# Cardiac screening of pathogenic *TTR* variant carriers: complementary value of echocardiographic global longitudinal strain imaging versus bone scintigraphy

Sanders-van Wijk S[1], Klaassen SHC[2,8], Weerts J[1], Oerlemans M[3], Michels M[4], van der Zwaag P[5,8], Slart RHJA[6,8], van Gemert M[1], van Veldhuisen DJ[2,8], Nienhuis HLA[7,8], Knackstedt C[1], van den Berg MP[2,8]

Department of [1]Cardiology, Maastricht University Medical Center/ CARIM, Maastricht, The Netherlands.
Departments of [2]Cardiology, [5]Clinical Genetics, [6]Nuclear Medicine and Molecular Imaging, [7] Internal Medicine, University Medical Center Groningen, Groningen , The Netherlands. Department of [3]Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands.
Department of [4]Cardiology, Thorax Center, Erasmus University Medical Center, Erasmus University Rotterdam, Rotterdam, The Netherlands
[8]Groningen Amyloidosis Center of Expertise, University Medical Center Groningen, Groningen, The Netherlands

## INTRODUCTION

Cardiac involvement is the major determinant of mortality in hereditary transthyretin-related amyloidosis (ATTRv). Treatments are most beneficial when initiated at an early disease stage, which makes early diagnosis important. Several imaging modalities for screening are proposed including bone scintigraphy, conventional and strain echocardiography but data on their relative value is limited.

## OBJECTIVE

To investigate the value of left ventricular global longitudinal strain (LV-GLS) for screening for cardiac involvement in pathogentic *TTR* variant carriers.

## METHODS

Fifty-three pathogenic *TTR* variant carriers from 2 university medical centers underwent transthoracic echocardiography and bone scintigraphy as part of routine patient care to assess cardiac involvement. LV-GLS was measured by 2 blinded reviewers. Abnormalities in LV-GLS (cut-off –21.5%) and conventional TTE (cTTE) parameters were evaluated in bone scintigraphy positive (≥ Perugini grade 1) and negative cases.

## RESULTS

Carriers with a positive bone scintigraphy (n=20) were 16 years older than those with a negative scan (n=33) (Table 1). When bone scintigraphy was negative, LV-GLS was abnormal in 11 cases (38%). Three out of them had diabetes and/or hypertension as potential additional explanation to ATTRv for the abnormal LV-GLS (Table 2). In the remaining 11 carriers, cardiac ATTRv was the sole most likely cause of abnormal LV-GLS. In 85% (17/20) of patients with a positive bone scintigraphy, LV-GLS was equally sensitive in determining the presence of cardiac ATTR as the combination of all cTTE parameters.

| | Bonescintigraphy negative (n=33) | Bonescintigraphy positive (n=20) | P-value |
|---|---|---|---|
| **Age (years)** | 49 (44-57) | 65 (64-74) | <0.001 |
| **Female sex** | 18 (55%) | 6 (30%) | 0.10 |
| **TTR mutation, V30M** | 21 (64%) | 11 (55%) | 0.21 |
| **Hypertension** | 3 (9.1%) | 4 (20%) | 0.41 |
| **Diabetes** | 2 (6.1%) | 0 | 0.52 |
| **Familial CVD** | 7 (21%) | 6 (30%) | 0.52 |
| **Systolic BP (mmHg)** | 130 (115-140) | 137 (130-149) | 0.09 |
| **Diastolic BP (mmHg)** | 75 (71-85) | 80 (73-85) | 0.42 |
| **Heart rate (bpm)** | 68 (60-78) | 80 (70-90)) | 0.01 |
| **Sinus rhythm** | 32 (97%) | 18 (90%) | 0.31 |
| **ECG abnormality** | 4 (12%) | 10 (50%) | 0.004 |
| **NT-proBNP (pg/ml)** | 79 (115-140) | 550 (317-1173) | <0.001 |
| **Hs-TnT (ng/L)** | 5 (3-10) | 26 (13-53) | <0.001 |
| **eGFR (ml/min)** | 91 (80-103) | 92 (76-99) | 0.60 |

***Table 1.*** Baseline characteristics — stratified by initial bone scintigraphy
Data are presented as medians with interquartile ranges. CVD: cardiovascular disease, BP: blood pressure, AF: atrial fibrillation, Hs-TNT: High sensitive troponin-T, eGFR: estimated glomerular filtration rate.

