Multimodal Artificial Intelligence for Cardiac Amyloidosis Diagnosis:

Integrating Echocardiography with Clinical and Laboratory Data for Improved Detection

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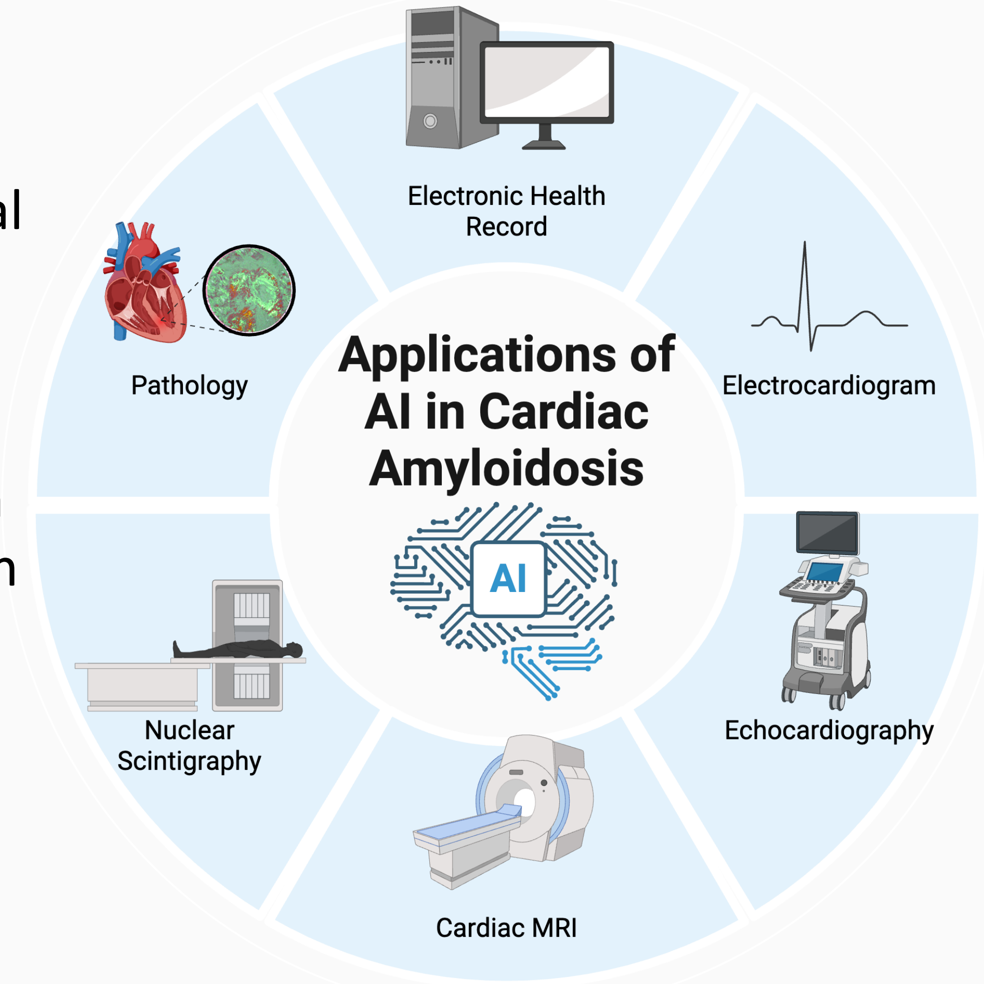
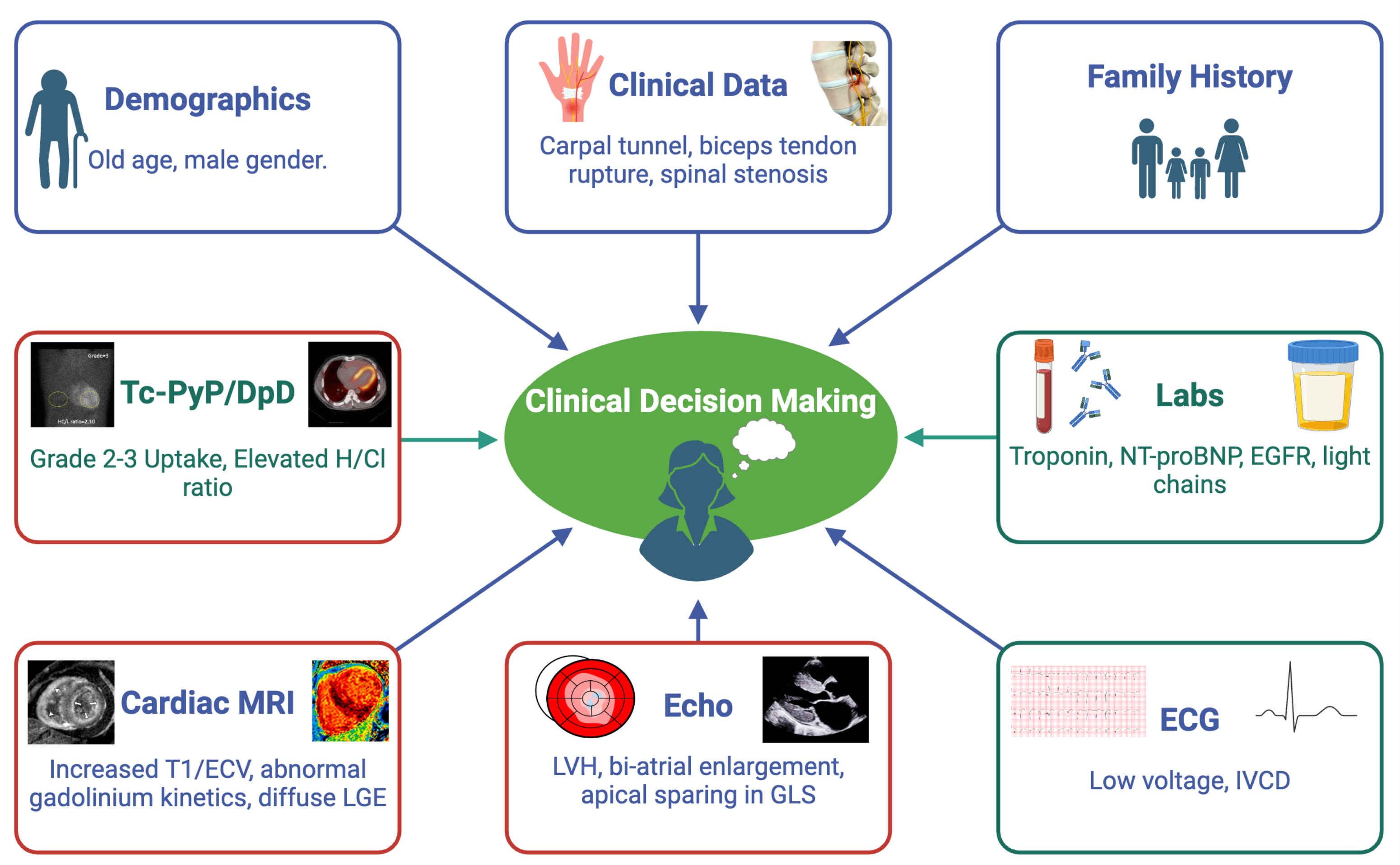
Disclosures

