Multimodality Imaging Approach to LA Remodeling in Subclinical Atrial Fibrillation

Hsuan-Ming Tsao, M.D

National Yang Ming Chiao Tung University Hospital, Yi-Lan, Taiwan

Korean Heart Rhythm Society
COI Disclosure

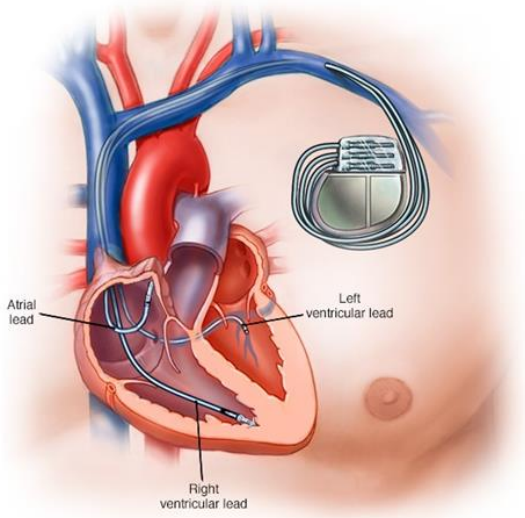
Name of First Author:Hsuan-Ming Tsao, M.D

The authors have no financial conflicts of interest to disclose concerning the presentation

Subclinical Atrial Fibrillation: Device Detected AF

Terminology: subclinical AF, atrial high-rate episodes

- As the technological advancement of cardiac implanted electronic device (CIED) enables the continuous detection of atrial activities, the asymptomatic atrial tachyarrhythmia can emerge as a relatively new entity and merit more considerations.
- These episodes are described as atrial high-rate episodes (AHRE) and are clinically asymptomatic, referred to subclinical AF (SCAF).
- They are clinically distinct from the ECG-documented paroxysmal AF due to the lower stroke rate, variability of different device detection and lacking of evidence-based approach to treatment.



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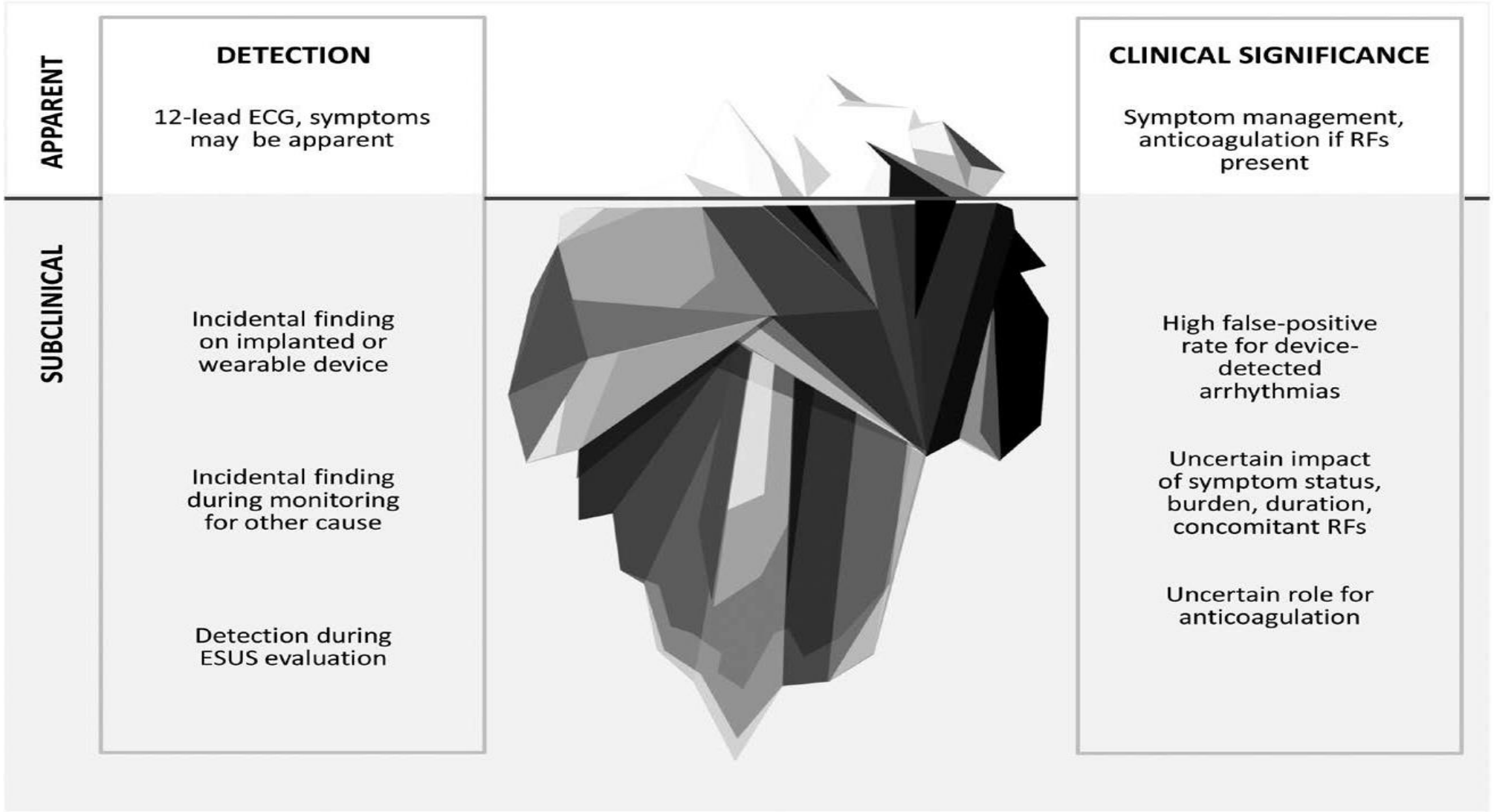
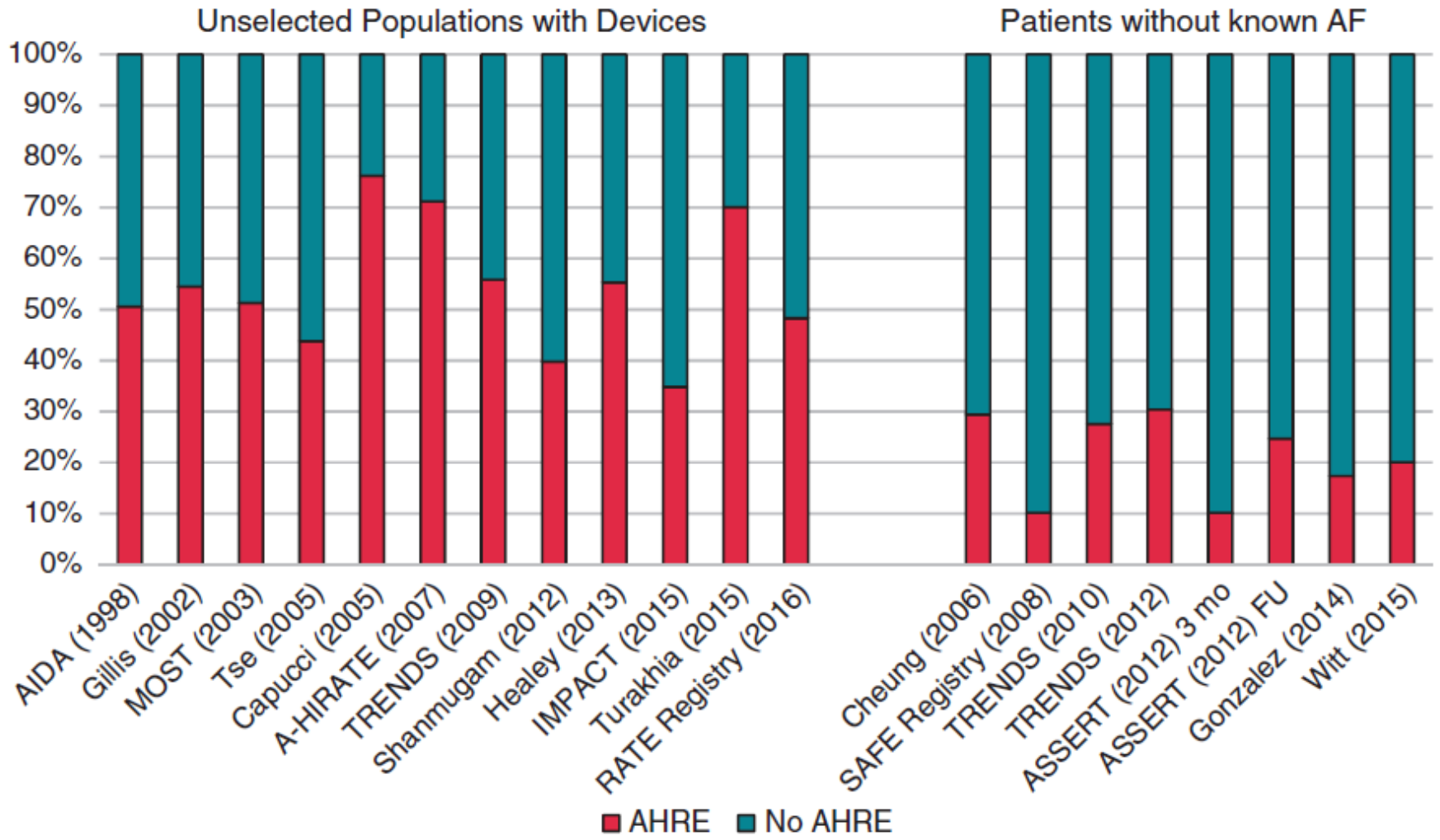
Tip of Iceberg Analogy of clinical and subclinical AF



