Echocardiographic screening for cardiac amyloidosis using artificial intelligence: A multi-site study for algorithm training and external validation

Basic & Translational Late-Breaking Science

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Background

Cardiac amyloid associated with high morbidity and mortality

ATTR more common than previously thought

Variable presentation and morphologic expression

Transthyretin stabilizers most effective in early disease

- Accurate diagnosis

Increasing complexity of our patients and their Doppler echocardiograms

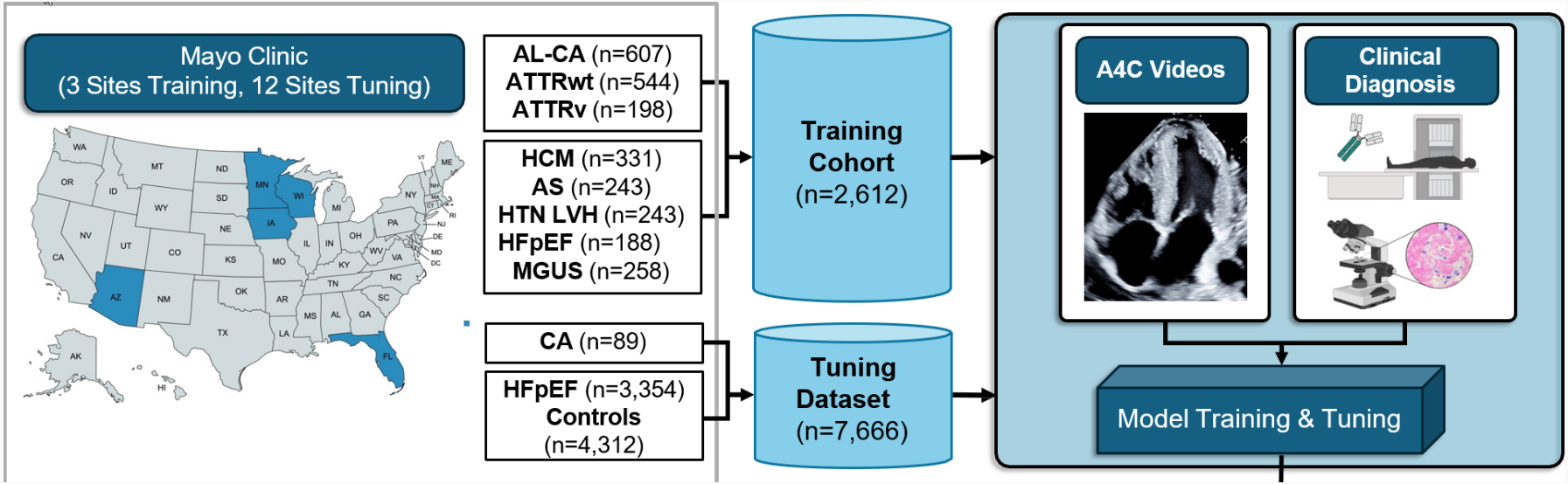
- Potential for missed diagnosis

Aims

- To develop an automated screening tool for cardiac amyloidosis (CA) using a single echocardiographic videoclip of the apical four-chamber view
- Distinguish CA from phenotypically similar hearts without CA
- Multi-site external validation

Training and tuning

- 3D convolutional neural network; apical 4 ch videoclips; videoclips divided into sequences of 30 frames
- Diagnosis of: AL cardiac amyloidosis, ATTR cardiac amyloidosis, hypertrophic cardiomyopathy (HCM), aortic valve stenosis, hypertension with increased LVMI, HFpEF, multiple myeloma, monoclonal gammopathy
- Patient selection stratified on age, sex, race and history of rhythm abnormalities