- Advisory boards: Alnylam, BridgeBio, Pfizer
- Consulting: GE Healthcare
- Study received with in kind support from Us2.AI

Background

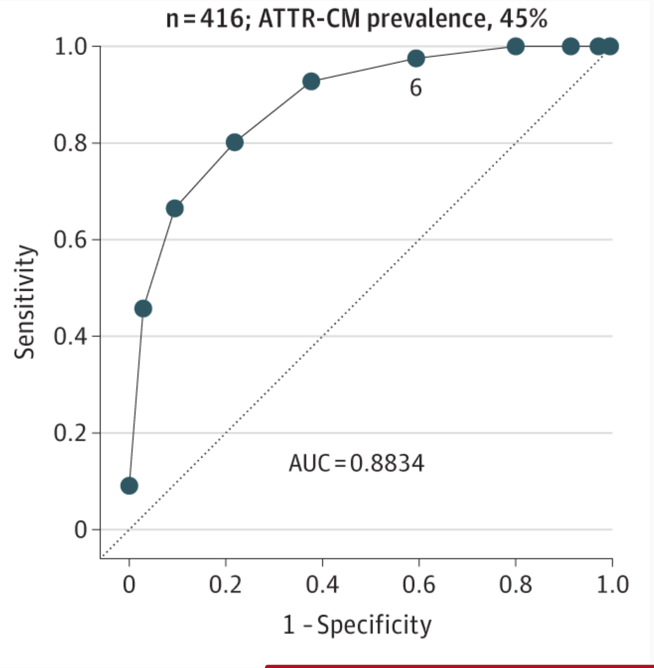
- AI algorithms have shown potential to improve cardiac amyloid detection.
- Ioannou, Fontana *et al* previously developed a deep learning pattern recognition model for CA detection from a single apical 4-chamber view (**AI-PRM**).
- Yet, a limitation of these models has been reliance on single modalities.