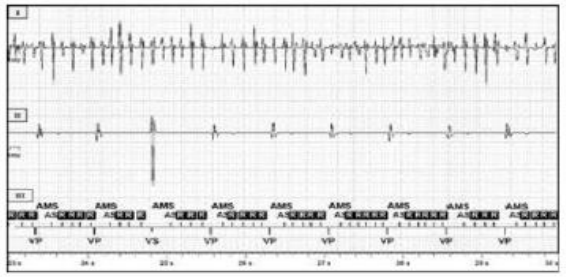
Incidence of AHRE



Bertaglia et at Europace 2019

KHRS 2023

Clinical Implication of AHRE



EGM showing AHRE

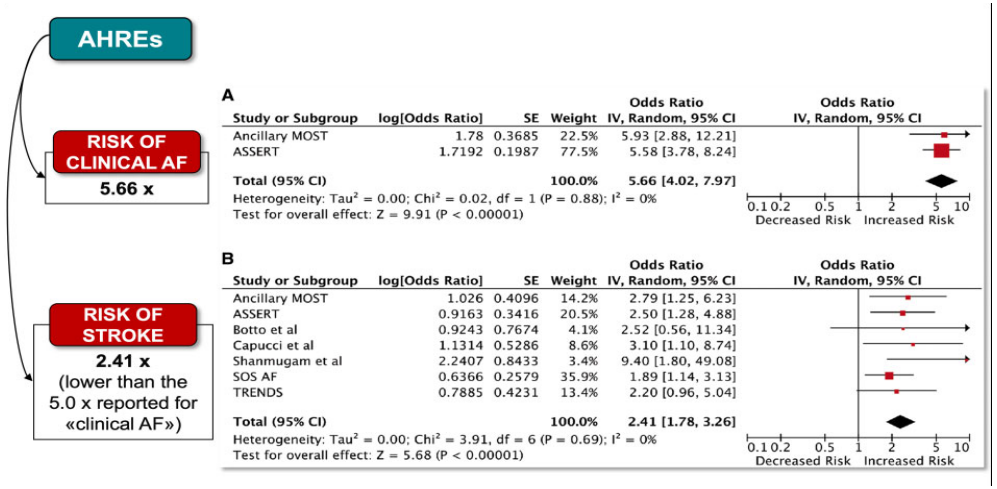
12-lead ECG showing AF

Duration of AHRE

CHA_2DS_2-VASc score

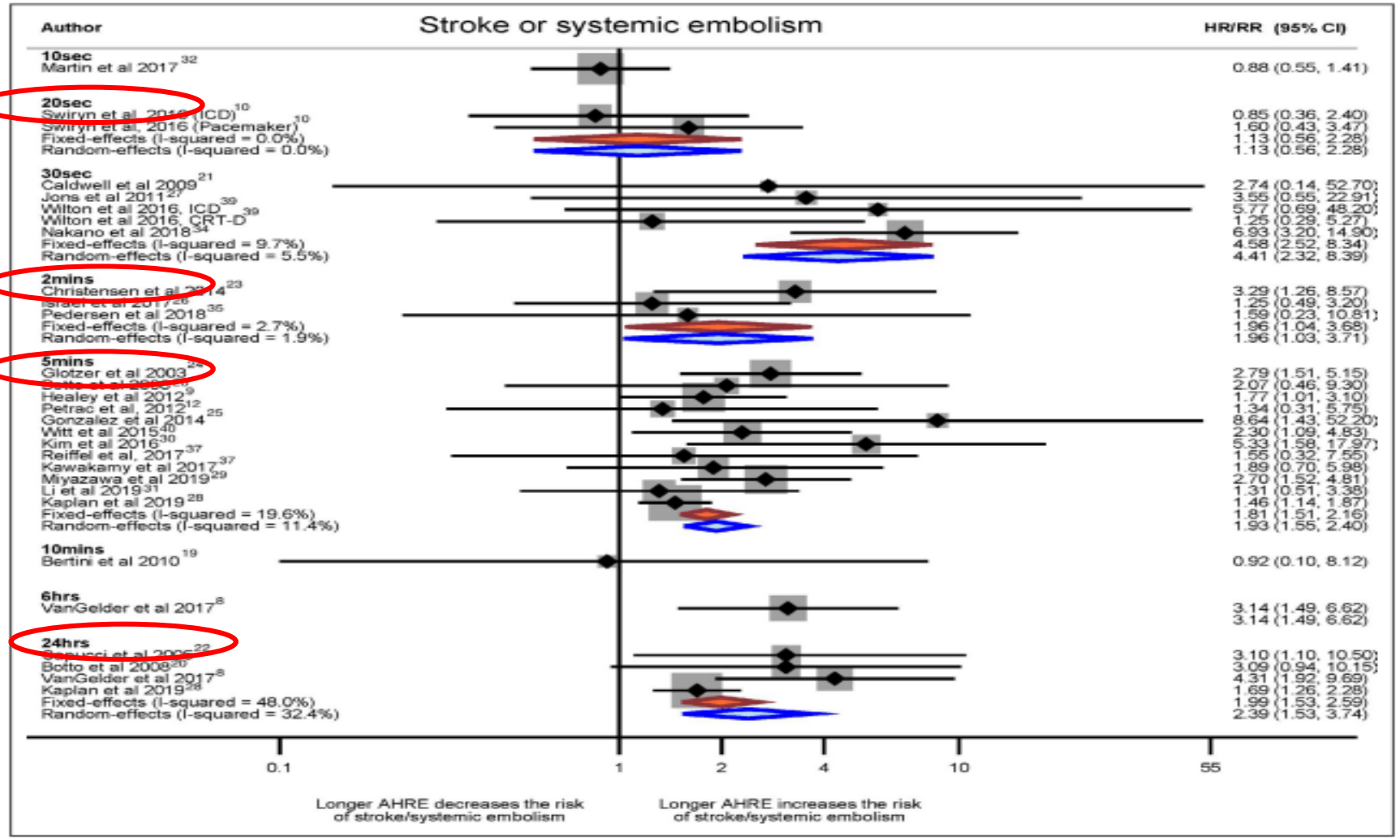
Anticoagulation

↑ thromboembolism risk including stroke [2.1 – 2.4% incidence (AHRE) vs 4 – 4.5% incidence (AF)]
↑ incidence of heart failure
↑ MACE



Lip G et al Clinic Research in Cardiol 2020

Atrial High-Rate Episode Duration Thresholds and Thromboembolic Risk: A Systematic Review and Meta-Analysis