## RESULTS

| | Bonescintigraphy negative (n=33) | Bonescintigraphy positive (n=20) | P-value |
|---|---|---|---|
| **LVEF (%)** | 56 (53-63) | 58 (49-66) | 0.61 |
| **LV-GLS** | 22.1 (21.0-23.7) | 16.1 (14.2-19.5) | <0.001 |
| **LVEDD (mm)** | 46 (42-51) | 44 (39-46) | 0.06 |
| **IVST (mm)** | 9.0 (8.0-10.0) | 15.0 (13.0-17.3) | <0.001 |
| **PWT (mm)** | 8.0 (7.0-9.6) | 13.8 (10.3-14.2) | <0.001 |
| **LAVI (ml/m2)** | 28 (25-33) | 33 (27-43) | 0.02 |
| **MV E velocity (cm/s)** | 65 (53-86) | 90 (57-114) | 0.07 |
| **E/A ratio** | 1.1 (0.83-1.37) | 1.02 (0.84-1.48) | 0.78 |
| **E' lateral (cm/s)** | 13.0 (10.6-14.8) | 6.7 (5.0-9.1) | <0.001 |
| **E' septal (cm/s)** | 10.3 (7.8-12.3) | 4.8 (3.3-6.5) | <0.001 |
| **E/e' ratio** | 5.9 (5.3-7.4) | 13.0 (8.3-25.9) | <0.001 |
| **TAPSE (mm)** | 24 (23-29) | 21 (18-24) | 0.004 |
| **RV S' (cm/s)** | 14.2 (12.7-15.3) | 11.8 (10.9-13.4) | 0.04 |
| **TR peak velocity (m/s)** | 2.2 (2.0-2.4) | 2.6 (2.5-2.7) | 0.001 |

***Table 2.*** Echocardiographic parameters — stratified by initial bone scintigraphy
Data are presented as medians with interquartile ranges. CVD: cardiovascular disease, BP: blood pressure, AF: atrial fibrillation, Hs-TNT: High sensitive troponin-T, eGFR: estimated glomerular filtration rate.

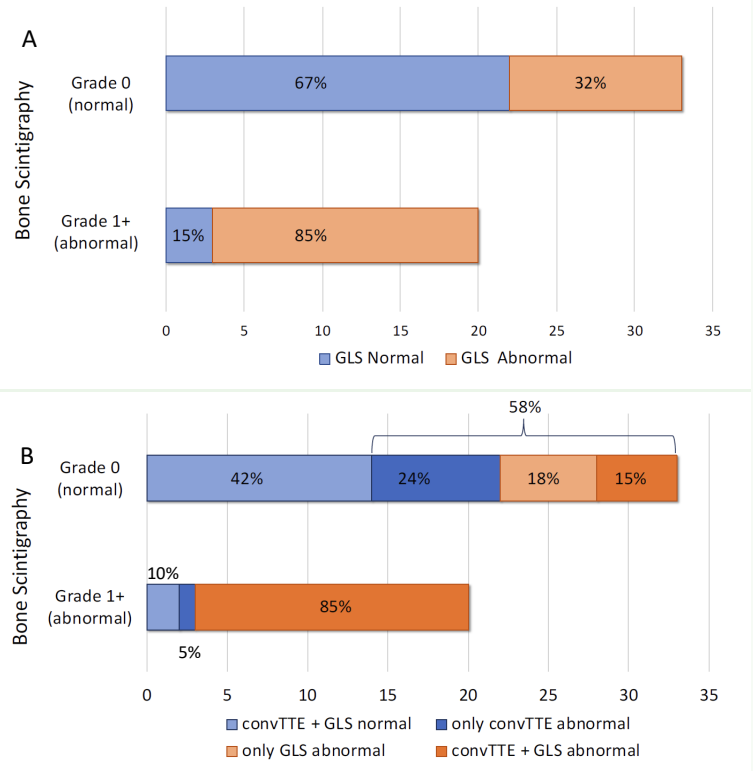


***Figure 1. A.*** Complementary value of GLS and bone scintigraphy. B. Complementary value of GLS, conventional TTR parameters and bone scintigraphy
GLS: global longitudinal strain (of the LV), convTTE: conventional transthoracic echocardiography parameters.

## CONCLUSION

LV-GLS and bonescintigraphy are complementary in screening TTR pathogenic variant carriers for cardiac involvement and should be used in conjunct. LV-GLS can play a significant role in repeated assessment in this population and our results suggest that LV-GLS may detect early disease

Corresponding author: h.l.a.nienhuis@umcg.nl