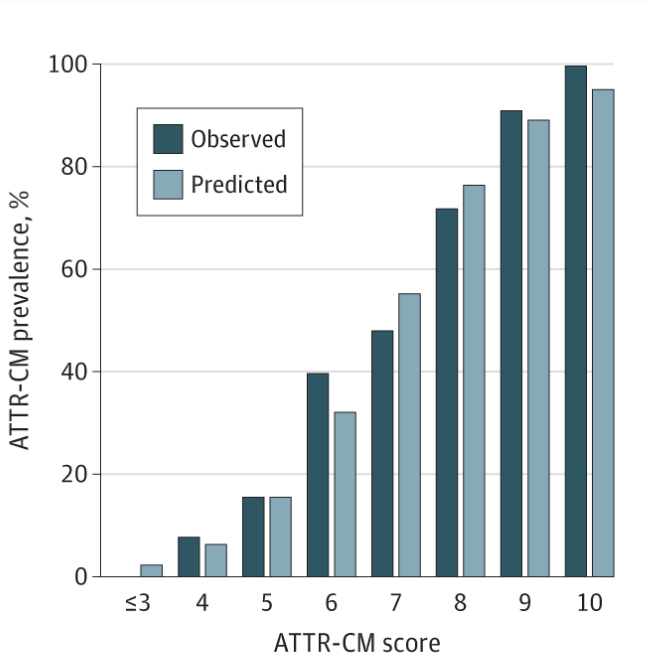




Demographics
Old age, male gender.
Clinical Data
Carpal tunnel, biceps tendon rupture, spinal stenosis
Family History
Tc-PyP/DpD
Grade 2-3 Uptake, Elevated H/Cl ratio
Clinical Decision Making
Labs
Troponin, NT-proBNP, EGFR, light chains
Cardiac MRI
Increased T1/ECV, abnormal gadolinium kinetics, diffuse LGE
Echo
LVH, bi-atrial enlargement, apical sparing in GLS
ECG
Low voltage, IVCD

Background





Input Features: Age, Male sex, hypertension, relative wall thickness, increased wall thickness, and LVEF

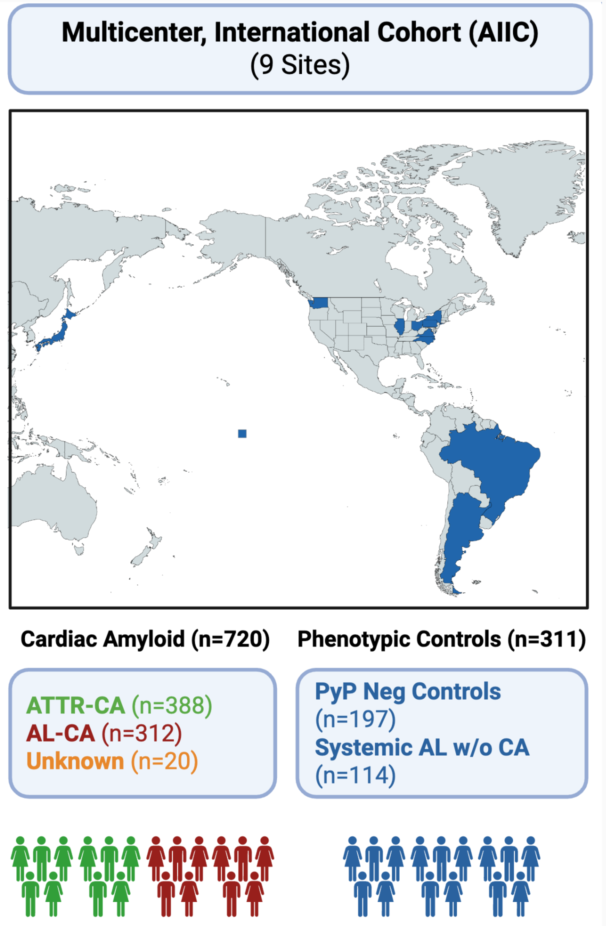
Davies *et al.* JAMA Cardiol. 2022

Hypothesis

- We hypothesized that a model (**AI-ECM**) integrating clinical, lab, and echo parameters into the AI echo model would similarly augment performance compared to **AI-PRM** alone

