Scientific Sessions

Artificial Intelligence-based Software for Checking REal-world Echocardiography to ideNtify hidden Cardiac Amyloidosis: AI-SCREEN-CA

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American Heart Association.

#AHA25

DISCLOSURES

- This study was funded by AstraZeneca. US2.ai and M3AI did not offer any financial support.
- Dr Kagiyama reported receiving research grants from AstraZeneca, Bristol Myers Squibb, AMI Inc. and EchoNous Inc. and speaker honoraria from Bristol Myers Squibb, Novartis, Otsuka Pharma, Eli Lilly, and Boehringer Ingelheim outside the submitted work.
- Dr. Kaneko reported receiving honoraria from Abbott Medical Japan and belongs to an endowed department funded by Abeam Consulting.
- No other disclosures were reported.

BACKGROUND

- Cardiac amyloidosis (CA) was traditionally regarded as rare, yet emerging evidence shows that many patients with cardiovascular disease may in fact harbor previously unrecognized, “hidden” CA.

Ioannou et al. Circulation. 2022;146:1657–1670
Aimo et al. Eur J Heart Fail 2022;24:2342–2351

- With the advent of effective therapies, early detection and timely intervention have become essential.

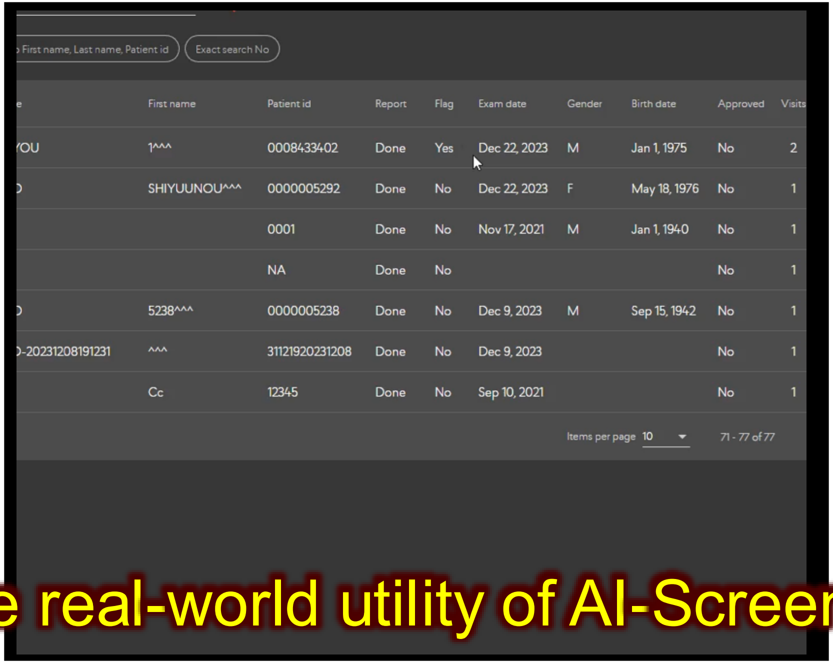
Kittlesen et al. JACC 2023;81:1076–1126

- Echocardiography remains a cornerstone for CA screening; however, most findings are non-specific. Although strain can provide greater specificity, it is time-consuming to obtain in routine clinical practice.

Fontana et al. JACC Img 2025;18:478–499

BACKGROUND 2

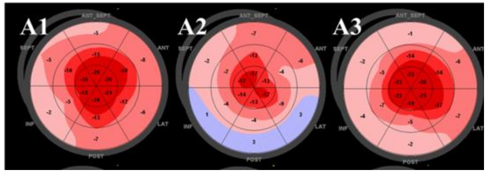
Fully-automatic echo parameters analysis
Both parameter- and deep learning-based CA detection



e	First name	Patient id	Report	Flag	Exam date	Gender	Birth date	Approved	Visits
YOU	1^^^	0008433402	Done	Yes	Dec 22, 2023	M	Jan 1, 1975	No	2
D	SHIYUUNOU^^^	0000005292	Done	No	Dec 22, 2023	F	May 18, 1976	No	1
		0001	Done	No	Nov 17, 2021	M	Jan 1, 1940	No	1
		NA	Done	No				No	1
D	5238^^^	0000005238	Done	No	Dec 9, 2023	M	Sep 15, 1942	No	1
D-20231208191231	^^^	31121920231208	Done	No	Dec 9, 2023			No	1
	Cc	12345	Done	No	Sep 10, 2021			No	1