Sagris et al JAHA 2021

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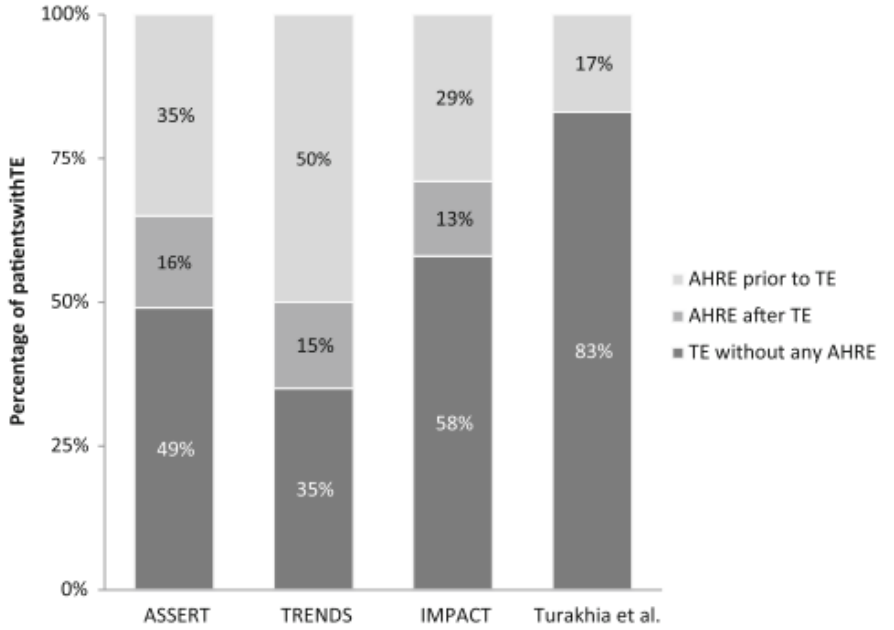
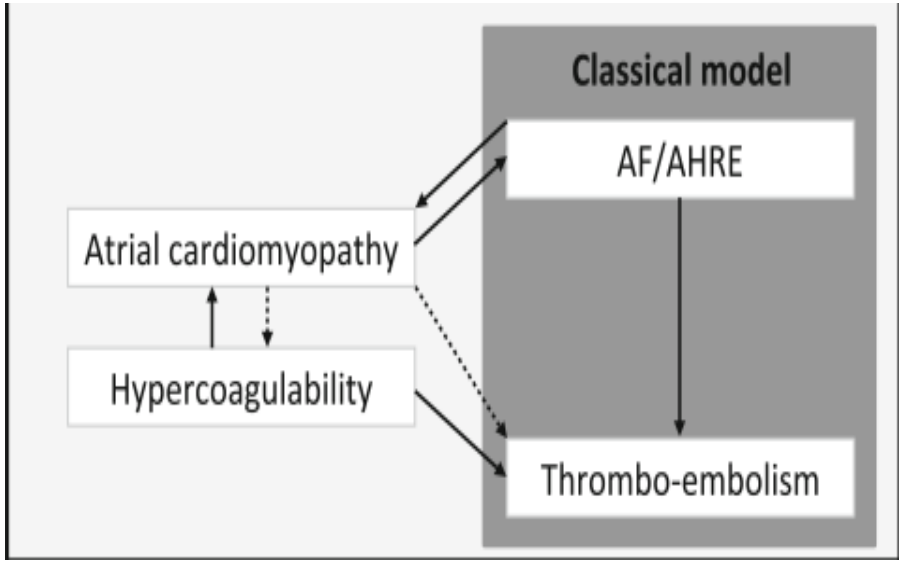
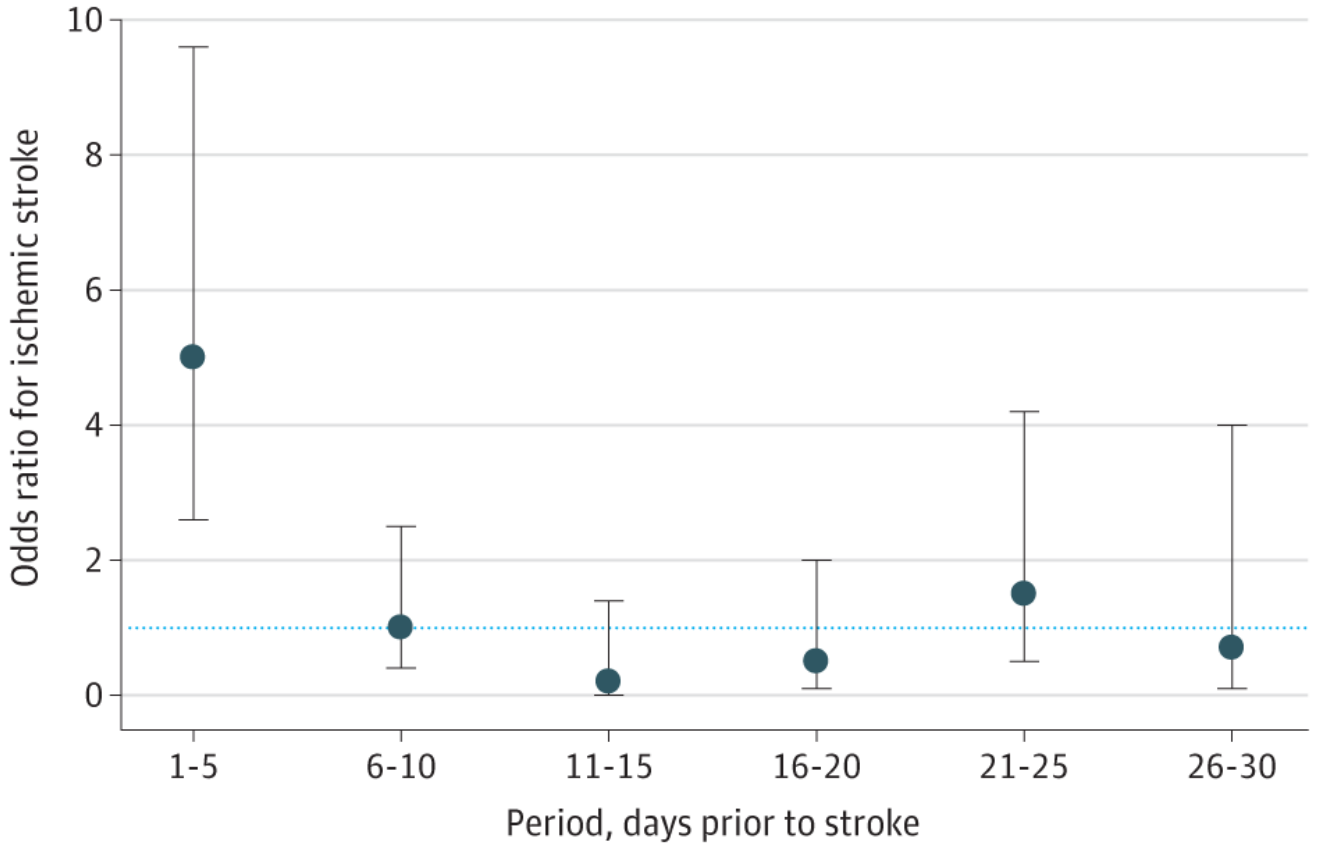
Lack of temporal relationship between AHRE and stroke?





