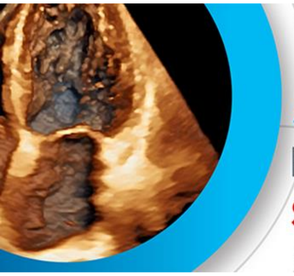

American Society of Echocardiography
ASE2025
Harmonizing Hearts
SEPTEMBER 5-7, 2025
#ASE2025 ASEScientificSessions.org

Echocardiography and Artificial Intelligence in the Cardiac Amyloidosis Referral Pathway

EchoGo™

A. P. AKERMAN [1], W. HAWKES [1], J. A. SLIVNICK [2], G. WOODWARD [1], C. G. SCOTT [3], M. S. MAURER [4], S. CUDDY [5], J. B. STROM [6], J. O'DRISCOLL [7], R. M. LANG [2], P. A. PELLIKKA [3], R. UPTON [1]

[1] Ultromics Ltd, Oxford, United Kingdom; [2] University of Chicago, Chicago, IL; [3] Mayo Clinic, Rochester, MN; [4] Columbia University, New York, NY; [5] Brigham and Women's Hospital, Boston, MA; [6] Beth Israel Deaconess Medical Centre, Boston, MA; [7] University of Leicester, Leicester, United Kingdom

PURPOSE / OBJECTIVES

Echocardiography is critical in identification of patients at risk of cardiac amyloidosis (CA). Low cost and high accessibility ensure that patients can be screened in high volumes, and appropriately referred for confirmatory testing, monitoring, and treatment. However, specific data and clear recommendations on how exactly such tools could integrate into clinical practice, and the impact for patient management is required. This study therefore aimed to aimed to examine how echocardiography and artificial intelligence (AI) may be utilized in the CA diagnostic pathway.

MATERIAL & METHODS

Retrospective, multi-site data comprising 4255 patients without CA, and 560 patients with CA was collected for external validation of an AI model for screening patients for CA[1] (AI-CA; EchoGo Amyloidosis, Ultromics Ltd). Using this data, clinical decision making was modelled (decision curve analysis) under two real-world scenarios; (1) patients considered high risk for CA (e.g., heart failure) have an echocardiogram to assess who should have a more in-depth "second read" by a clinician; and (2) patients who have already been pre-screened for key selection criteria (older, heart failure, structural remodelling) have an echocardiogram to assess who should be referred for confirmatory CA testing (PYP). Modelling compared the clinical utility of making decisions to refer for a second read or confirmatory testing based on an echocardiographic red flag for CA (increased wall thickness) or an AI-indicated presence of heart failure with preserved ejection fraction[2] (AI-HF; EchoGo Heart Failure, Ultromics Ltd), compared with an AI indication of CA, or the AI-CA in combination with increased wall thickness or AI-HF.

RESULTS

Patient characteristics are highlighted in **Table 1**. The modelled clinical decision-making scenarios are presented in **Figure 1**. Standardized net benefit represents the proportion of patients with CA who would be correctly referred, and net reduction in interventions represents the number of incorrect referrals avoided without missing a patient with CA. Threshold probability (x-axis), represents the preference of the clinician to be more concerned with missing the disease (*lower threshold*) than the risk of the decision (*higher threshold*). Using wall thickness alone to decide which patients should be sent for a second read or confirmatory testing would result in up to 65% correct referrals, whereas incorporating AI-CA information to wall thickness or AI-HF results in up to 77% correct referrals, similar to decisions based on AI-CA alone (~80%; *panel A and B*). Similarly, compared with referring for a second read or confirmatory testing based on wall thickness alone, unnecessary referrals are reduced by up to 18% and 14% (respectively) when AI-CA information is combined with either wall thickness or AI-HF.

Combining **echocardiography** and **AI** demonstrated clinical utility at different stages of the **CA diagnostic pathway**.

In low-risk decisions for further patient examination, or higher-risk decisions for confirmatory testing, the **integration of AI** could **increase detection rates** and **decrease unnecessary referrals**.