ORIGINAL RESEARCH

Multiparametric Echocardiography Scores for the Diagnosis of Cardiac Amyloidosis



IWT Score

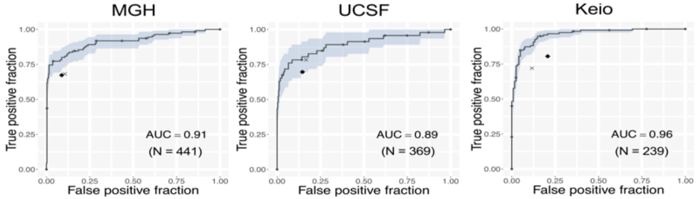
AUC = 0.87
(95% CI: 0.85-0.90)

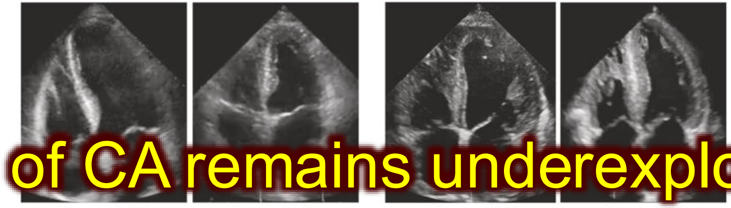
RWT >0.6	3 points
E/e' >11	1 point
TAPSE ≤19 mm	2 points
LS ≥ -13%	1 point
SAB> 2.9	3 points

ARTICLE

https://doi.org/10.1038/s41467-021-22877-8 OPEN

Artificial intelligence-enabled fully automated detection of cardiac amyloidosis using electrocardiograms and echocardiograms





The real-world utility of AI-Screening of CA remains underexplored

Boldrini, Fontana, et al. JACC Img 2020 [PMID 31864973]

Goto S, et al. Nat Commun 2021 [PMID 33976142]

OBJECTIVES

- To investigate the AI software's real-world diagnostic performance and determine its potential to uncover the hidden burden of previously unrecognized CA.

METHODS: Study design

A retrospective analysis of consecutive echo exams

Inclusion criteria:

- Adult patients (≥20 years) who underwent echo at Juntendo Univ. between Apr 2023 – Mar 2024

Exposure:

- AI-based screening for CA

Primary endpoint:

- Number of patients flagged as suspected CA by AI

Secondary endpoint:

- Characteristics of patients flagged as s/o CA by the AI
- Prevalence and characteristics of newly identified CA
- Diagnostic accuracy of the AI against clinical standards

All echo between Apr 2023 – Mar 2024
n = 13,511 (16,764 exams)

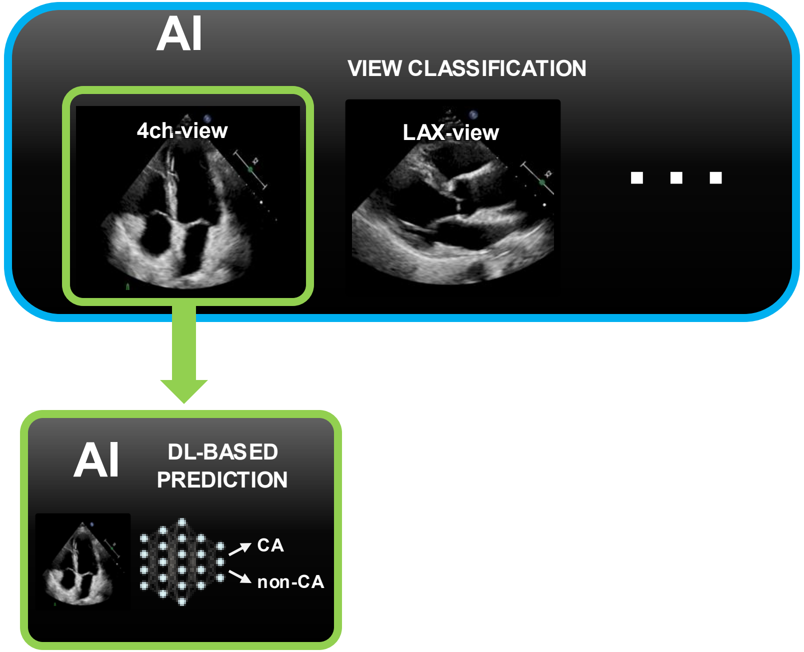
Exclusion:
- Poor images (n = 2691)
- AI non analyzable (n = 22)