Erkuner et al Neth Heart J 2018

Odds Ratios for Ischemic Stroke for Sequential, with> 5.5 Hours AHRE



Singer et al. JAMA Cardiol 2021

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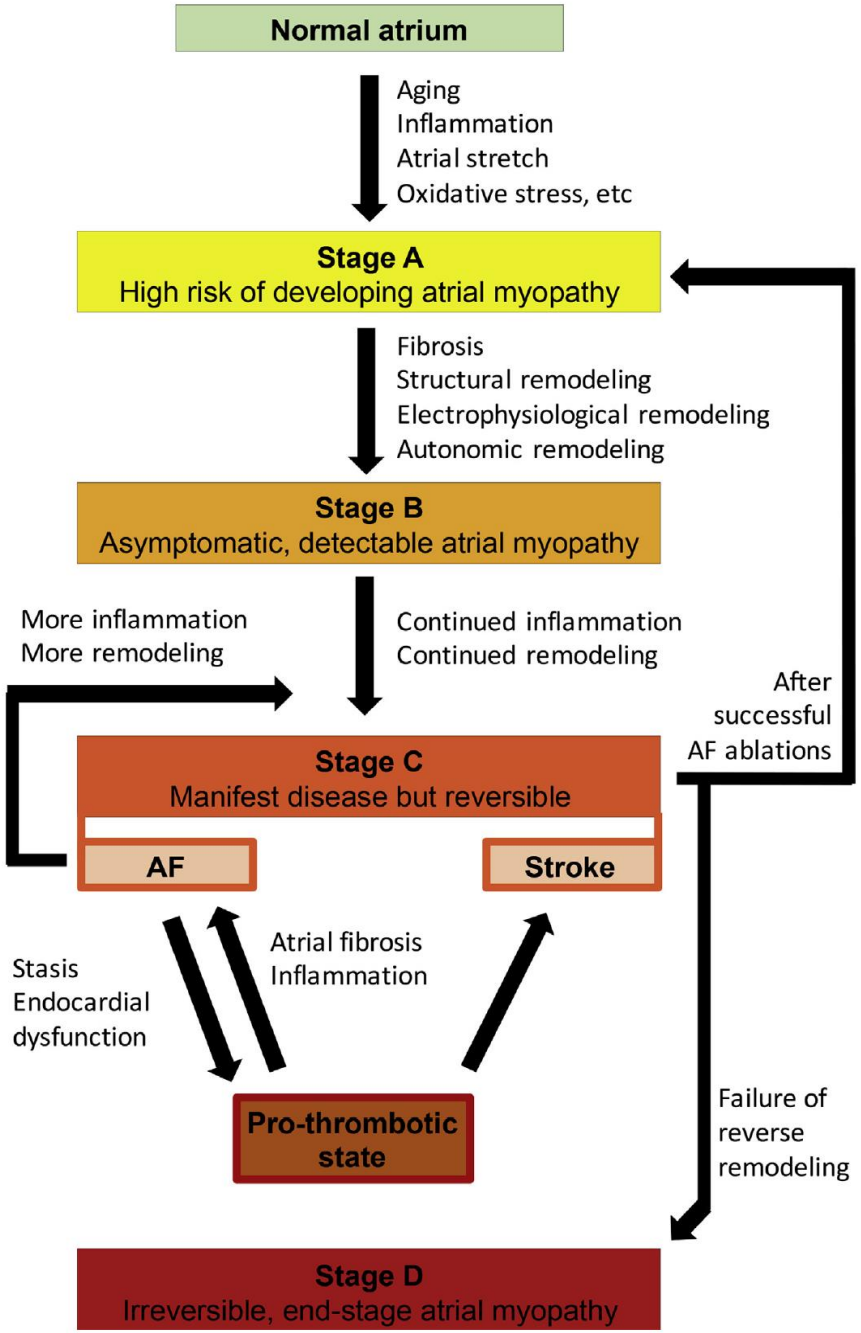
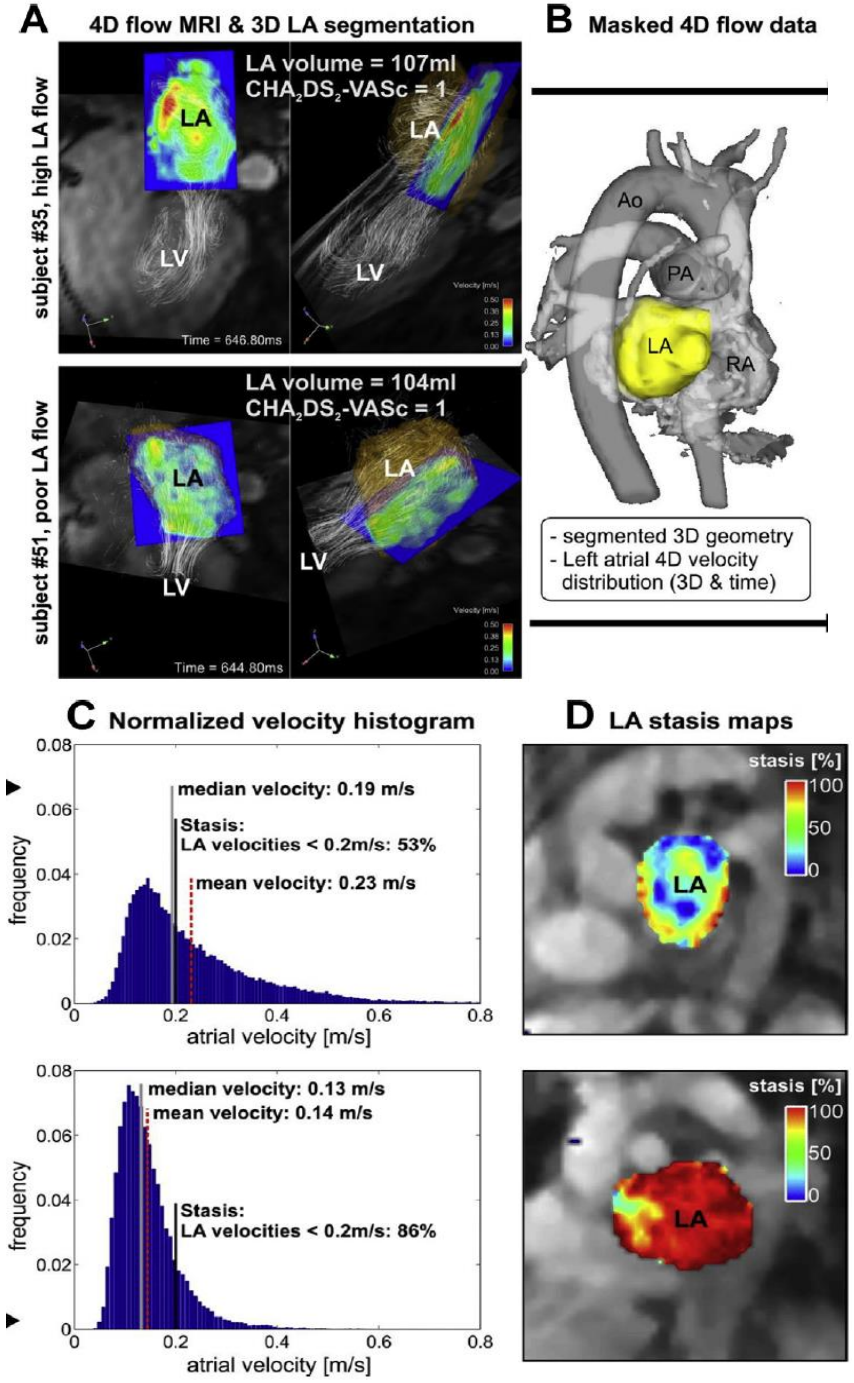
FIGURE 1 Stages of Atrial Myopathy





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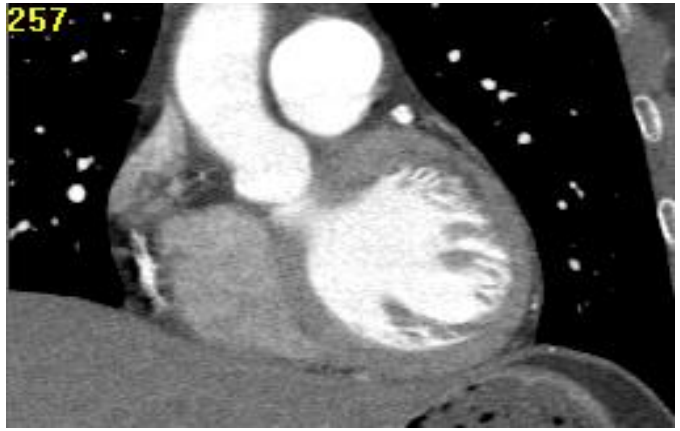
What is the relationship between **Atrial Remodeling** and **AHRE**?

- **Part 1:**

Distinguish the atrial structure and function between AF and AHRE (>6 minutes, 6 minutes-6 hours, >6 hours)