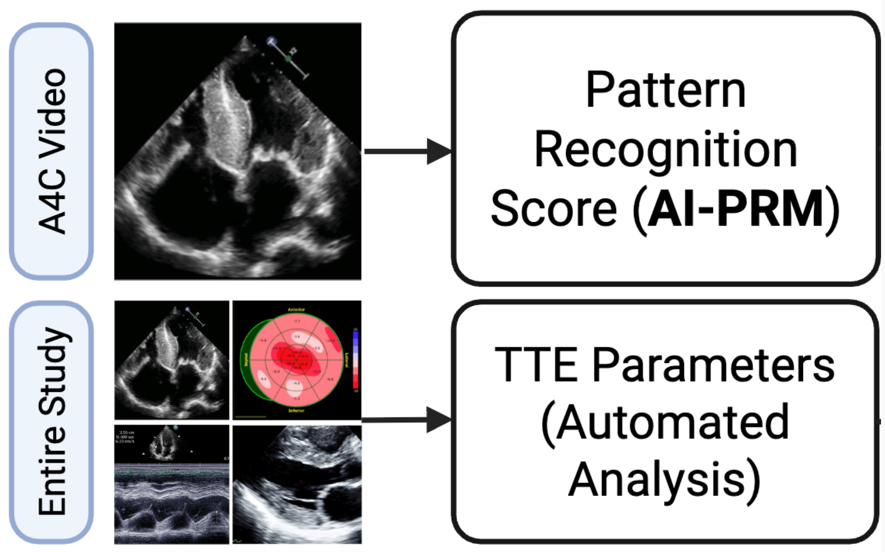
Methods

- Amyloidosis International Imaging Collaborative Study.
- 1,031 Patients
  - 720 Cardiac Amyloidosis
  - 311 Phenotypic Controls



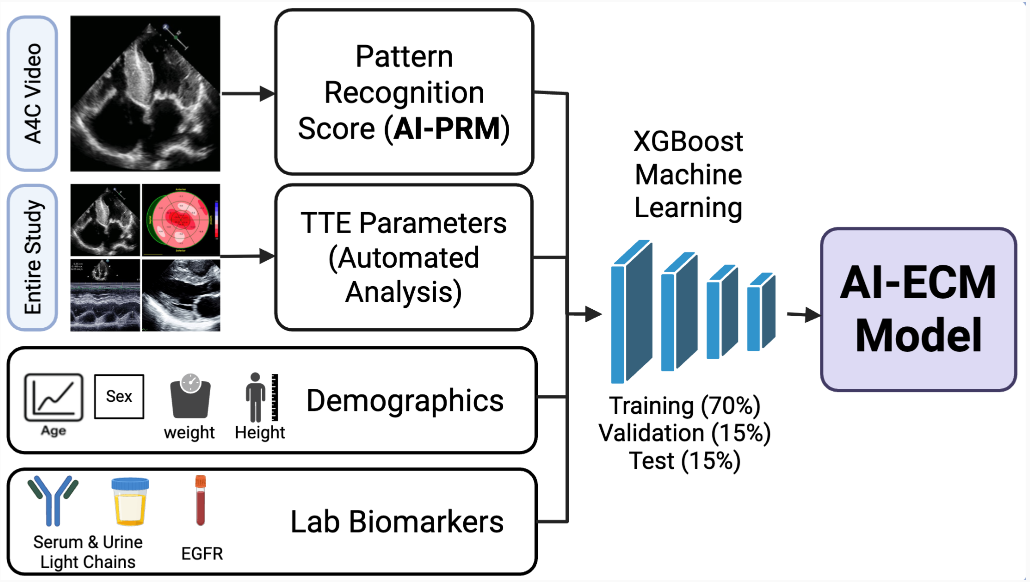
Methods

- A4C automatically detected and analyzed by deep learning model (**AI-PRM**).
- Echocardiographic Parameters automatically quantified using commercially available AI platform (Us2.AI):
  - Septal apical-to-basal ratio (SAB)
  - Relative Wall Thickness (RWT)
  - RV S'
  - Doppler E/e' Ratio
  - TAPSE