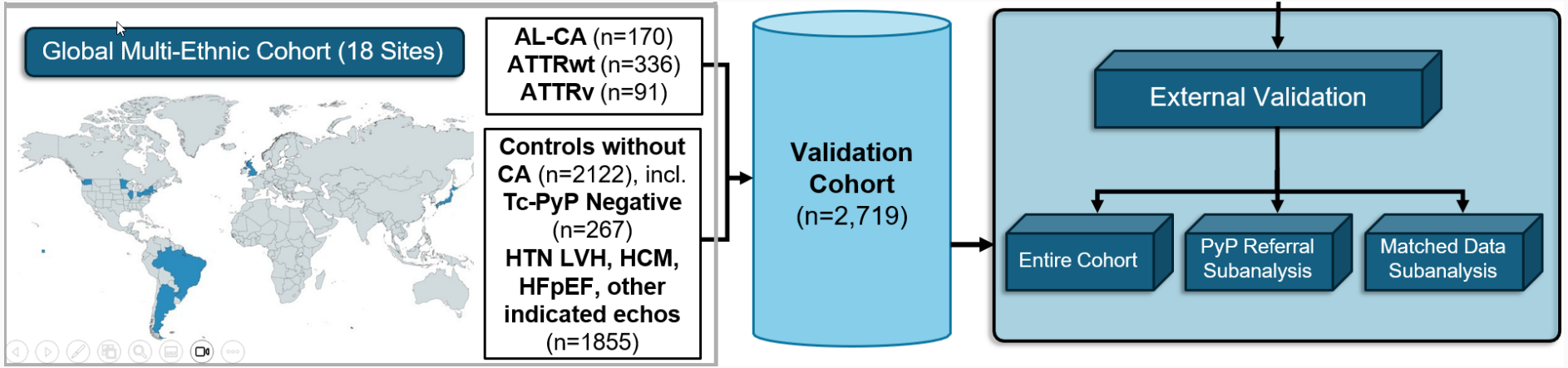
External validation

Global multi-ethnic cohort

597 with CA (55% ATTRwt, 28% AL, 15% ATTRv)

2122 controls

Testing in entire cohort, patients referred for PYP, and age, sex, and wall thickness matched subgroup



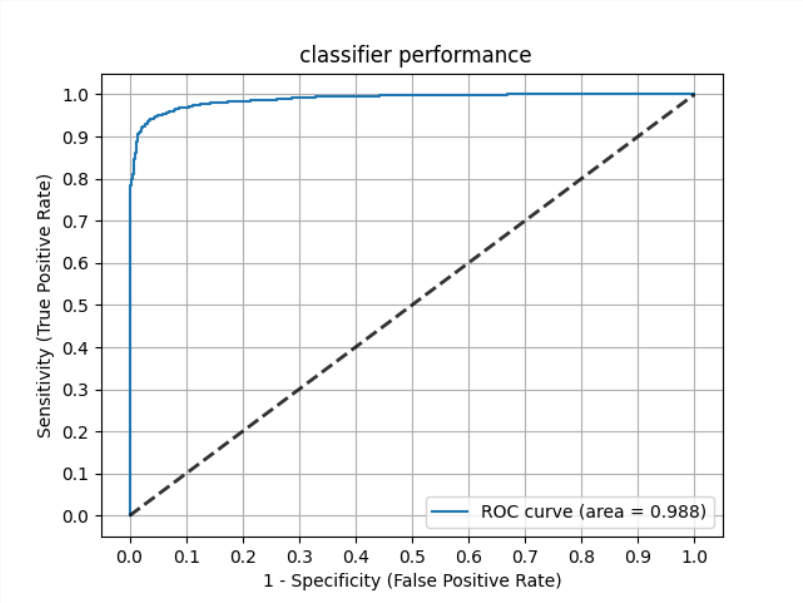
Clinical and echo features of training, tuning & external validation cohorts

Variable*	Training N=2,612	Tuning N=7,666	External Validation N=2,719
Age, years	70 (61, 77)	66 (54, 76)	71 (60, 80)
Body mass index, kg/m2	27.6 (24.6, 31.5)	28.2 (22.4, 32.9)	27.6 (24.2, 32.0)
Male	1916 (73.4)	3562 (46.5)	1524 (56.6)
Black	328 (13.1)	75 (1.3)	522 (21.5)
Other race	160 (6.4)	266 (4.6)	393 (16.2)
White	2007 (80.4)	5422 (94.1)	1512 (62.3)
ATTRwt CA	544 (40.3)	24 (27.0)	329 (55.1)
ATTRv CA	198 (14.7)	5 (5.6)	89 (14.9)
AL CA	607 (45.0)	60 (67.4)	166 (27.8)
Hypertension	1068 (40.9)	4378 (57.2)	1618 (70.9)
Diabetes mellitus	507 (19.4)	1984 (25.9)	694 (30.2)
LV ejection fraction	60 (49, 65)	63 (59, 66)	61 (55, 66)
Interventricular septal thickness, mm	14 (12, 17)	10 (9, 12)	13 (10, 15)
LV posterior wall thickness, mm	13 (11, 15)	10 (9, 11)	11 (10, 14)
LV mass index, g/m2	127.0 (103.0, 156.0)	90.0 (76.0, 108.0)	113.0 (90.0, 141.7)

* Median (IQR) or number (%)