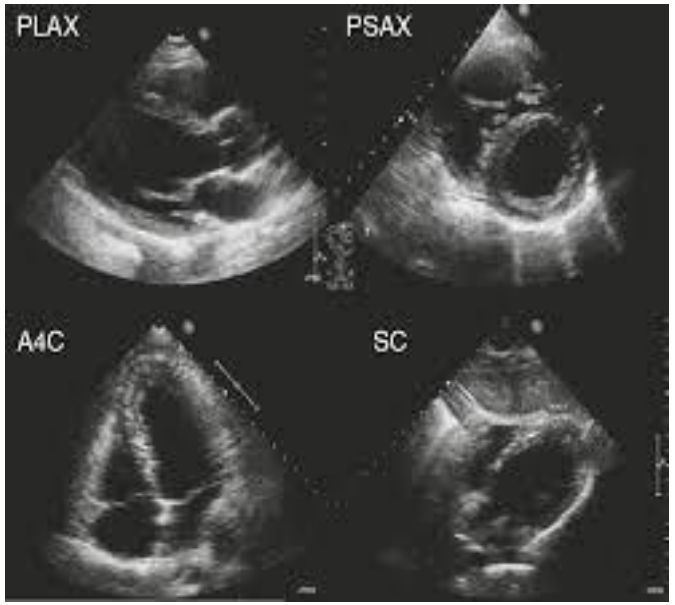
Dynamic Function of LA/LV



Oblique View

Sagittal View

Transverse View

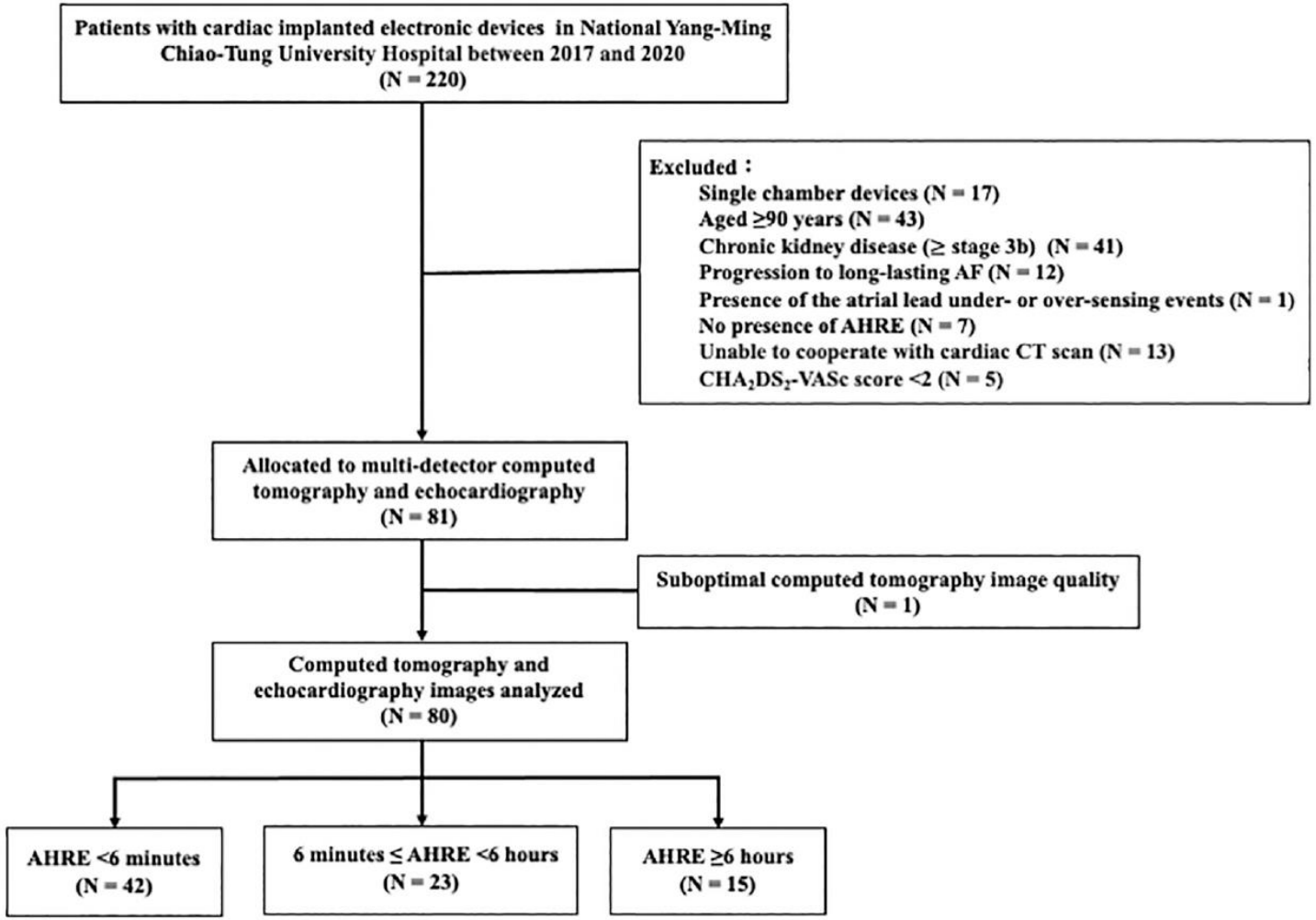


Echocardiography

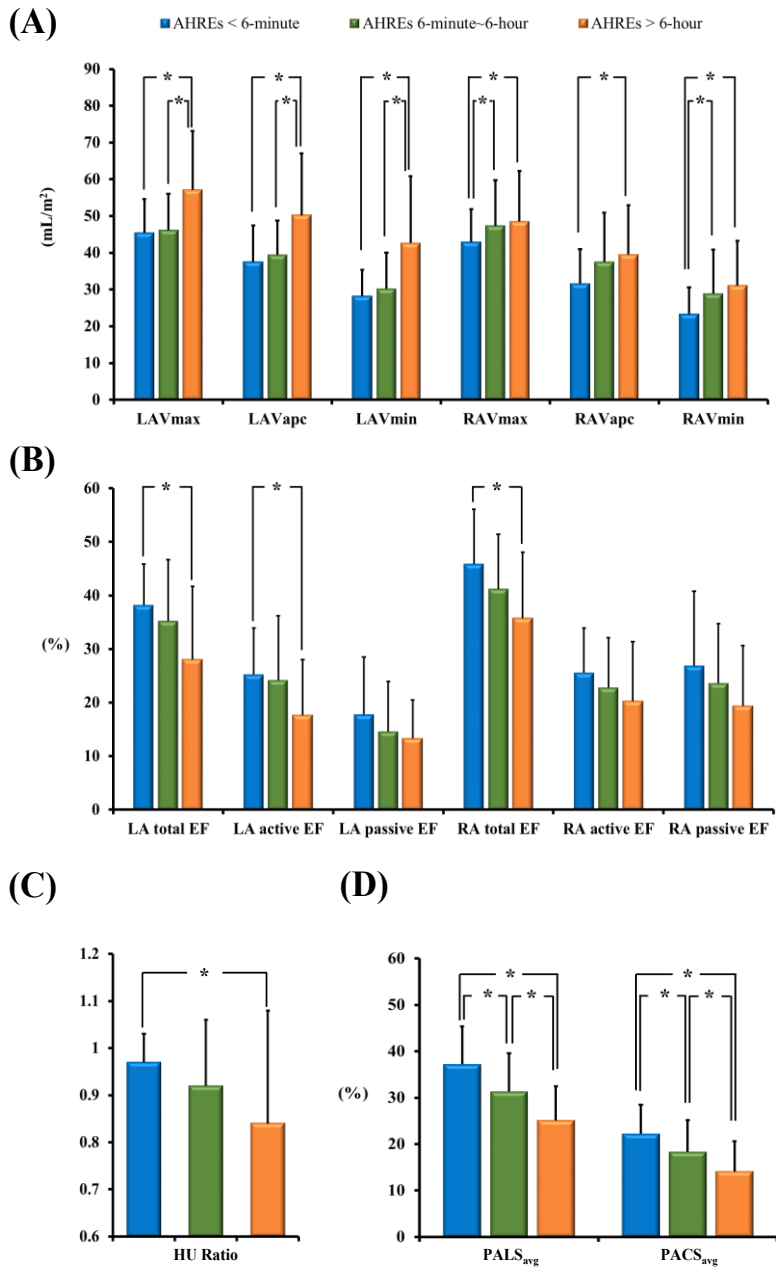
Multimodality imaging assessment of the Biatrial remodeling of the burden of atrial high-rate episodes in patients with cardiac implanted electronic devices

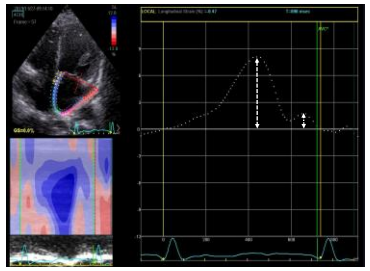
Int J Cardiol 2023

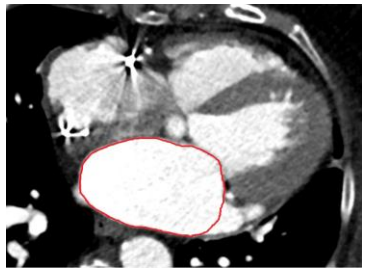
Sung-Hao Huang [a], Hsuan-Ming Tsao [a,b,*], Chao-Feng Liao [a], Zu-Yin Chen [a], Tze-Fan Chao [b,c],



Comparison among AHRE<6min, 6min-6hours, >6 hours



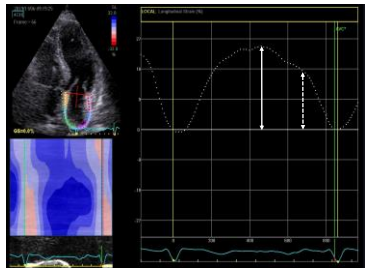


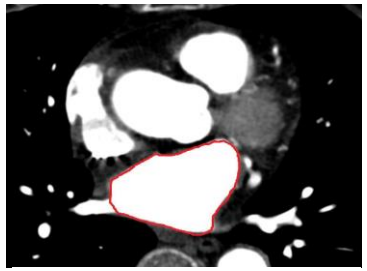


(A) AHREs > 6 hours

- **AHREs burden = 2.3 (%)**
- **LAV_{max} = 55.01 (mL/m²)**
- **LAV_{min} = 38.85 (mL/m²)**
- **LA total EF = 29.36 (%)**
- **4CH PALS = 8.25 (%)**
- **4CH PACS = 1.62 (%)**