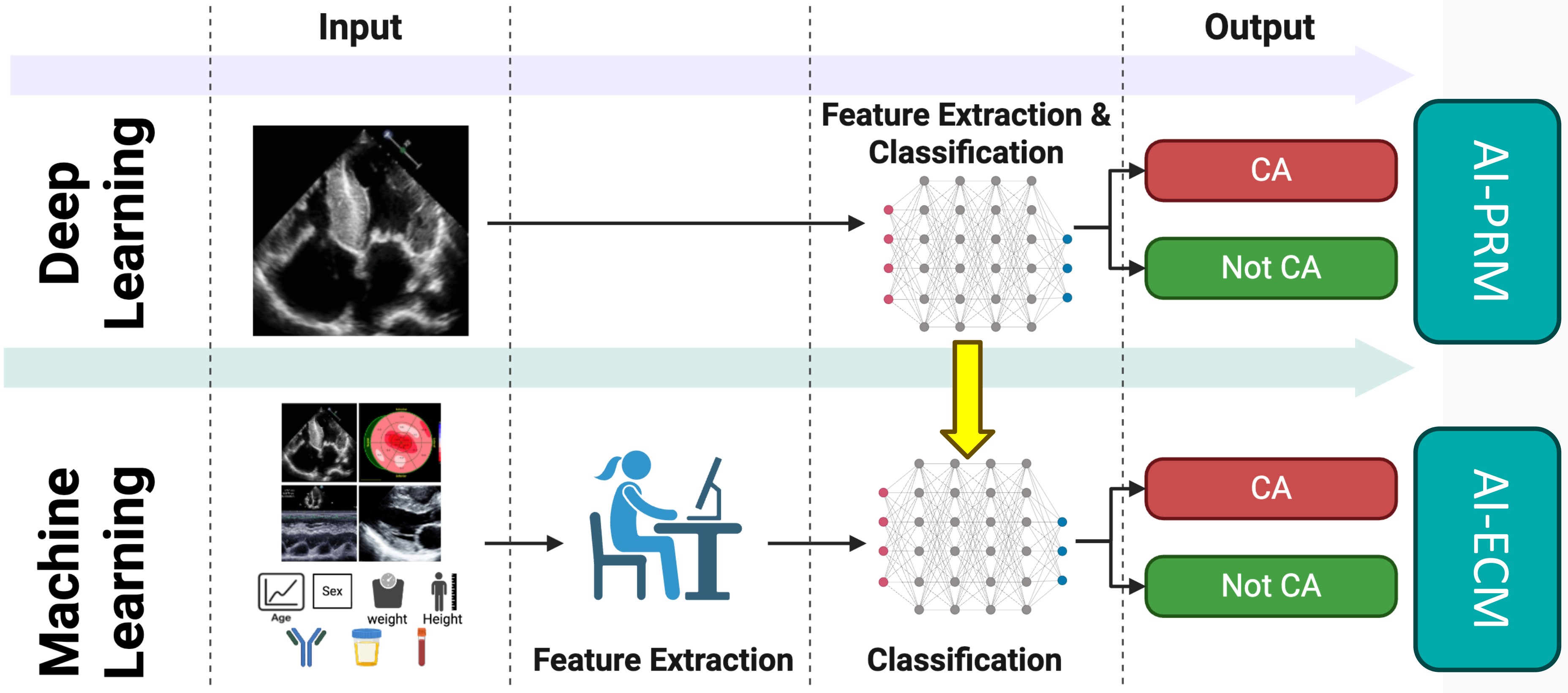
Methods

- Dataset split into training, validation, and test (70%/15%/15%) datasets.
- AI Combined Echo Clinical Model (**AI-ECM**) trained using XGBoost model* in step-wise manner.
- Hyperparameters optimized via 5-fold cross-validation in training and validation datasets



Input Features: AI-PRM, RWT, SAB, age, gender, height, weight, BMI, EGFR, light chain biomarkers

