was expressed as an absolute value.

Results: LV GLS and free-wall RV longitudinal strain were impaired in all patients (LV GLS: 11.9 ± 2.9% in ALCA, 12.5 ± 3.8% in TTRwt, 14.9 ± 2.7% in TTRm, and 21.9 ± 2.6% in control subjects [P < .01]; free-wall RV longitudinal strain: 13.1 ± 6.8%, 14.9 ± 4.5%, 17.2 ± 3.4%, and 22.1 ± 3.1%, respectively [P < .01]). LV and RV ARs were higher in ALCA compared with both TTRwt, TTRm, and control subjects (LV AR: 1.1 ± 0.2, 0.8 ± 0.2, 0.9 ± 0.1, and 0.7 ± 0.1, respectively [P < .001]; RV AR: 1.1 ± 0.2, 0.6 ± 0.2, 0.6 ± 0.1, and 0.6 ± 0.1, respectively [P < .001]). Cutoff values of LV AR > 0.98 and RV AR > 0.8 showed high accuracy to differentiate between ALCA and transthyretin-derived CA.

Conclusions: RV dysfunction is common in patients with CA. Analysis of RV strain showed an apical sparing pattern, as previously described in the left ventricle, with a higher AR as a specific finding in patients with ALCA. RV AR may be a parameter that can differentiate the subtypes of amyloidosis on the basis of speckle-tracking echocardiographic analysis. (J Am Soc Echocardiogr 2019;32:845-53.)

Keywords: Amyloidosis, Right ventricle, Speckle-tracking, Longitudinal strain, Apical ratio
The aims of this study were to characterize RV involvement in patients with CA and to identify parameters that may help in the differential diagnosis between ALCA and transthyretin-derived CA subtypes.

Results: LV GLS and free-wall RV longitudinal strain were impaired in all patients.

LV and RV ARs were higher in ALCA compared with both TTRwt, TTRm, and control subjects.

Cutoff values of LV AR > 0.96 and RV AR > 0.8 showed high accuracy to differentiate between ALCA and transthyretin-derived CA.
A

**Peak Strain**

**HR (Avg):** 65 bpm

**EBV (Bi-Plane):** 95.3 ml

**ESV (Bi-Plane):** 52.4 ml

**EF (Bi-Plane):** 44.5%

**Time SVL:** 0.7 ml

**APQ L Strain:** -6.9%

**APQ L Strain:** -15.3%

**APQ L Strain:** -12.8%

**Global L Strain:** -13.0%

**Deform. pico**

**FC (Prom.):** 85 bpm

**Desv. síst.:** 1.8 m/s

**LV Apical ratio 1.1**

B

**RV Apical ratio 1.1**

C

**LV Apical ratio 0.7**

D

**RV Apical ratio 0.5**
RV dysfunction is common in patients with CA. Analysis of RV strain showed an apical sparing pattern, as previously described in the left ventricle, with a higher AR as a specific finding in patients with ALCA.

RV AR may be a parameter that can differentiate the subtypes of amyloidosis on the basis of speckle-tracking echocardiographic analysis. (J Am Soc Echocardiogr 2019)

This study showed that in patients with AL amyloidosis, free wall RVLS < 17% (absolute value) identified patients with marked RV dysfunction and a higher risk for death.
In patients with hypertrophy and high LV filling pressures with suspicion for CA, **the first step** would be to analyze LV GLS.

-The presence of LV **apical sparing** should increase the suspicion for CA.

Then, **the second step** should be checking the presence of RV apical sparing, and if RV apical ratio is >0.96, strong suspicion of ALCA would prompt us to complete diagnostic testing for CA.

- Furthermore, **if apical ratio is <0.96**, a pyrophosphate scan should be performed to assess for ATTR.
bortezomib-induced systolic dysfunction has been described (in the treatment of AL)

a subacute deterioration in clinical status after cardiac biopsy, particularly with worsening right heart failure, should prompt a search for iatrogenic tricuspid regurgitation.
Cardiomyopathies

Echo Parameters for Differential Diagnosis in Cardiac Amyloidosis
A Head-to-Head Comparison of Deformation and Nondeformation Parameters

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Background—A plethora of echo parameters has been suggested for distinguishing cardiac amyloidosis (CA) from other causes of myocardial thickening with, however, scarce data on their head-to-head comparison. This study aimed at comparing the diagnostic accuracy of various deformation and conventional echo parameters in differentiating CA from other hypertrophic substrates, especially in the gray zone of mild hypertrophy (maximum wall thickness ≤16 mm) or normal ejection fraction (EF).