Type	ID#	Date	Time hh:mm	Duration hh:mm:ss	Avg bpm A/V	Max bpm A/V	Activity at Onset
AT/AF	1984	01-Mar-2018	04:36	:02:00	265/72	333/80	Rest
AT/AF	1983	23-Feb-2018	10:24	:34:53	279/80	500/118	Rest
AT/AF	1982	20-Feb-2018	08:51	02:01:15	305/91	400/130	Active
AT/AF	1981	11-Feb-2018	02:19	07:18:50	351/78	500/109	Rest

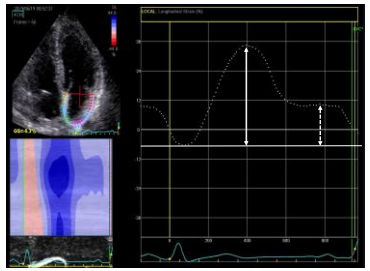


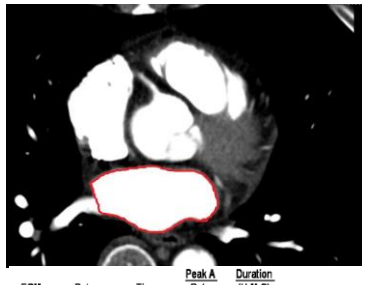


(B) 6 minutes < AHREs < 6 hours

- AHREs burden <0.1 (%)
- LAV_{max} = 30.54 (mL/m²)
- LAV_{min} =19.17 (mL/m²)
- LA total EF = 37.21 (%)
- 4CH PALS = 24.96 (%)
- 4CH PACS = 17.32 (%)

Type	ID#	Date	Time hh:mm	Duration hh:mm:ss	Avg bpm A/V	Max bpm A/V	Activity at Onset
AT/AF	6186	03-Aug-2017	05:58	:10:37	133/70	188/76	Rest



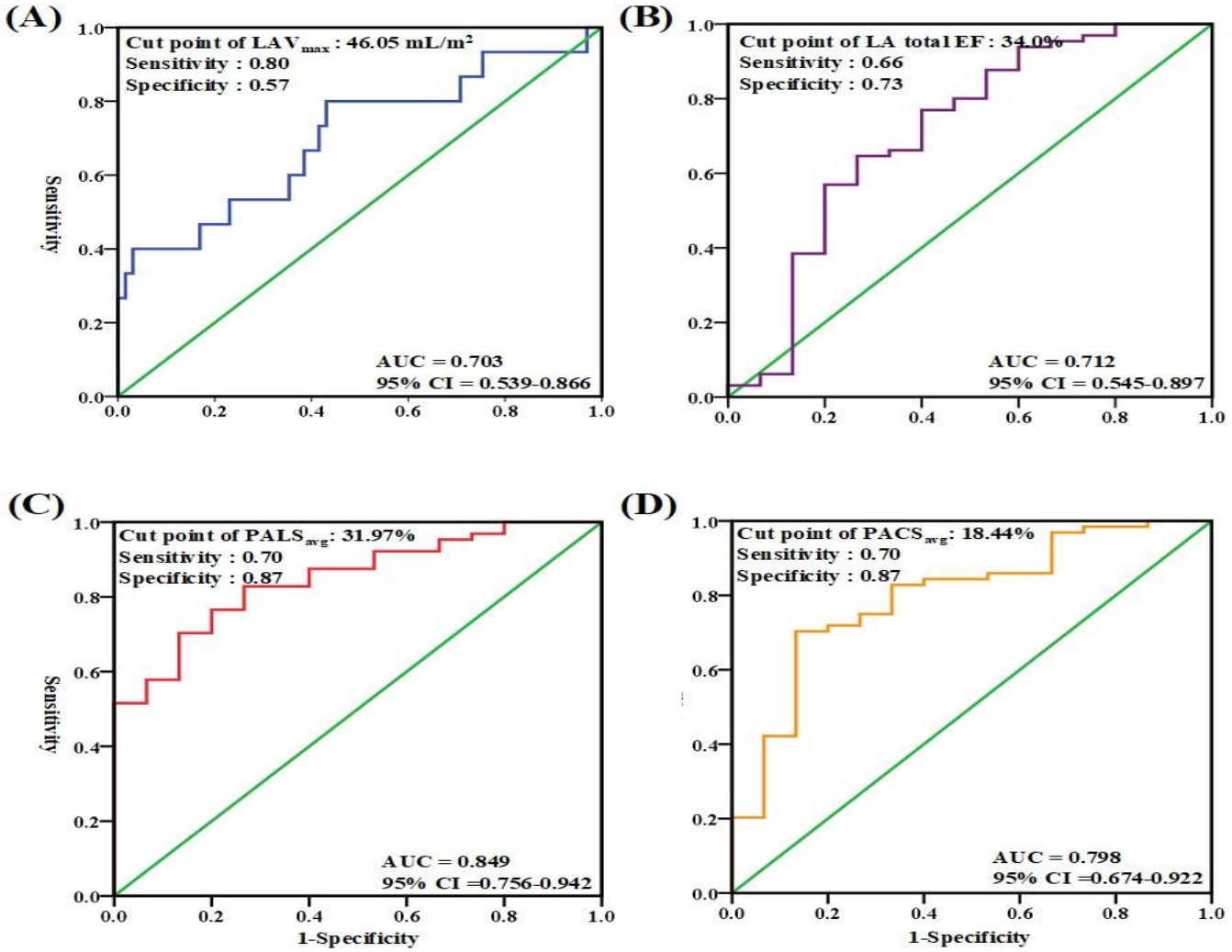


(C) AHREs < 6 minutes

- AHREs burden <0.1 (%)
- LAV_{max} = 33.85 (mL/m²)
- LAV_{min} = 19.38 (mL/m²)
- LA total EF = 42.75 (%)
- 4CH PALS = 34.81 (%)
- 4CH PACS = 10.81 (%)

EGM	Date	Time	Peak A Rate	Duration (H:M:S)	
	29 Jan 2019	05:18	187	00:00:08	Most Recent
	21 Jan 2019	08:32	197	00:00:05	
	13 Jan 2019	08:53	179	00:00:04	
	15 Dec 2018	16:57	179	00:00:06	
	14 Nov 2018	09:46	197	00:00:08	
	29 Oct 2018	02:02	208	00:00:10	Highest A Rate
	16 Oct 2018	07:34	202	00:00:05	
	6 Oct 2018	05:30	192	00:00:28	Longest
	1 Oct 2018	17:25	179	00:00:04	

