High-sensitivity cardiac troponin T to exclude cardiac involvement in *TTR* variant carriers and ATTRv amyloidosis patients

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INTRODUCTION

TTR gene variant (*TTRv*) carriers are at high risk of developing hereditary transthyretin (ATTRv) amyloidosis. Regular screening for disease onset is advised in this population[1-8]. Currently, there is no international consensus on how *TTRv* carriers should be screened[1-8]. The screening of *TTRv* carriers aims to detect onset of subclinical amyloid deposition to facilitate early initiation of disease[2]. However, maintaining a good balance between frequent screening tests required for early disease detection and minimizing unnecessary tests is essential.

OBJECTIVE

This study aims to evaluate whether the cardiac biomarkers N-terminal pro B-type natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin T (hs-cTnT) can be used to rule out ATTRv cardiomyopathy (ATTRv-CM).

METHOD

In this retrospective case-control study, 46 ATTRv-CM patients and 101 *TTRv* carriers and ATTRv amyloidosis patients without cardiomyopathy were included. Binary logistic regression models were used to assess the ability of NT-proBNP and hs-cTnT to predict the diagnosis of ATTRv-CM. An optimal cutoff for the relevant biomarker(s) was determined based on a sensitivity of ≥99% and highest possible percentage of additional tests avoided (%ATA) in the index dataset. Performance of the cutoff and clinically used cut-offs were assessed in a validation cohort of 30 ATTRv-CM patients and 34 controls. (Figure 1)

RESULTS

Hs-cTnT demonstrated the highest predictive capabilities for ATTRv-CM. The addition of NT-proBNP did not improve the predictive model. A hs-cTnT cutoff of <6 ng/L resulted in a 97% sensitivity and negative predictive value of 95% with a %ATA of 30% in the validation dataset. One ATTRv-CM patient would have been missed (Figure 2). The previously proposed hs-cTnT cutoffs of 14 ng/L and 28.6 ng/L are inadequate in excluding ATTRv-CM in *TTRv* carriers without or with amyloidosis.

CONCLUSION

- **Hs-cTnT performs better in the screening for ATTRv-CM than NT-proBNP or a combination of these biomarkers.**
- **Hs-cTnT <6 ng/L can rule out ATTRv-CM with a sensitivity of 97% and a negative predictive value of 95%.**
- **30% of diagnostic procedures can be avoided by using a two-step screening approach with hs-cTnT <6 ng/L as the first step.**

REFERENCES

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ABBREVIATIONS

TTRv = TTR gene variant, ATTRv = hereditary transthyretin, GrACE = Groningen Amyloidosis Centre of Expertise, ATTRv-CM = hereditary transthyretin amyloidosis related cardiomyopathy, CM = cardiomyopathy, hs-cTnT = high-sensitivity cardiac troponin T, NT-proBNP = N-terminal pro B-type natriuretic peptide, Sens = sensitivity, NPV = negative predictive value, FN = false negatives, Spec = specificity, PPV = positive predictive value, FP = false-positives, n ATA = number of patients in whom additional tests are avoided,%ATA = percentage of additional tests avoided.

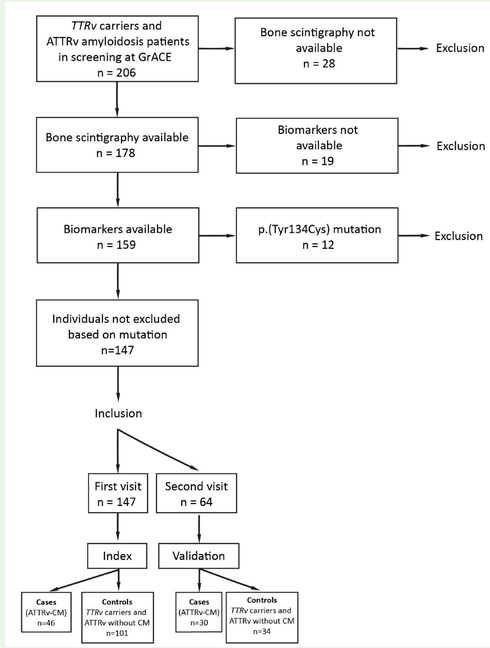

Figure 1. Flowchart of inclusion.