Final analysis set
n = 11,454 (14,051 exams)

AI screening for CA

AI-based echo screening of CA

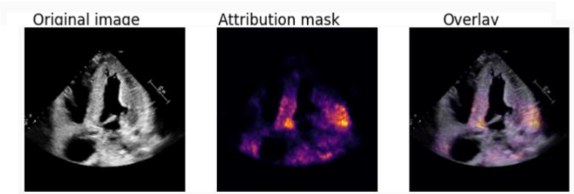
Integration of two AI workflows



Deep learning-based

DL-based prediction

1). Vision Transformer-based deep learning architecture
2). Trained on 4371 patients, of which 2241 were Amyloid-positive.
3). Externally tested in 1647 patients, showing generalizability.
4). FDA approved in July, 2025.



Cohort	No. of patients classified	Accuracy	Sensitivity	Specificity
NAC internal validation split	289 (100%)	93.3%	93.3%	93.4%
NAC internal test split	284 (100%)	94.5%	94.7%	93.8%
Duke testing dataset	1149 (100%)	82.1%	83.1%	81.7%
NCVC testing dataset	406 (100%)	85.75	81.4%	89.2%

Ioannou et al. Presented at EuroEcho-Imaging 2024 (https://esc365.escardio.org/presentation/293580)

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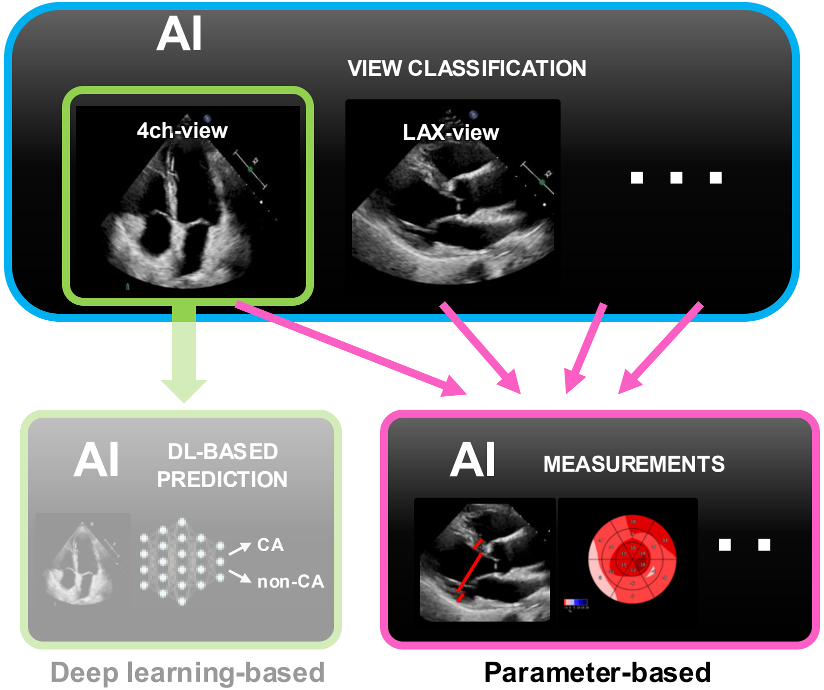


Parameter-based prediction

1). DL models automatically measure traditional echo parameters
2). Based on the published ESC position statement *
3). LVH (≥ 12 mm) + either of the following criteria is met:

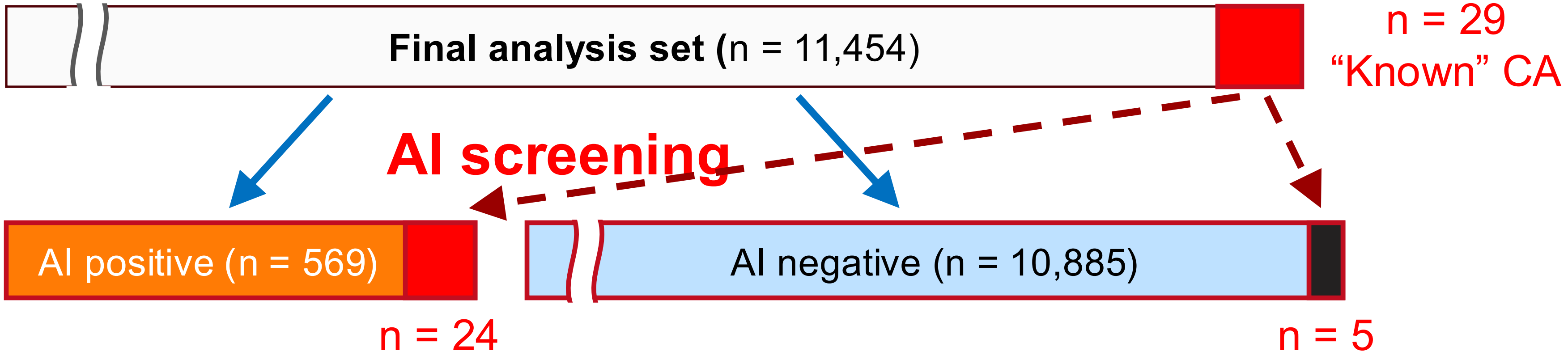
1. Criteria 1	
Parameters: ≥ 2 points are positive	point
a. Grade 2 or 3 diastolic dysfunction	1
b. Reduced mitral s', e', and a' waves (<5 cm/s)	1
c. Decreased global longitudinal LV strain (< 15%)	1
2. Criteria 2 (IWT score)	
Parameters: ≥ 8 points are positive	point
a. Relative LV wall thickness (RWT) >0.6	3
b. E/e' >11	1
c. TAPSE ≤ 19 mm	2
d. Decreased global longitudinal LV strain (≤ 15%)	1
e. Longitudinal strain apex to base ratio > 2.9	3

** Garcia-Pavia et al. Eur Heart J 2021;42:1554–1568*

RESULTS

AI-positive vs. AI-negative

AI-Screening Flow Chart



AI flagged 569 as s/o CA (5.0% of patients undergoing echocardiography)

Among 29 patients with known diagnosis of CA, AI successfully flagged 24 patients (Sensitivity: 82.8% for detecting known CA)

AI-positive vs. AI-negative

	n	AI-positive (n = 569)	AI-negative (n = 10,885)	p value	SMD [95%CI]
Subtype of CA	29			>0.999	0.14 [-0.83–1.10]
ATTR-CA		16 (66.7%)	3 (60.0%)		
AL-CA		8 (33.3%)	2 (40.0%)		
Age, years	11,454	77 [69 - 83]	69 [57 - 78]	<0.001	-0.59 [-0.67–-0.51]
Female	11,454	204 (35.9%)	5,067 (46.6%)	<0.001	0.22 [0.13–0.30]
Significant aortic stenosis	11,427	81 (14.3%)	368 (3.4%)	<0.001	0.39 [0.31–0.48]
Carpal tunnel syndrome	11,454	16 (2.8%)	77 (0.7%)	<0.001	-0.16 [-0.24–-0.08]
LVEF, %	11,449	61.0 [53.0 - 67.0]	64.0 [59.0 - 68.0]	<0.001	0.34 [0.25–0.42]
LVDd, mm	11,449	46.3 ± 6.7	45.9 ± 5.8	0.109	-0.07 [-0.16–0.01]
IVSd, mm	11,448	11.6 ± 2.0	9.5 ± 1.7	<0.001	-1.10 [-1.20–-1.10]
Relative wall thickness	11,449	0.50 ± 0.11	0.42 ± 0.08	<0.001	-0.89 [-0.97–-0.80]
LA diameter, mm	11,443	42.8 ± 8.0	37.0 ± 7.2	<0.001	-0.76 [-0.84–-0.67]
E/e'	11,383	15.5 [11.0 - 22.5]	9.9 [7.7 - 13.1]	<0.001	-0.76 [-0.85–-0.68]
*Global longitudinal strain, %	10,402	-16.0 ± 4.4	-18.7 ± 3.8	<0.001	-0.64 [-0.73–-0.56]
*Strain apical to basal ratio	11,251	1.8 [1.3 - 2.5]	1.3 [1.0 - 1.7]	<0.001	-0.20 [-0.28–-0.12]
*IWT score	11,454	3 [2 - 5]	0 [0 - 2]	<0.001	-1.20 [-1.20–-1.10]

