Overview of Cardiac Amyloidosis and the Utility of $^{99m}$Tc-labelled Tracers Scintigraphy for Diagnosis of Transthyretin Cardiac Amyloidosis

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Toru Kubo
I have received consulting fees or honoraria and remuneration for lecture from Pfizer Japan Inc.

Name of Authors: Toru Kubo
Management of cardiac amyloidosis

✓ Invasive diagnostic procedure
  (endomyocardial biopsy)
  ➔ Utility of $^{99m}$Tc-labelled tracer scintigraphy

✓ Recognition as a rare disease
  ➔ Major important cause of HF in the elderly

✓ Treatment with supportive care
  ➔ Emergence of disease-modifying therapies
Utility of $^{99m}$Tc-labelled Scintigraphy

Prevalence of ATTR-CA in HFpEF Patients

HF + LVEF ≥ 50% + MWT ≥ 12mm
164 patients

44 patients refuse to participate

99mTc-DPD SCINTIGRAPHY
120 patients

(-) 104 patients (86.6%)

(+) 16 patients (13.3%)

TTR Genetic testing

No mutations

4 patients EMB

Prevalence of ATTR-CA in Severe AS

6% of ATTR-CA in AVR for severe AS


16% of ATTR-CA in TAVI for severe AS

Prognosis of ATTRwt-CA Patients

Heart Failure Resulting From Age-Related Cardiac Amyloid Disease Associated With Wild-Type Transthyretin
A Prospective, Observational Cohort Study

Lawrence H. Connors, PhD; Flora San, MD; Martin Sh通讯, MD; Francesco Sullano, MD; Fangcai Sun, PhD; Frederick L. Reberg, MD; John L. Berk, MD; David C. Soldin, MD, PhD

5-year survival rate: 35.7%

Prognosis of Japanese ATTRwt-CA Patients

ATTRwt-CA patients in Kochi Medical School Hospital

1-year survival rate: 79%
2-year survival rate: 68%
5-year survival rate: 34%

The ATTR-ACT Clinical Trial

Analysis of All-Cause Mortality

Probability of Survival

Hazard ratio, 0.70 (95% CI, 0.51–0.96)

Months since First Dose

Pooled tafamidis
Placebo

JCS 2020 Guideline on Diagnosis and Treatment of Cardiac Amyloidosis

Hiroaki Kitaoka; Chisato Izumi; Yasuhiro Izumiya; Takayuki Inomata; Mitsuharu Ueda; Toru Kubo; Jun Koyama; Motoaki Sano; Yoshiki Sekijima; Nobuhiro Tahara; Nobuhiro Tsukada; Kenichi Tsujita; Hiroyuki Tsutsui; Takeshi Tomita; Masashi Amano; Jin Endo; Atsushi Okada; Seitaro Oda; Seiji Takashio; Yuichi Baba; Yohei Misumi; Masahide Yazaki; Toshihisa Anzai; Yukio Ando; Mitsuaki Isobe; Takeshi Kimura; Keiichi Fukuda on behalf of the Japanese Circulation Society Joint Working Group
3 Subtypes of Cardiac Amyloidosis

<table>
<thead>
<tr>
<th>Precursor protein</th>
<th>Underlying disorder</th>
<th>Organ involvement</th>
<th>Other</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>Monoclonal immunoglobulin light chain</td>
<td>Plasma cell dyscrasia</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>ATTRwt</td>
<td>Wild-type TTR</td>
<td>Aging</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>ATTRv</td>
<td>Mutant TTR</td>
<td>Mutations in TTR gene</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>AA</td>
<td>SAA</td>
<td>Inflammatory disorders (RA, JIA)</td>
<td>−/+</td>
<td>+++</td>
</tr>
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</table>

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Algorithm for Diagnosis of Cardiac Amyloidosis

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Question 1
Which ECG findings strongly suspect cardiac amyloidosis in patients with cardiac hypertrophy?