Results

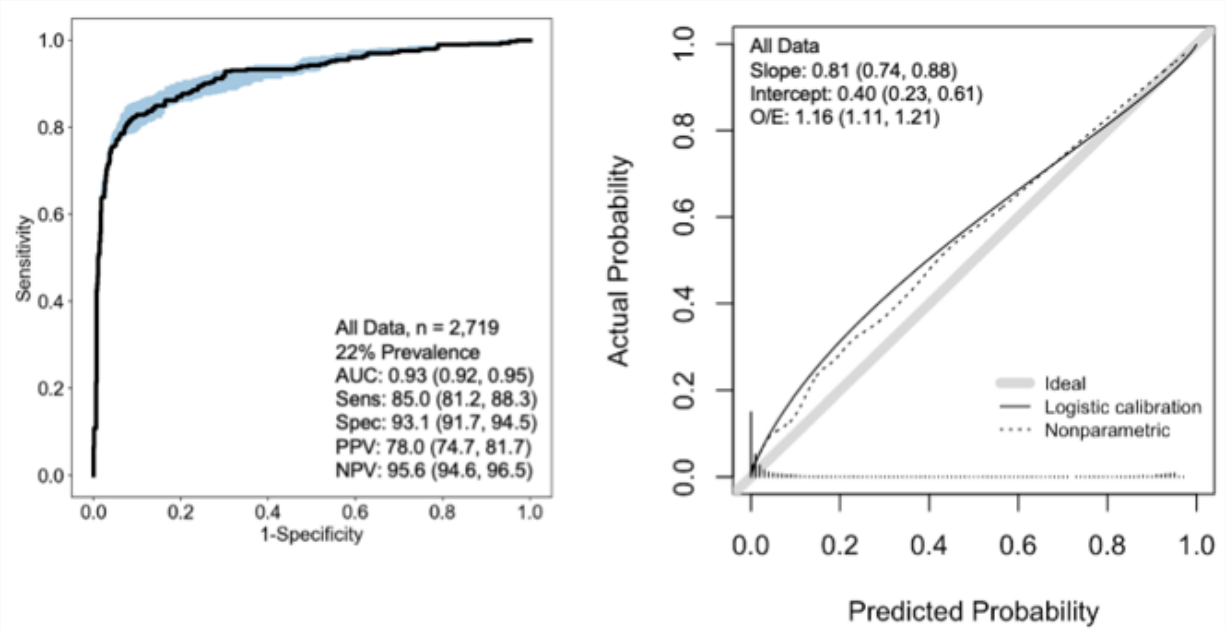
Training and Tuning Performance



- Performance on tuning data, n= 7666; 3354 with HFpEF, CA in 89 (1.2%)
  - AUC: 0.928
  - Sensitivity: 81.4%
  - Specificity: 92.8%
  - PPV: 13.2%
  - NPV: 99.7%

External validation in 2,719 patients

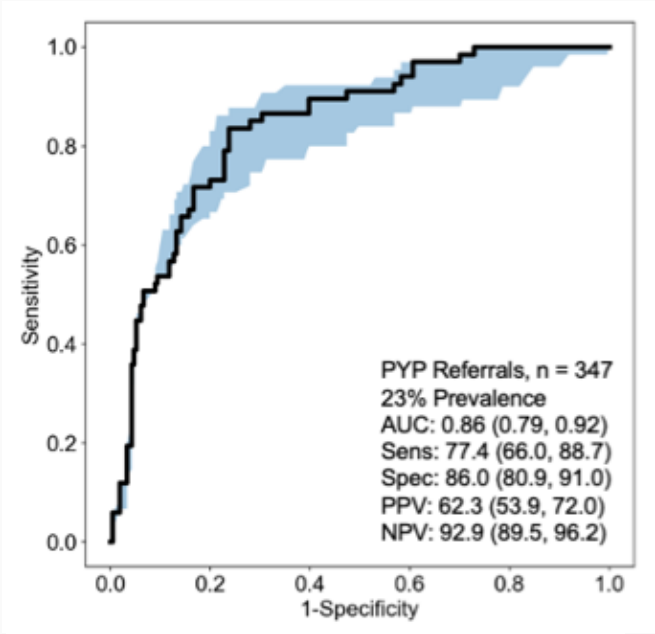
Predictions in 2,356 (86.6%); uncertain in 363 (13.4%)