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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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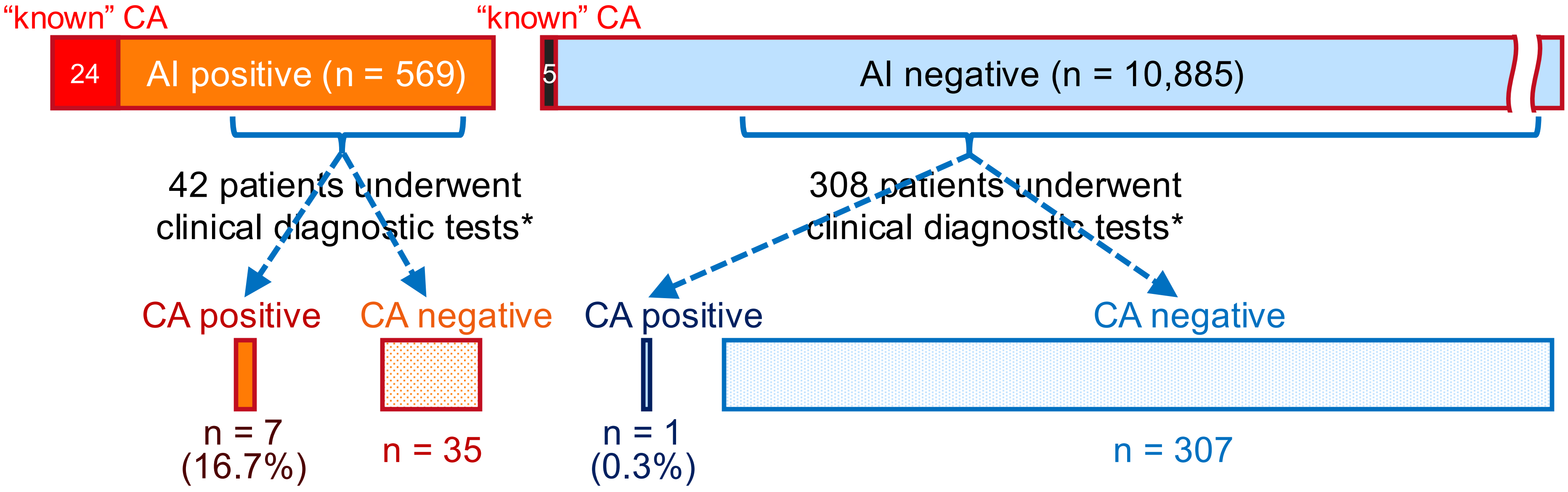
Despite using only echocardiographic images,
the AI identified patients with clinical features characteristic of CA.

Proportion of "Hidden" CA



AI-positive patients were **50 times more likely** to be CA

*Clinical diagnostic tests include cardiac biopsy, 99mTc-PYP scintigraphy, cardiac MRI, and/or monoclonal protein assessment with cardiac tests

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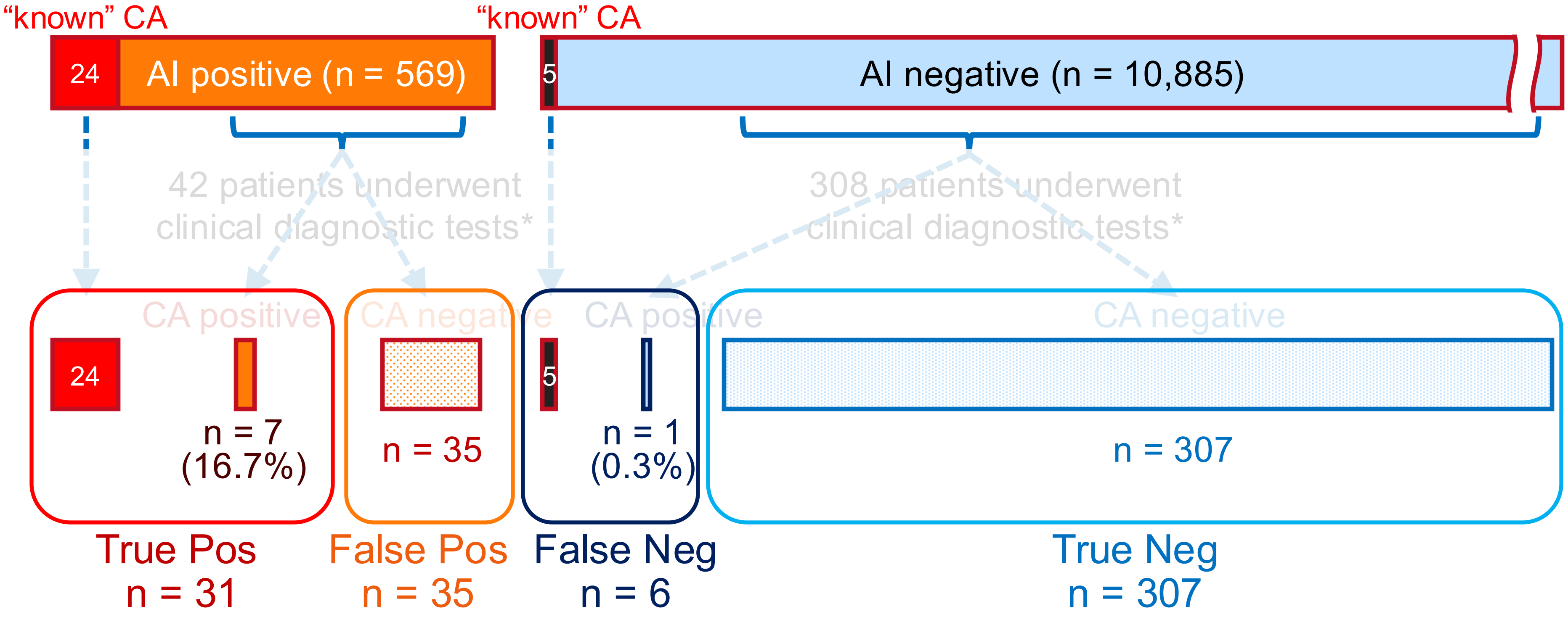