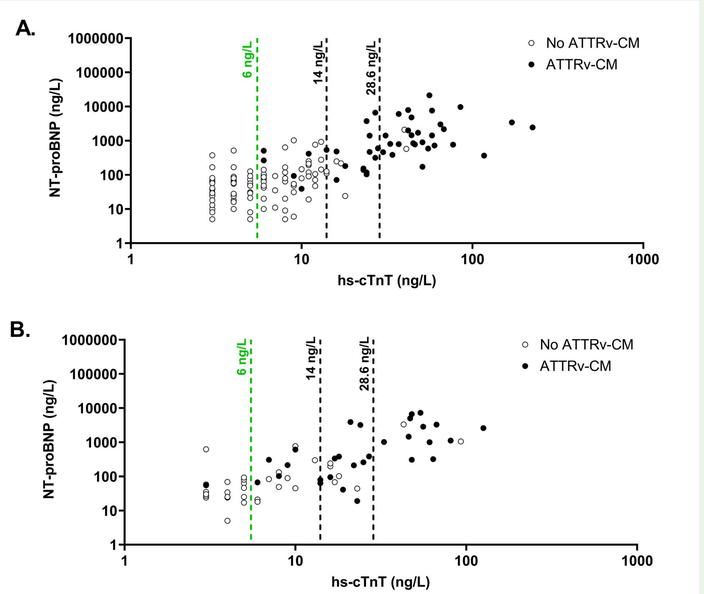

Figure 2. Diagnostic accuracy of the proposed cutoff of hs-cTnT <6ng/L and clinically used cutoffs of <14 ng/L and <28.6 ng/L to predict ATTRv-CM in the index dataset (A) and the validation dataset (B).

Table 1. Diagnostic performance of various hs-cTnT cutoffs to predict ATTRv-CM.

	Index dataset								Validation dataset							
Hs-cTnT cutoff	*Sens*	*NPV*	*FN*	*Spec*	*PPV*	*FP*	*n ATA*	*%ATA*	*Sens*	*NPV*	*FN*	*Spec*	*PPV*	*FP*	*n ATA*	*%ATA*
<6 ng/L	100%	100%	0	50%	48%	50	51	35%	97%	95%	1	53%	64%	16	19	30%
<14 ng/L	89%	95%	5	93%	85%	7	99	68%	80%	82%	6	79%	77%	7	33	52%
<28.6 ng/L	59%	84%	19	98%	93%	2	118	80%	40%	64%	18	94%	86%	2	50	78%

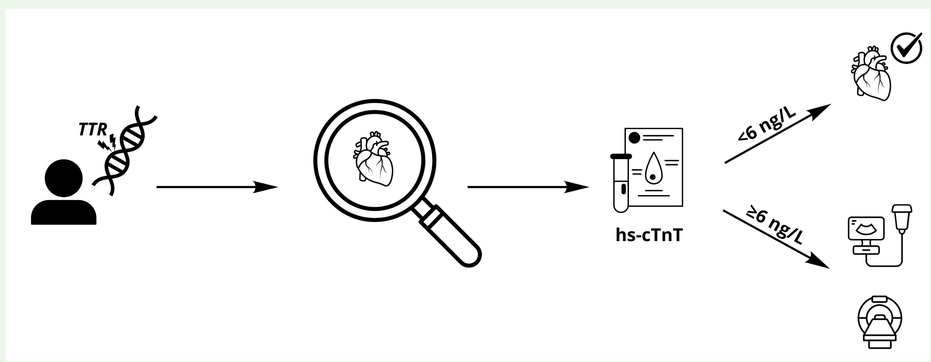

Figure 3. Conclusion of the study. A hs-cTnT cutoff of <6 ng/L can be used in a two-step screening approach for cardiac onset of disease in *TTRv* carriers.

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