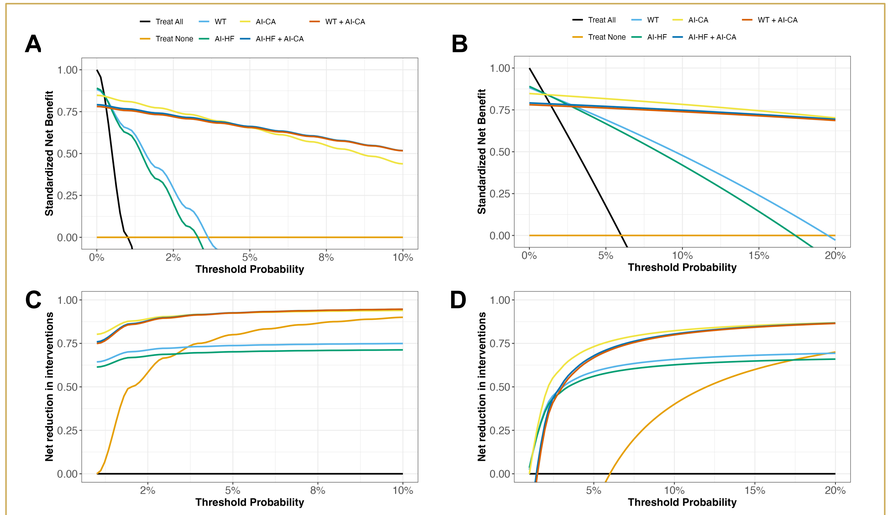

Figure 1. Decision curve analysis modelling referral decisions in the cardiac amyloidosis (CA) diagnostic pathway at two distinct phases; an assumed low prevalence (1%) scenario where patients are assessed to decide who should be further examined for possible CA ("second read"; *A and C*), and an assumed higher prevalence (6%) scenario where patients are pre-screened and then assessed to decide who should be referred for confirmatory testing (PYP; *B and D*). Clinical utility was assessed when decisions were based on: (i) increased wall thickness on echocardiography ("WT"; PWT or IVS ≥ 12 mm) as a key echocardiographic red flag; (ii) AI-indicated presence of heart failure ("AI-HF"; EchoGo Heart Failure) as an AI red flag; (iii) AI-indicated presence of CA ("AI-CA"; EchoGo Amyloidosis); and (iv) joint probabilities of a red flag plus AI-indicated presence of CA. Decisions to refer all ("Treat All") and refer none ("Treat None") are provided as clinical benchmarks.

Table 1. Descriptive Statistics

Outcome	Not CA	CA
Age (years)	58 (20) [3928]	72 (11) [555]
Sex (Female)	2100 (49%)	152 (27%)
BMI (kg/m2)	26.8 (6.2) [3933]	27.0 (7.0) [377]
Race		
Asian	1174 (28%)	75 (13%)
Black	575 (14%)	195 (35%)
White	1962 (46%)	255 (46%)
Other	266 (6%)	28 (5%)
Coronary Artery Disease	358 (8%)	86 (15%)
Diabetes Mellitus	662 (16%)	89 (16%)
History of AF	485 (11%)	129 (23%)
Hypertension	1481 (35%)	218 (39%)
AL		192 (34%)
ATTRv		70 (13%)
ATTRwt		298 (53%)
Echocardiography		
Ejection Fraction (%)	62.2 (6.2) [3883]	52.6 (13.1) [534]
IVS (mm)	9.6 (3.1) [3617]	14.9 (3.2) [377]
PWT (mm)	9.7 (2.9) [4098]	14.3 (4.3) [550]
LVMi (g/m2)	78.1 (35.3) [2888]	128 (42) [370]
iWT	1118 (26.3%)	489 (87%)

Note: Data are presented as mean (sd) [n] for continuous measures and count (proportion) for categorical measures. AF, atrial fibrillation; AL, Light Chain Amyloidosis; ATTRv, Hereditary Transthyretin Amyloidosis; ATTRwt; Wild-type Transthyretin Amyloidosis; BMI, body mass index; CA, Cardiac Amyloidosis; IVS, intra-ventricular septum; iWT, increased Wall Thickness (PWT ≥ 12 mm or IVS ≥ 12 mm); LVMi, Left Ventricular mass indexed to body surface area; PWT, Posterior Wall Thickness.

CONCLUSION

Integrating AI tools into clinical decision-making demonstrated increased clinical utility compared with using only traditional echocardiographic red flags for CA, resulting in more patients being correctly managed in the CA diagnostic pathway. This strategy of combining sources of information has the potential to increase the number of patients with CA being detected and reduce the number of incorrect referrals for follow-up assessment.

REFERENCES

1. https://doi.org/10.1093/eurheartj/ehaf387 2. https://doi.org/10.1016/j.jacadv.2023.100452

APA, WH, GW, and RU are employees of Ultromics Ltd. The staff of Ultromics would like to dedicate this presentation to the memory of Roberto Lang. It was a pleasure to work closely with this giant of the industry, and he shall be missed widely.