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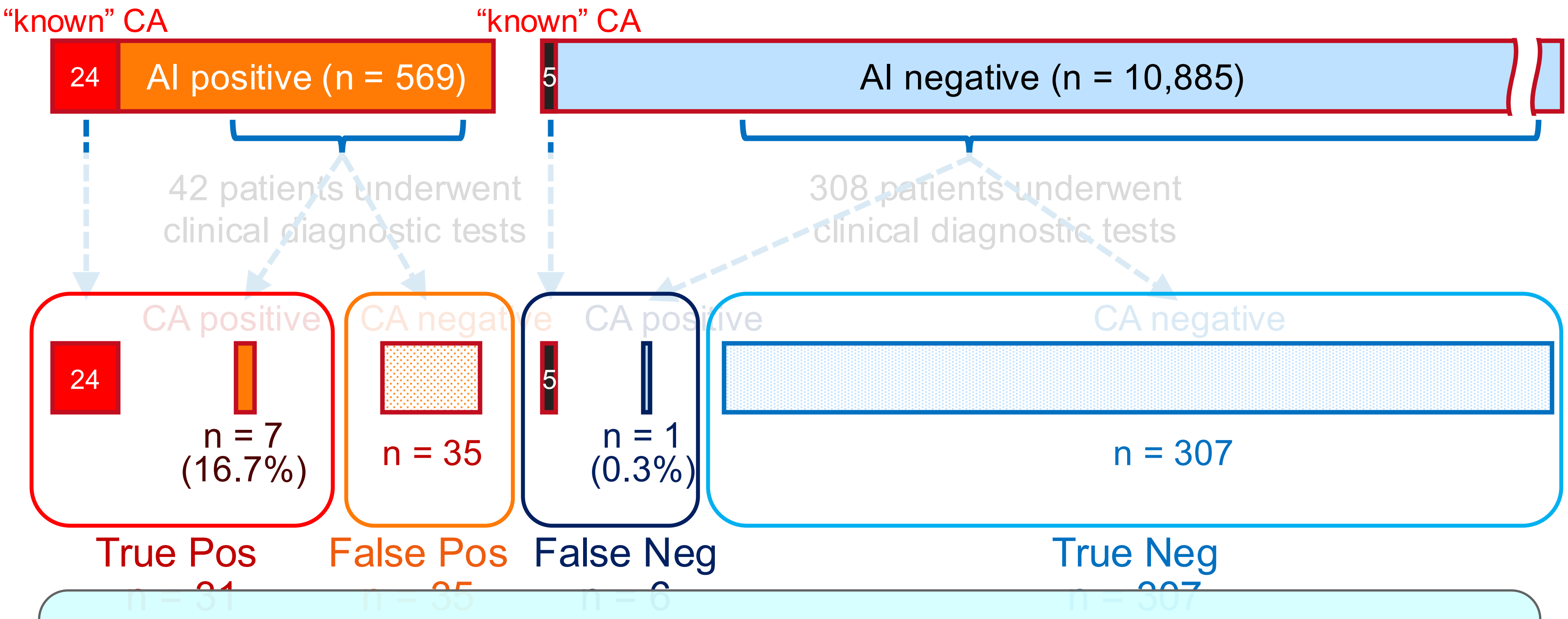

