Fast-tracking Transthyretin cardiac amyloidosis detection from 12-lead ECG: Validating the deep learning model Willem

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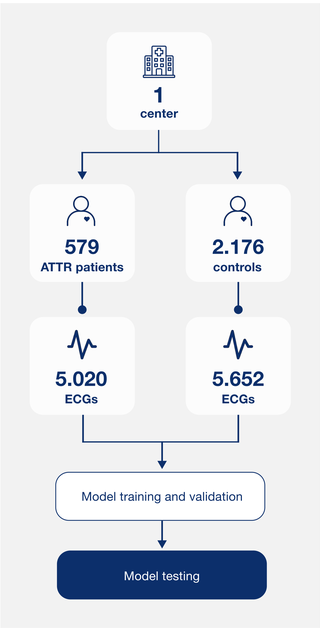
Purpose

Misdiagnosis and delay in diagnosis are frequent in patients with **transthyretin cardiac amyloidosis (ATTR-CA)**. Despite recent improvements, ATTR-CA may take up to ~4 years to be diagnosed *(1)*. **Artificial Intelligence (AI) solutions** applied to the simple and widely available 12-lead electrocardiogram (ECG) **have the potential to improve ATTR-CA detection** for earlier and better patient management. We sought to develop and validate a deep-learning model based on the Willem AI platform to discriminate ATTR-CA patients and controls.

Methods



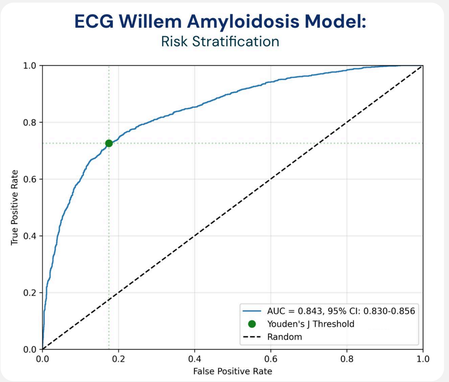
- CONCERTO is a **single-center**, **retrospective** study conducted at **Hospital Universitario Puerta de Hierro, Madrid**, expert center in ATTR-CA.
- All subjects undergoing 3,3-diphosphono-1,2- propanodicarboxylic acid (DPD) scintigraphy for ATTR-CA assessment from 2009 to 2023 were included.
- Signal normalization, class weighting, quality and temporal filtering methods were applied, yielding a total of **10,672 ECGs** for model training and testing.
  - **5,020 ECGs from 579 ATTR-CA patients, and 5,652 ECGs from 2176 controls**.
  - **Temporal thresholds** were defined to keep ECGs **from 2 years prior to diagnosis** for ATTR-CA patients, **and up to 6 months after negative diagnosis** for controls.
- The study data was split in training, validation and testing datasets. All results are computed from the testing dataset.
- The final model selected was a **Time-Slicing Convolutional Neural Network**.
- The CONCERTO Study is funded by **AstraZeneca**.

References

1. Rozenbaum MH, Large S, Bhambri R, et al. Cardiol Ther. 2021;10(1):141-159

Results

The Area Under the Receiver Operating Characteristic curve (AUC) for correct ATTR-CA classification by Willem was **0.84 (CI 95%: 0.83–0.86)**. Subgroup performance analysis showed consistent performance even in populations with similar symptoms and comorbidities, such as patients with **Heart Failure with Reduced Ejection Fraction** (0.86 AUC), with **Carpal Tunnel Syndrome** (0.91 AUC), and in **asymptomatic** patients (0.81 AUC).



0.84

Area under the Curve (AUC)

ATTR Amyloidosis	No ATTR Amyloidosis
1.185 True positives (TP)	**322** False positives (FP)
448 False negatives (FN)	**1.521** True negatives (TN)
Sensitivity = 72.6%	**Specificity = 82.5%**

Group	Positive / Total ECGs	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	OR (95% CI)
All	1633/3476	0.843 (0.830 - 0.856)	72.6% (70.4 - 74.7)	82.5% (80.7 - 84.2)	78.6% (76.5 - 80.6)	77.2% (75.3 - 79.0)	12.47 (10.61-14.66)
HFpEF	1062/1888	0.830 (0.810 - 0.851)	75.0% (72.4 - 77.6)	79.4% (76.5 - 82.0)	82.4% (79.9 - 84.7)	71.2% (68.2 - 74.1)	11.57 (9.30-14.39)
HFrEF	499/739	0.857 (0.836 - 0.870)	71.9% (67.8 - 75.7)	84.2% (79.0 - 88.2)	90.4% (87.1 - 92.9)	59.1% (53.8 - 64.1)	13.46 (9.06-20.00)
LVH	1611/2577	0.833 (0.819 - 0.852)	72.3% (70.1 - 74.4)	80.8% (78.2 - 83.2)	86.3% (84.4 - 88.0)	63.7% (60.9 - 66.3)	11.00 (9.06-13.35)
Carpal Tunnel Syndrome	645/701	0.913 (0.895 - 0.931)	74.3% (70.8 - 77.5)	94.6% (85.4 - 98.2)	99.4% (98.2 - 99.8)	24.2% (19.0 - 30.3)	44.02 (14.72-131.67)
Asymptomatic	179/431	0.807 (0.781 - 0.822)	65.4% (58.1 - 71.9)	84.5% (79.5 - 88.5)	75.0% (67.7 - 81.1)	77.5% (72.2 - 82.0)	10.16 (6.43-16.06)

Conclusion

- Willem AI platform identifies ATTR-CA in a large cohort of subjects suspected of ATTR-CA and assessed for diagnosis in an expert center. Controls are not healthy volunteers, and thus this is a hard-to-discriminate population with higher prevalence compared to the general population.
- Future work includes external validation in an ongoing multicentric study to further evaluate model generalizability and capacity for early identification.