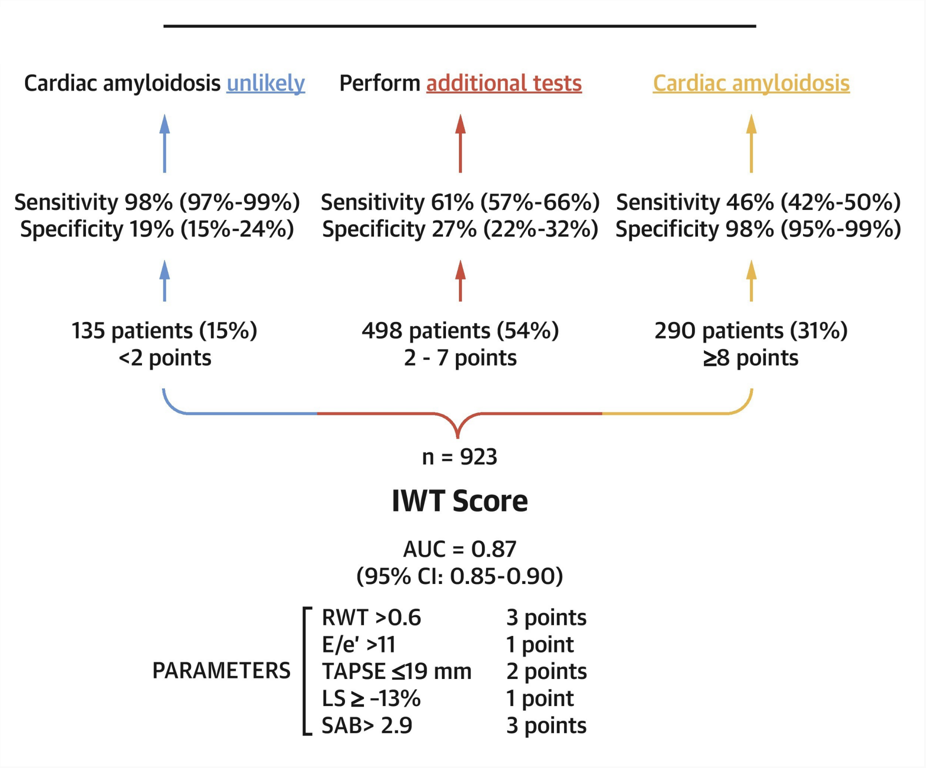
*Supervised, machine learning model utilizing sequential decision trees to integrate multimodal data sources. Data sources are weighted based on their respective learning contributions.


Input
Output
Deep Learning
Feature Extraction & Classification
CA
Not CA
AI-PRM
Machine Learning
Age
Sex
weight
Height
Feature Extraction
Classification
CA
Not CA
AI-ECM

Methods

- Model accuracy evaluated using AUC, sensitivity, specificity, and accuracy.
- AUC of **AI-ECM** compared to **AI-PRM** and conventional **IWT** score using DeLong method.
- Sub-analysis comparing AI-ECM to IWT and AL score performed in relevant subpopulations.