Overall performance of AI-based echo screening for CA

PPV=47.0% [95%CI 34.6%–59.7%] NPV=98.1% [95%CI 95.8%–99.3%]

Known, Newly-identified, vs. false-positive CA

	n	Known CA (n = 24)	Newly identified CA (n = 7)	CA-false positives (n = 35)	p value
Age, years	66	77 [72 - 80]	80 [68 - 84]	74 [59 - 78]	0.246
Female	66	3 (12.5%)	5 (71.4%)	10 (28.6%)	0.010
NT-proBNP, ng/L	63	1,808 [919 - 4,994]	1,792 [1,161 - 4,726]	2,007 [899 - 7,426]	0.971
HCM	66	0 (0%)	0 (0%)	8 (22.9%)	0.015
Aortic stenosis	65	3 (12.5%)	0 (0%)	2 (5.9%)	0.800
Carpal tunnel syndrome	66	3 (12.5%)	1 (14.3%)	0 (0%)	0.063
LVDd, mm	66	44.4 ± 4.5	43.6 ± 6.0	50.7 ± 9.1	0.008
IVSd, mm	66	14.2 ± 2.2	12.0 ± 2.2	12.2 ± 1.9	0.008
LVEF, %	66	53.5 [41.0 - 62.0]	62.0 [59.0 - 65.0]	56.0 [32.0 - 67.0]	0.376
LA diameter, mm	66	43.5 ± 9.1	44.1 ± 5.0	47.1 ± 10.9	0.369
Relative wall thickness	66	0.63 ± 0.11	0.58 ± 0.14	0.48 ± 0.12	<0.001
E/e'	66	21.9 [15.4 - 25.9]	16.6 [13.3 - 18.4]	17.5 [14.3 - 23.8]	0.212
*Global longitudinal strain, %	59	-13.9 ± 4.2	-13.7 ± 1.7	-15.0 ± 4.9	0.537
*Strain apical to basal ratio	65	2.7 [1.6 - 3.9]	1.3 [1.2 - 3.9]	1.6 [1.3 - 2.3]	0.021
*IWT score	66	6 [4 - 9]	5 [1 - 9]	3 [1 - 4]	0.002

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HCM	66	0 (0%)	0 (0%)	8 (22.9%)	0.015
Aortic stenosis	65	3 (12.5%)	0 (0%)	2 (5.9%)	0.800
Carpal tunnel syndrome	66	3 (12.5%)	1 (14.3%)	0 (0%)	0.063
LVDd, mm	66	44.4 ± 4.5	43.6 ± 6.0	50.7 ± 9.1	0.008
IVSd, mm	66	14.2 ± 2.2	12.0 ± 2.2	12.2 ± 1.9	0.008
LVEF, %	66	53.5 [41.0 - 62.0]	62.0 [59.0 - 65.0]	56.0 [32.0 - 67.0]	0.376
LA diameter, mm	66	43.5 ± 9.1	44.1 ± 5.0	47.1 ± 10.9	0.369
Relative wall thickness	66	0.63 ± 0.11	0.58 ± 0.14	0.48 ± 0.12	<0.001
E/e'	66	21.9 [15.4 - 25.9]	16.6 [13.3 - 18.4]	17.5 [14.3 - 23.8]	0.212
*Global longitudinal strain, %	59	-13.9 ± 4.2	-13.7 ± 1.7	-15.0 ± 4.9	0.537
*Strain apical to basal ratio	65	2.7 [1.6 - 3.9]	1.3 [1.2 - 3.9]	1.6 [1.3 - 2.3]	0.021
*IWT score	66	6 [4 - 9]	5 [1 - 9]	3 [1 - 4]	0.002

COMPARISON WITH CLINICAL SCORE

AI-SCREENING vs. Kumamoto Criteria

Kumamoto criteria:

- hs-cTnT ≥0.0308 ng/mL
- QRS duration ≥120 ms
- LV PWT ≥13.6 mm

Circ J 2019;83:1698-1708

Reclassification by AI

NRI (Categorical)	**0.452 [0.198–0.707]**	**p<0.001**
IDI	**0.452 [0.192–0.713]**	**p<0.001**