The association of LAV, LAEF ,PALS and PACS with AHRE> 6 hours



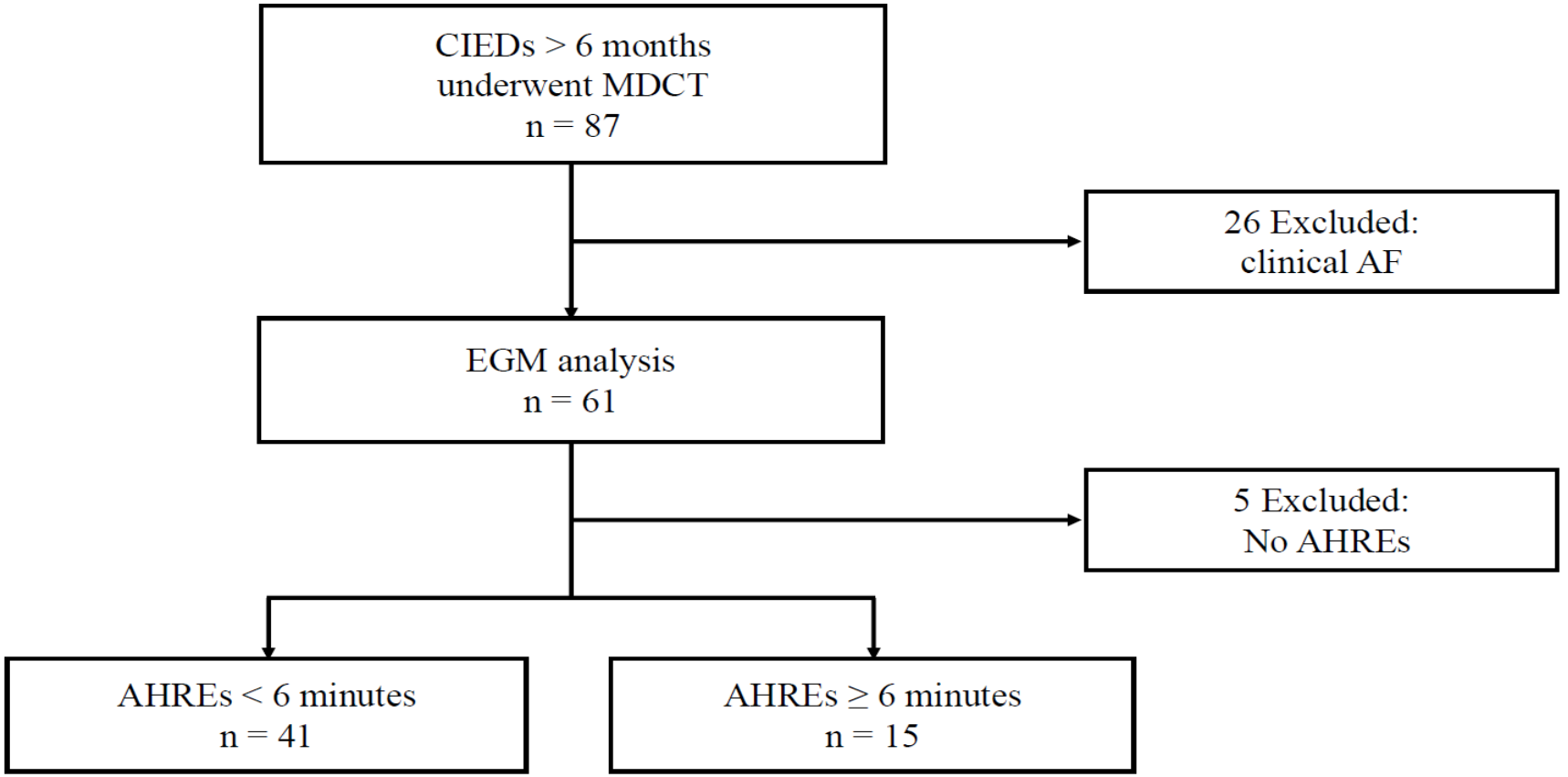
Conclusion: Functional remodeling of the atria manifested after AHRE >6 min. Increased biatrial volumes and decreased LA reservoir and pump function occurred when AHRE were > 6 h. These LA structural and functional may be considered surrogate imaging markers for stroke risk assessment in patients with CHA_2DS_2-VASc $\geq$2 and AHRE.

- **Part 2:**

  Explore the parameters of LA remodeling to predict the longer AHRE (>6 minutes)

Distinct atrial remodeling in patients with subclinical atrial fibrillation: Lessons from computed tomographic images

Sung-Hao Huang[1] | Chao-Feng Liao[1] | Zu-Yin Chen[1] | Tze-Fan Chao[2,3] | Shih-Ann Chen[2,3,4] | Hsuan-Ming Tsao[1,3]



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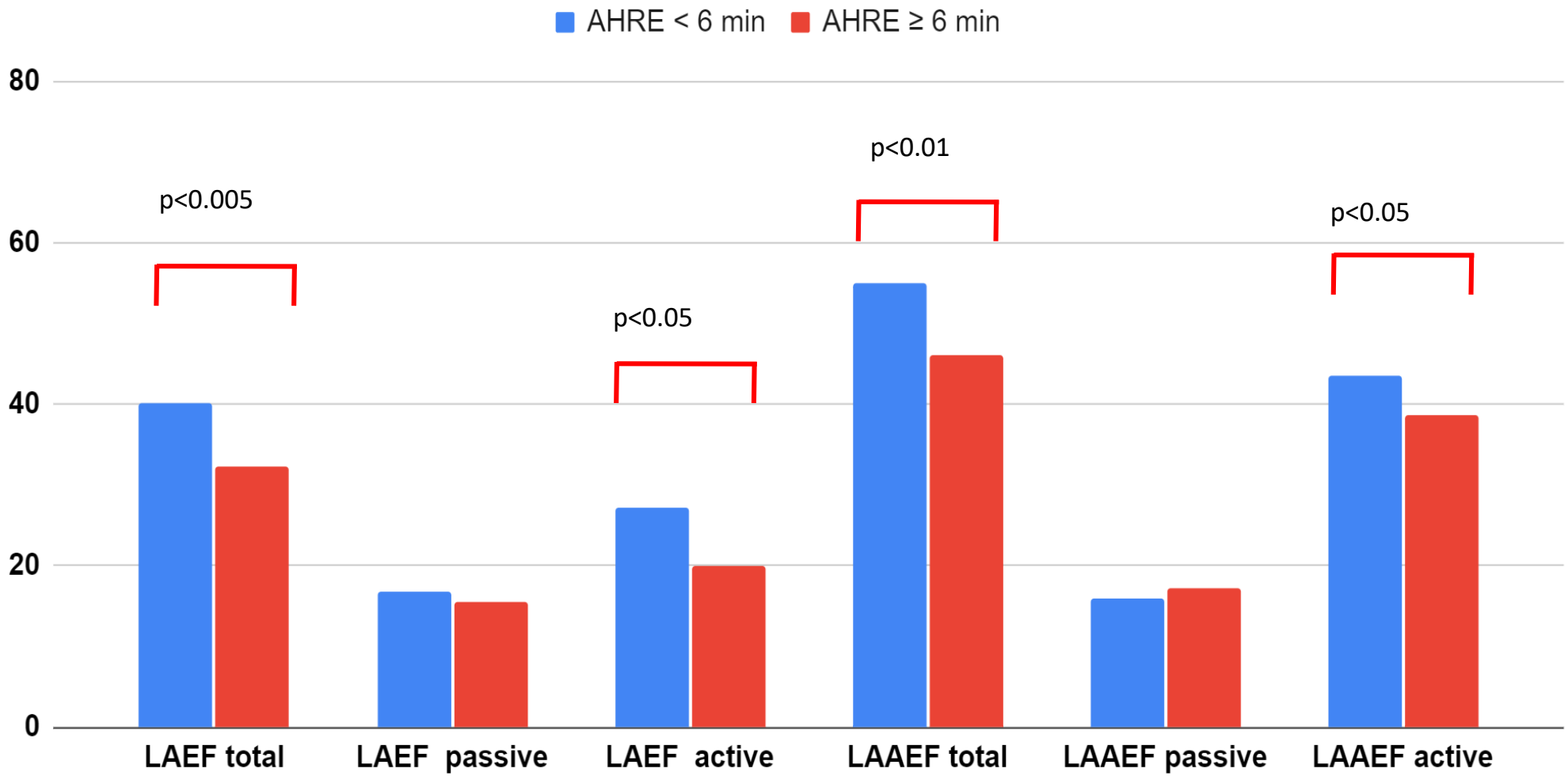
Results

TABLE 1 The clinical and computed tomographic (CT) characteristics of the patients with atrial high-rate episodes (AHREs) =0, <6, and ≥6 min*

	AHREs = 0 (*n* = 12)	AHREs <6 min (*n* = 45)	AHREs ≥6 min (*n* = 21)	*p*-value
Clinical characteristics				
Age	76.1±8.4	75.0±11.9	74.9±7.9	0.941
Prior stroke	1(8)	3(7)	1(5)	0.450
CAD	4(33)	12(27)	4(19)	0.640
CHA_2DS_2-VASc	3.7±1.0	3.5±1.5	3.3±1.2	0.934
Mean AHREs burden (%)	–	0.11±0.07	1.83±4.04	<0.01
Median length of the Longest AHREs (hour:minute:second)	–	00:00:06	01:05:26	–
LAV max (mL)	67.1±15.5	71.6±15.1	80.8±15.1	<0.05
LAV min (mL)	40.6±12.0	43.7±11.7	54.6±18.1	<0.005
LAV precontraction (mL)	57.0±15.5	59.4±13.7	68.6±17.1	<0.05
LA total EF (%)	39.6±8.2	38.8±7.4	31.3±10.5	<0.05
LA passive EF (%)	15.6±8.3	16.8±9.9	15.6±10.6	0.876
LA active EF (%)	29.9±7.5	26.4±9.7	18.9±10.3	<0.05
LAAV max (mL)	5.1±2.1	7.6±3.2	8.5±2.4	<0.05
LAAV min (mL)	2.4±1.1	3.6±1.8	4.2±1.8	<0.05
LAAV precontraction (mL)	4.6±1.7	6.3±2.5	6.6±2.5	0.097
LAA total EF (%)	58.7±11.4	51.3±14.4	45.9±9.6	<0.05
LAA passive EF (%)	20.7±13.3	15.7±7.6	20.6±10.9	0.083
LAA active EF (%)	44.8±10.7	43.1±16.4	37.1±13.7	0.515
HU ratio of LAA/AA	0.97±0.05	0.98±0.03	0.91±0.18	<0.05
Total EAT (cm^3)	25.0±11.8	26.2±8.5	20.7±9.2	0.084
LVEF (%)	59.0±12.9	54.0±13.6	53.0±9.5	0.707