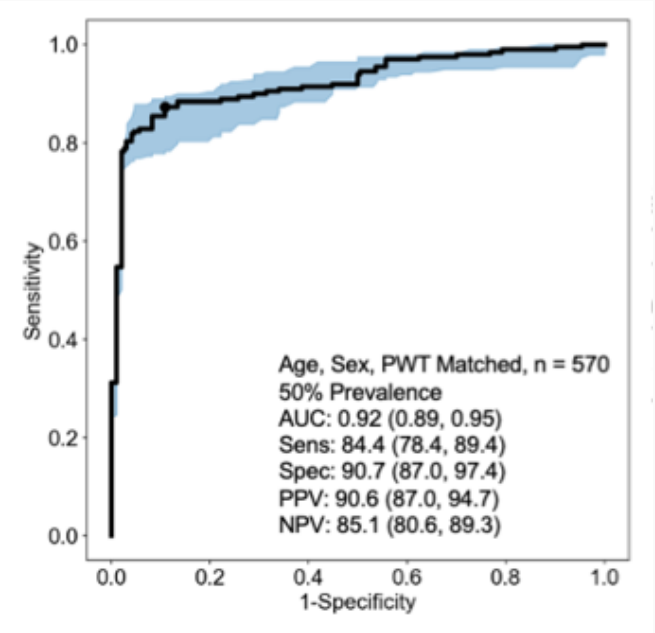


AUC 0.93, sens 85%, spec 93%, PPV 78%, NPV 96%

Model performance consistent: sensitivity 84% AL, 85% ATTRwt, 86% ATTRv

PYP and age, sex, wall thickness matched subgroups





23% CA; uncertain prediction in 16.7%

AUC 0.86

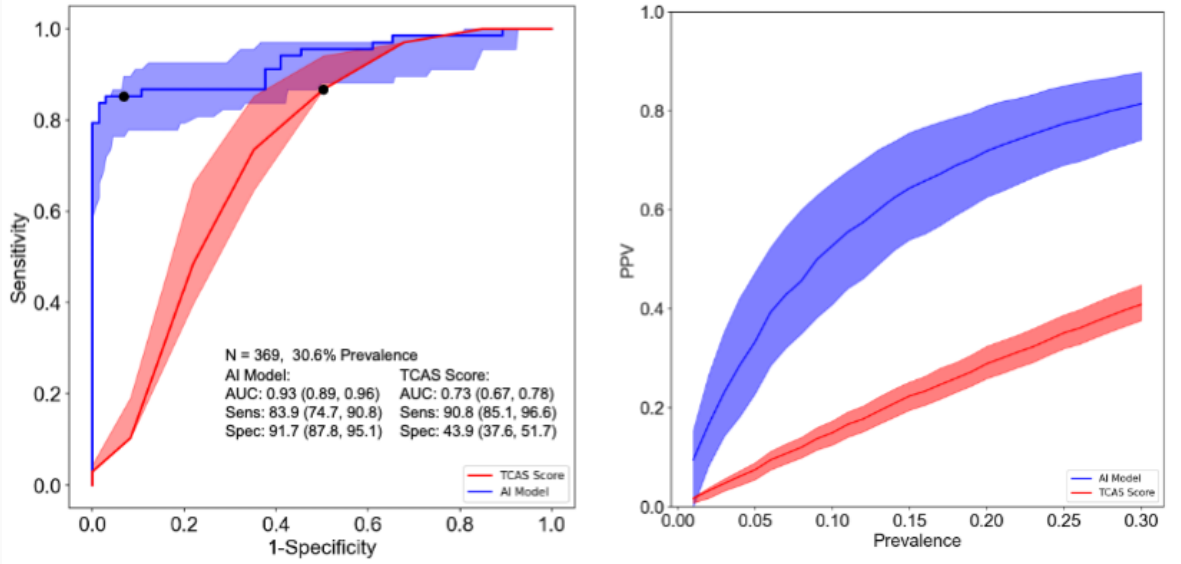
50% CA; uncertain prediction in 13.5%

AUC 0.92

Sensitivity: consistent performance of AI model across various strata of age, sex, race, comorbidities, LVEF, and wall thickness

Comparison to Transthyretin Cardiac Amyloid Score*

- 369 ATTR-CA and control patients ≥60 years of age with clinical HFpEF and interventricular septum or PWT ≥ 12mm and complete data
- Score ≥ 6 considered positive for ATTR-CA



* TCAS: Validated risk model for ATTR-CA detection using age, sex, HTN, PWT, RWT

Summary

- AI screening model for CA using apical 4 chamber videoclip
- In the 86.6% with certain predictions, model discrimination and classification were high
  - AUC 0.93 in all, 0.86 PYP, and 0.92 matched, respectively
  - NPV 96%, 93%, and 85%, respectively
- Performance consistent among CA types (sensitivity 84%, 85%, 86% for AL, ATTRwt, ATTRv, respectively
- Outperformed TCAS in pts ≥ 60 yrs with HFpEF and increased LV wall thickness (AUC 0.93 vs 0.73)
- AI screening model may improve echo detection of CA, facilitating early access to therapy