IWT Score

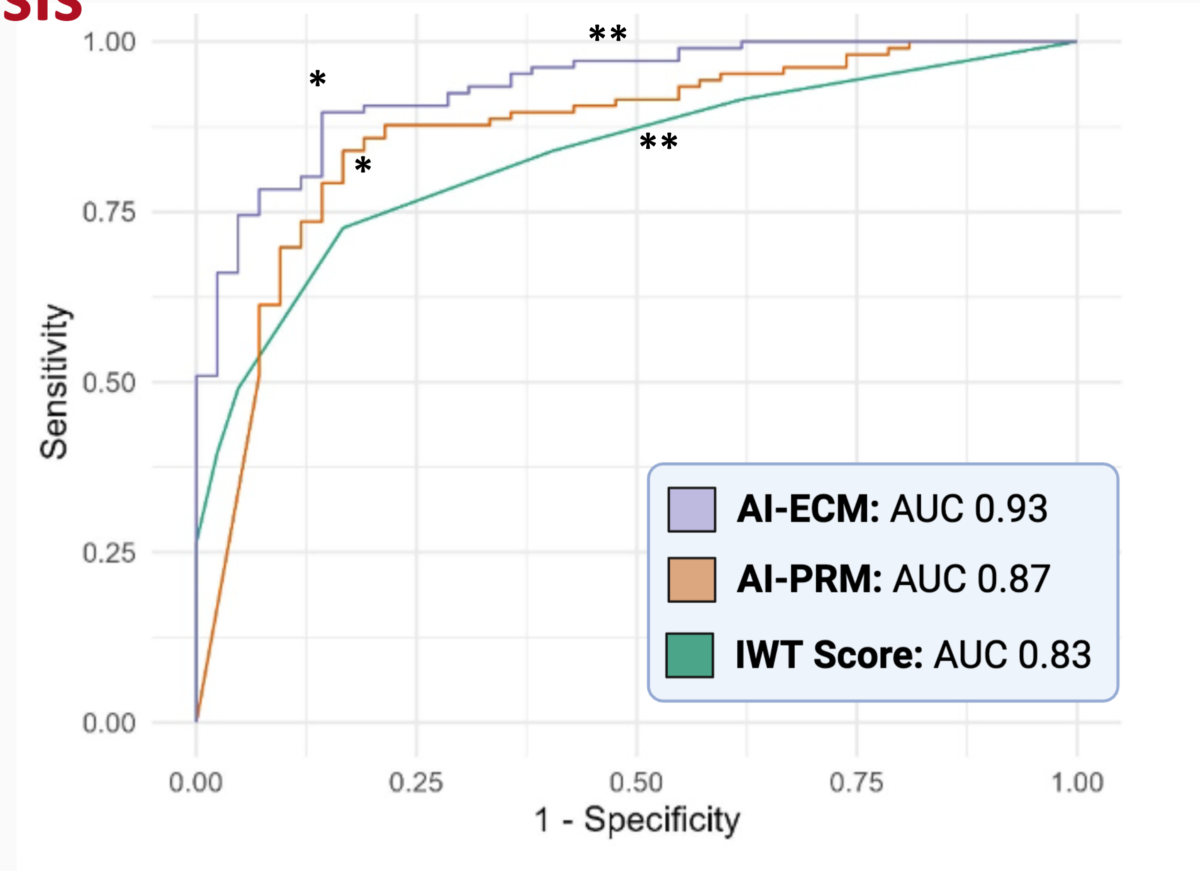


Boldrini *at al.* J Am Coll Cardiol Img. 2020.

Study Population

Clinical characteristic	CA Cases (N=720)	Controls (N=311)
Age, years, mean ± SD	70.9 ± 11.0	69.3 ± 13.8
Weight, kg, mean ± SD	78.4 ± 19.8	82.5 ± 22.0
Height, cm, mean ± SD	170.7 ± 11.6	169.1 ± 11.4
BMI, kg/m2, mean ± SD	26.8 ± 6.1	28.9 ± 7.6
Gender, male, n (%)	531 (73.8%)	179 (57.6%)
Ethnicity, n (%)		
- Black	211 (29.3%)	102 (32.8%)
- Hispanic or Latino	118 (16.4%)	19 (6.1%)
- White	279 (38.8%)	162 (52.1%)
- Others/ Not reported	112 (15.6%)	28 (9.0%)
NT-proBNP, pg/ml, median (IQR)	2492.0 (710.5-6542.3)	812.7 (182.0-3804.0)
BNP, pg/ml, median (IQR)	514.0 (240.0-931.0)	87.0 (41.0-280.9)
Creatinine, mg/dL, median (IQR)	1.22 (0.95-1.69)	1.14 (0.88-1.82)
eGFR, mL/min/1.73m2, median (IQR)	56.3 (36.9-72.0)	59.0 (34.0-80.0)
RWT, mean ± SD	0.7 ± 0.2	0.5 ± 0.1
TAPSE, mm, mean ± SD	17.8 ± 4.9	21.8 ± 5.2
E/e' Mean, mean ± SD	17.0 ± 6.5	12.6 ± 6.0
A4C LV GLS, %, mean ± SD	-13.9 ± 5.1	-16.2 ± 5.1
A4C LV SAB, mean ± SD	2.2 ± 1.1	1.5 ± 0.7
LV SAB, mean ± SD	2.2 ± 1.0	1.4 ± 0.5

ROC Analysis



*: p=0.007 (AI-ECM vs AI-PRM)

**: p=0004 (AI-ECM vs IWT Score)

Feature Importance

Feature	Feature Importance
AI-PRM	10.99
RWT	3.35
Abnormal Urine Monoclonal Protein Present (Immunofixation)	2.13
Gender	2.00
Abnormal Serum Monoclonal Protein Present (Immunofixation)	1.83
EGFR	1.44
LV Apex-to-Basal Strain Ratio	1.41
Serum Kappa	1.28
Age	1.15
Serum Lambda	1.15
Weight	1.12
Height	1.06
BMI	1.02
Creatinine	0.94

Model Comparison

Model	Accuracy (%)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	AUC (95% CI)	Yield (%)
IWT Score	56%	40%	98%	0.83 (0.76 - 0.90)	100%
AI-PRM Score	81%	77%	90%	0.87 (0.80-0.94)	92%
AI-PRM+TTE Parameters	84%	83%	86%	0.89 (0.84 - 0.94)	100%
AI-PRM+TTE+Clin	82%	81%	86%	0.90 (0.85-0.95)	100%
AI-ECM	89%	90%	86%	0.94 (0.90 - 0.97)	100%

Subgroup Analysis

ATTR Subgroup

(ATTR-CA vs PyP-negative Controls)