1. High voltage with ST-T changes
2. Low voltage in limb leads
3. Short PQ interval
### Clinical Findings of Cardiac Amyloidosis

<table>
<thead>
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<th>(ECG findings)</th>
<th>(Echo findings)</th>
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<td>Low voltage in limb leads</td>
<td>Ventricular wall thickening (including RVH)</td>
</tr>
<tr>
<td>QS pattern in V1-3</td>
<td>Atrial septal thickening</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Conduction disorder</td>
<td>Restrictive pattern</td>
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<tr>
<td>Ventricular arrhythmia</td>
<td>Apical sparing</td>
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</table>

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Apical Sparing Pattern

Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis

Dermot Phelan, Patrick Collier, Paaladinesh Thavendiranathan, Zoran B Popović, Mazen Hanna, Juan Carlos Plana, Thomas H Marwick, James D Thomas
A Typical Case of ATTR-CA

A case in the Kochi Medical School Hospital

ATTRwt-CA
**Not Always Typical Findings in CA Patients**

Especially in the early stages of CA or ATTR type

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<th>(Echo findings)</th>
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# Rate of ECG Findings of Cardiac Amyloidosis

## Table 13. Rate of Electrocardiogram Findings Among Different Types of Cardiac Amyloidosis

<table>
<thead>
<tr>
<th>Types</th>
<th>Low voltage</th>
<th>Pseudoinfarct pattern</th>
<th>Atrioventricular block</th>
<th>Atrial fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>23–64%</td>
<td>15–69%</td>
<td>15–26%</td>
<td>6–32%</td>
</tr>
<tr>
<td>ATTRwt</td>
<td>13–40%</td>
<td>18–71%</td>
<td>11–33%</td>
<td>27–67%</td>
</tr>
<tr>
<td>ATTRv</td>
<td>23–38%</td>
<td>18–69%</td>
<td>25–45%</td>
<td>5–17%</td>
</tr>
</tbody>
</table>

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Question 2

Which are the extracardiac findings that suspect cardiac amyloidosis?

1. Achilles tendon xanthoma
2. Angiokeratomas
3. Carpal tunnel syndrome
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A Case of ATTRwt-CA with CTS

A case in the Kochi Medical School Hospital

80 y.o.
Woman
Dyspnea
Bil. carpal
tunnel syndrome
If the patient is suspected of having CA,

- **M protein detection**
  - Serum FLC
  - Serum protein electrophoresis
  - Serum immunofixation
  - Urine immunofixation

- **99mTc PYP scintigraphy**
  - Grade 0
  - Grade 1
  - Grade 2-3

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99mTc Scintigraphy with High Sensitivity and Specificity

H/CL ratio (heart / contralateral)

H/CL > 1.5 (1-h imaging)

ATTR-CA

Sensitivity 87%
Specificity 100%

99mTc Scintigraphy with High Sensitivity and Specificity

ATTX-CA
Sensitivity 99%
Specificity 86%

Nonbiopsy diagnostic approach

✓ 99mTc Scintigraphy positive
✓ FLC negative

ATTR-CA

Gillmore JD, et al. Circulation 2016;133:2404-12
Question 3

Which patients have ATTR cardiac amyloidosis?
Which patients have ATTR cardiac amyloidosis?

1. Late 60s, Woman, Family Hx of ATTRv
2. Late 70s, Woman, TTR (+) in CTS tissue
3. Late 70s, Man, Shortness of breath
99mTc-PYP Scintigraphy

1. Late 60s, Woman, Family Hx of ATTRv
2. Late 70s, Woman, TTR (+) in CTS tissue
3. Late 70s, Man, Shortness of breath

Grade 0
Grade 0
Grade 3

No findings of cardiac amyloidosis → follow-up
TTR (+) in endocardial biopsy
TTR mutation (-) → Diagnosis of ATTRwt-CA

Diagnosis of ATTRwt-CA
Take Home Message

✓ Importance of awareness of cardiac amyloidosis in HF and arrhythmic patients

✓ Utility of $^{99m}$Tc-PYP Scintigraphy as a noninvasive diagnostic modality for ATTR-CA with high sensitivity and specificity