AI was correct | Kumamoto was correct

Patients without CA

Kumamoto score	AI prediction: negative	AI prediction: positive	% reclassified
negative	110	20	15
positive	27	5	84

Patients with CA

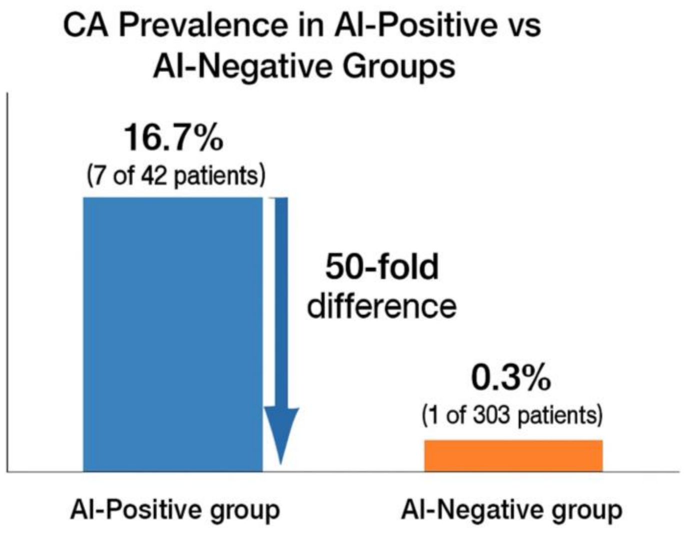
Kumamoto score	AI prediction: negative	AI prediction: positive	% reclassified
negative	4	10	71
positive	1	7	12

Combined data

Kumamoto score	AI prediction: negative	AI prediction: positive	% reclassified
negative	114	30	21
positive	28	12	70

SUMMARY

AI flagged 5% of population as s/o CA



Positive Predictive Value

47.0%

95% CI: 34.6%–59.7%

Among AI-positive patients without prior diagnosis who underwent diagnostic evaluation, 47% had confirmed cardiac amyloidosis. This high PPV validates the AI's utility in selecting patients for advanced, costly testing.

Negative Predictive Value

98.1%

95% CI: 95.8%–99.3%

Among AI-negative patients, only 0.3% had confirmed CA. This exceptionally high NPV demonstrates the AI's powerful ability to safely rule out cardiac amyloidosis in the general population.

Improved prediction over clinical score

DISCUSSION

In >11,000 real-world patients, the AI system showed strong screening performance for CA.

AI advantages beyond routine practice

- **Parameter-based model:** Routine strain assessment for all LVH patients is impractical given the high prevalence of LVH; automation enables universal analysis.
- **Deep-learning model:** May detect subtle alterations in myocardial texture and motion changes that appear before overt hypertrophy, helping flag early-stage disease.
- The combination of these approaches yielded robust performance and identified patients who may not trigger clinical suspicion.

Context and significance

Prior studies elegantly showed AI's performance, but were in curated case-control cohorts; this is the first large-scale evaluation in an unselected population. As early CA treatment improves outcomes, the ability to surface potential early cases in routine workflow has meaningful clinical implications.

Goto S, et al. Nat Commun. 2021;12:2726
Hourmozdi J, et al. JACC Adv. 2025;4:101901
Slivnick JA, et al. Eur Heart J. 2025;46:4090-4101
Duffy G, et al. JACC Adv. 2025:102067

LIMITATIONS

- The retrospective, single-center design in a Japanese cohort limits generalizability and necessitates multi-center, multi-ethnic validation.

- Significant verification bias exists, as diagnostic testing was not systematic. Thus, the true prevalence is unknown, and the observed PPV may be overestimated because it was calculated in a clinically selected, high-risk subgroup.

- Although the PPV of 47% may appear modest as a standalone diagnostic level, the intended role of this AI is screening and enrichment. In the context of a low-prevalence disease, this level of enrichment represents meaningful clinical value rather than definitive diagnosis.

CONCLUSIONS

- In a large, real-world cohort, AI-based echocardiographic screening showed strong diagnostic performance and high practical yield in identifying previously unrecognized cardiac amyloidosis.

- Prospective studies in which all AI-positive patients undergo systematic diagnostic evaluation, and efforts to integrate AI-echo screening with other screening modalities, are warranted to refine and optimize this approach.

THANK YOU

Scientific Sessions

#AHA25

AI-SCREEN-CA

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