	Accuracy (%)	Sens (%)	Spec (%)	AUC	Yield (%)
IWT Score	61%	46%	96%	0.84	100%
AI-PRM	84%	82%	88%	0.86	98%
AI-ECM	90%	91%	88%	0.94	100%

AL Subgroup

(AL-CA vs AL controls without CA)

	Accuracy (%)	Sens (%)	Spec (%)	AUC	Yield (%)
AL Score	51%	34%	100%	0.86	100%
AI-PRM	76%	68%	93%	0.89	84%
AI-ECM	86%	87%	81%	0.91	100%

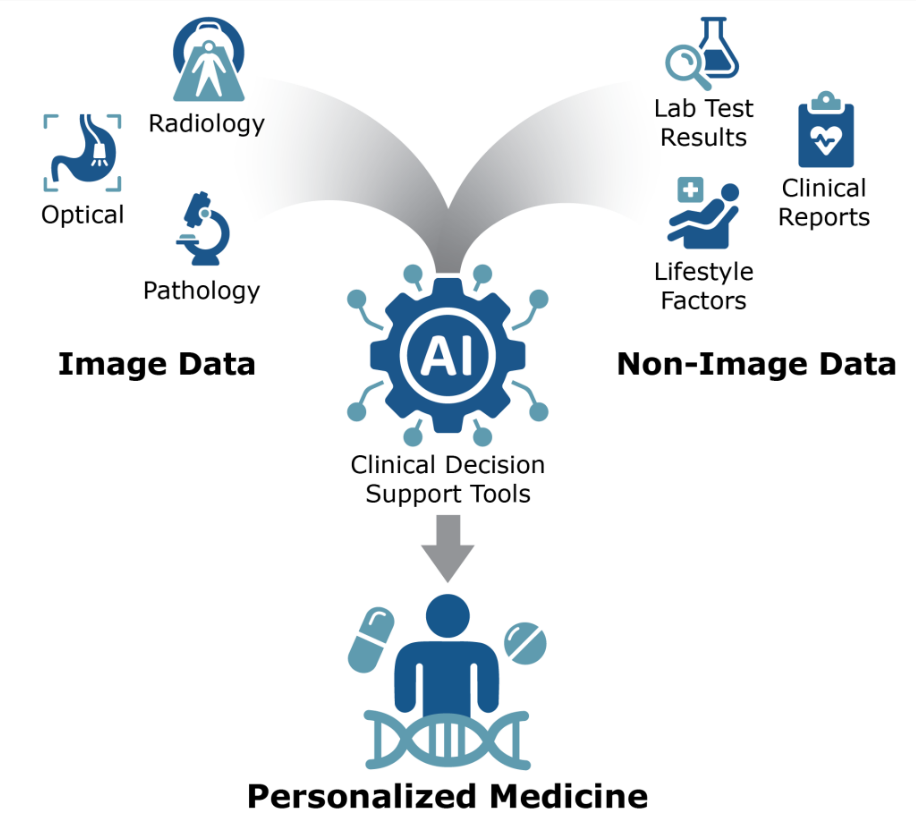
Limitations

- External validation is needed.
- Prevalence does not mimic real world screening.
- Did not incorporate traditional red flag clinical parameters.
- Performance in early-stage disease is unknown.

Conclusions

- The **AI-ECM** outperformed **AI-PRM** and **IWT** scores for CA detection in a large, multi-ethnic international dataset without the use of indeterminate classifications.
- Although more work is needed prior to deployment in clinical practice, the integration of clinical, lab, and echo biomarkers has the potential to augment AI-based echocardiographic detection of CA.

Potential Future Implications



https://commonfund.nih.gov/primed-ai

Thank You

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WEXNER MEDICAL CENTER

産業医科大学
University of Occupational and Environmental Health, Japan

Endeavor Health



In Memorium to Roberto Lang

Model From Clinical Perspective

Model	Accuracy (%)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	AUC (95% CI)	Yield (%)
IWT Score	56%	40%	98%	0.83 (0.76 - 0.90)	100%
AI-PRM Score	81%	77%	90%	0.87 (0.80-0.94)	92%
Clin Only	47%	31%	86%	0.67 (0.57-0.77)	92%
Clin + Lab	71%	65%	86%	0.85 (0.77-0.92)	100%
Clin + Lab + TTE Parameters	81%	79%	86%	0.91 (0.86-0.95)	100%
AI-ECM	89%	90%	86%	0.93 (0.89-0.97)	100%

Collinearity Between Parameters

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