Methods and Results—We included 100 subjects, of which 40 were patients with newly diagnosed, biopsy-proven CA (65.5±10.8 years, 65% male, 62.5% amyloidosis light chain [AL] type), 40 patients with hypertrophic cardiomyopathy matched for demographics and maximum wall thickness (60.1±14.8 years, 85% male), and 20 hypertensives with prominent myocardial remodeling. Quantifiable conventional morphological and functional parameters along with multidimensional strain and strain-derived ratios indices, previously suggested to diagnose CA, were analyzed. EF global longitudinal strain ratio showed the best performance to discriminate CA (area under the curve, 0.95; 95% confidence intervals, 0.89–0.98; P<0.00005). Traditional echo indices showed overall low sensitivities and high specificities (among them myocardial contraction fraction ratio had the highest area under the curve, 0.80; 95% confidence intervals, 0.7–0.87; P<0.0001). In the challenging subgroups (maximum wall thickness ≤16 mm and EF>55%), EF global longitudinal strain ratio remained the best predicting parameter of CA diagnosis (multiple logistic regression models P<0.00005 and P<0.0002, respectively) independent of the CA type.

Conclusions—Our study demonstrated that in patients with thickened hearts, EF global longitudinal strain ratio has the best accuracy in detecting CA, even among the most “challenging” patient subgroups as those with mild hypertrophy and normal EF. (Circ Cardiovasc Imaging. 2017;10:e005588. DOI: 10.1161/CIRCIMAGING.116.005588.)
in patients with thickened hearts, **EF global longitudinal strain ratio has the best accuracy in detecting CA**, even among the most “challenging” patient subgroups as those with mild hypertrophy and normal EF.
CENTRAL ILLUSTRATION  Diagnostic Algorithms With Echocardiographic Scores in 2 Different Clinical Scenarios

A

PARAMETERS
- RWT > 0.52 2 points
- E/e’ > 10 2 points
- TAPSE ≤ 19 mm 1 point
- LS ≥ -14% 1 point

AUC = 0.9
(95% CI: 0.87–0.92)

Systemic AL Score
n = 487

< 1 point 74 patients (15%)
- Sensitivity 100% (99–100%)
- Specificity 0% (0–2%)

1–4 points 243 patients (50%)
- Sensitivity 93% (87–96%)
- Specificity 43% (35–50%)

≥ 5 points 170 patients (35%)
- Sensitivity 54% (48–59%)
- Specificity 98% (95–100%)

Cardiac AL amyloidosis unlikely. Perform additional tests. Cardiac AL amyloidosis

B

Cardiac amyloidosis unlikely. Perform additional tests. Cardiac amyloidosis

Sensitivity 98% (97–99%)
Specificity 19% (15–24%)

135 patients (15%)
< 2 points

Sensitivity 61% (57–66%)
Specificity 27% (22–32%)

498 patients (54%)
2–7 points

Sensitivity 46% (42–50%)
Specificity 98% (95–99%)

290 patients (31%)
≥ 8 points

n = 923

IWT Score

AUC = 0.87
(95% CI: 0.85–0.90)

PARAMETERS
- RWT > 0.6 3 points
- E/e’ > 11 1 point
- TAPSE ≤ 19 mm 1 point
- LS ≥ -13% 2 points
- SAB > 2.9 3 points

Proposed diagnostic algorithms with highly sensitive and highly specific cutoffs to diagnose or exclude cardiac amyloidosis in patients with (A) systemic AL amyloidosis (AL score) and (B) increased wall thickness (IWT score).
Because it is essential to avoid misdiagnosis of CA because effective treatments are now available, the primary aim of the different cutoffs provided (including those that are highly specific and highly sensitive) is to guide the diagnostic algorithm and the use of second-level tests in the most efficient way.

When the score points denote a **very high likelihood of CA**, searching for a clonal dyscrasia and performing a diphosphonate scintigraphy should be the next diagnostic steps to confirm CA and help differentiate the AL from ATTR subtypes

However, **CMR or endomyocardial biopsy should be considered if AL is in the differential**, that is, in a patient who has a hypertrophic phenotype and a clonal gammopathy
High risk indexes in CA by echo

- Relative regional strain ratio’ (RRSR): median RRSR of greater than 1.19 was associated with increased progression to death or heart transplantation.

- In a Mayo Clinic study, GLS proved to be an important prognostic marker compared with clinical, echocardiographic and serological markers in patients with light-chain CA.

- Even in the patients who did not have cardiac involvement, GLS predicted all-cause mortality.

- A low MAPSE value, is also associated with poor outcomes in patients with heart failure with preserved LVEF.
Compared with the conventional diastolic parameters like E’ and E/E’, speckle tracking imaging-derived diastolic deformation, *longitudinal early diastolic strain rate (LSRdias)* was superior in predicting outcomes in patients with CA with preserved LVEF (>50%).

*LSRdias* < 0.85 s⁻¹ alone was associated with fourfold increased mortality in these patients.

RV longitudinal could be added to TAPSE as a valuable RV-derived prognostic marker in patients with cardiac AL amyloidosis.
Thank you for your attention