LA and LAA EF and active EF were related to future development of AHRE longer than 6 minutes



Multivariate analysis Results

	Univariate			Multivariate		
LAV min	1.06	1.02–1.10	<0.01	1.02	0.92–1.08	0.572
LAV precontraction	1.04	1.01–1.08	<0.05	–	–	–
LA total EF	0.90	0.84–0.97	<0.01	0.91	0.81–1.01	0.068
LAA total EF	0.96	0.93–1.00	<0.05	0.97	0.93–1.01	0.161
LAA passive EF	0.99	0.98–1.10	0.130	–	–	–
LAA active EF	0.98	0.95–1.01	0.258	–	–	–
HU ratio of LAA/AA	0.86	0.75–0.98	<0.05	0.91	0.79–1.02	<0.05
Total EAT	0.94	0.86–0.98	<0.05	0.94	0.90–1.03	0.267

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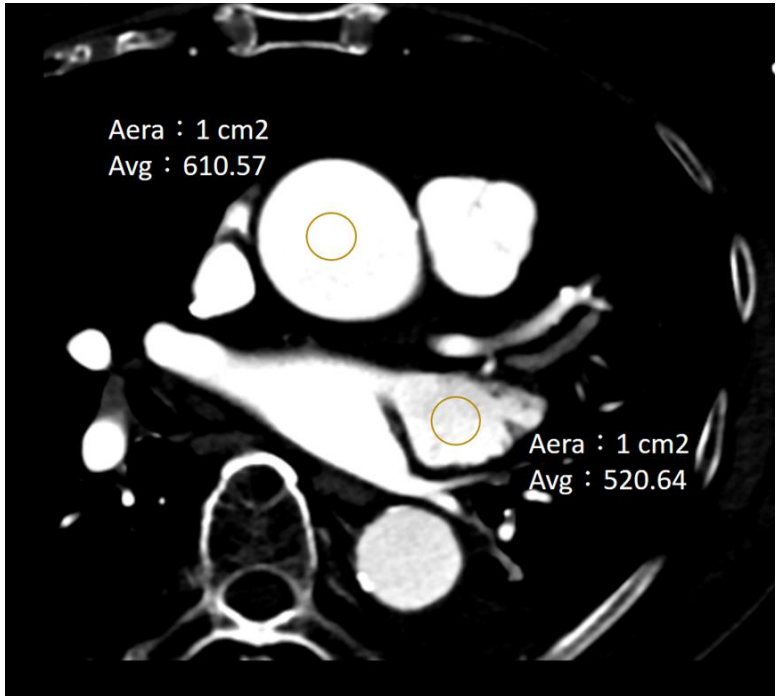
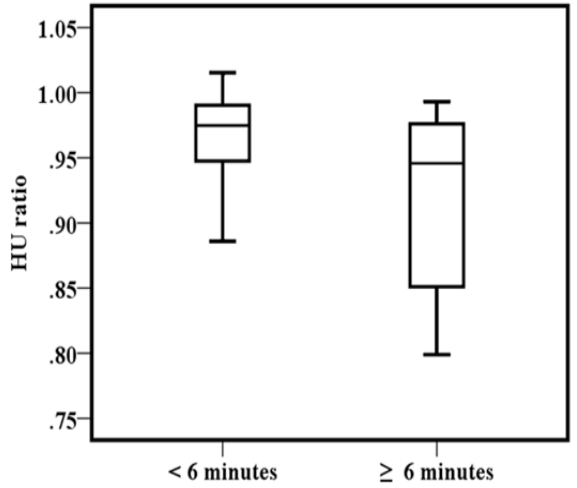
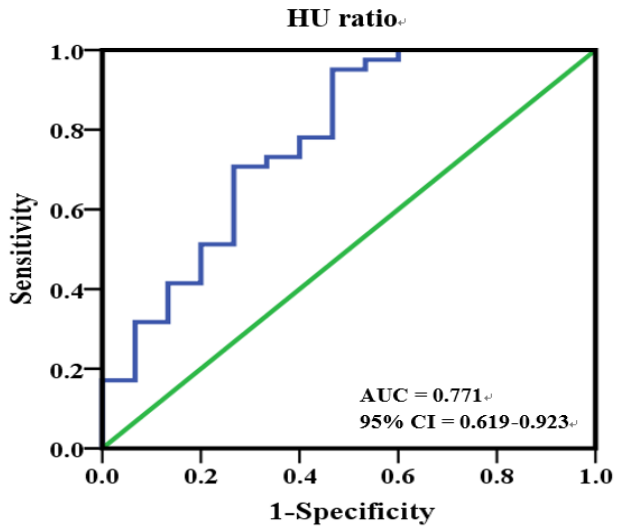
HU ratio of LAA/AA could predict subsequent AHRE> 6 mins



1-cm2 ROI was sampled within the LAA to show the lowest HU values and inside the filling defect, if it existed.
At the same level, another 1-cm2 region was selected in the contrast- enhanced lumen of the ascending aorta



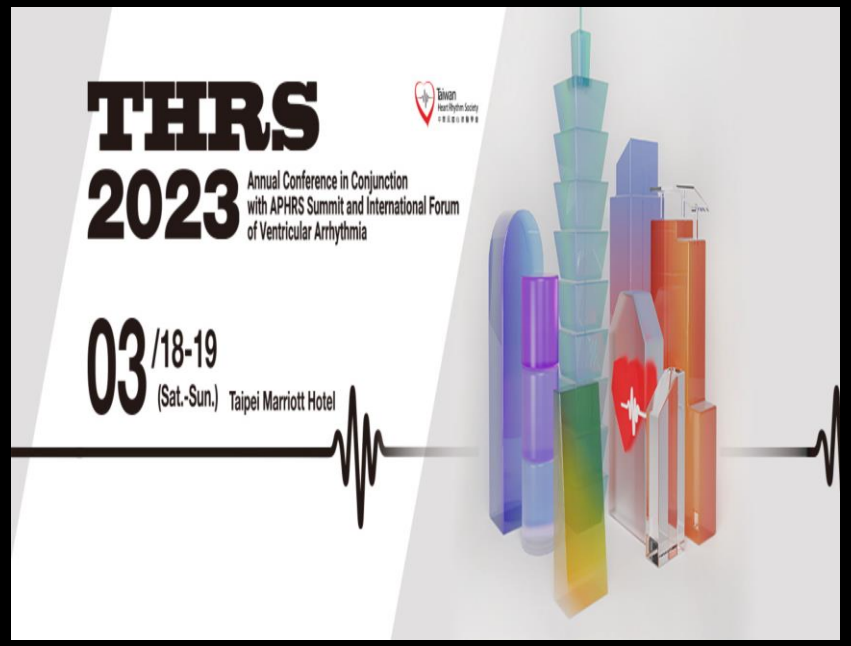
A cutoff point of 0.93 was determined with a 95% sensitivity and 47% specificity.



Conclusions

- Subclinical AF defined as AHRE>6 minutes showed a more favorable remodeling of LA structure and function (compared with clinical AF), which might correlate to the burden of AHRE
- Echocardiography and cardiac CT can delineate the changes of a trial substrate and provide an incremental value to justify the appropriate treatment.
- HU ratio of LAA/AA can serve as a reliable parameter to predict the occurrence of AHRE > 6 minutes and prompt the use anticoagulant in the high risk patients.

國立陽明交通大學附設醫院
National Yang Ming Chiao Tung University Hospital



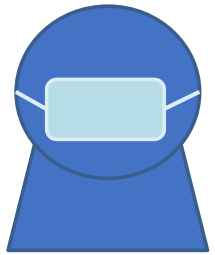
Machine Learning-Enabled Multi-Spectrum Approach Intracardiac Electrogram in Prediction of Atrial High-rate Episodes Sustainability

*Sung-Hao Huang MD[1], *Yu Huang PhD[2], Ting-En Zhao MD[2], Chun-Ti Chou MD[2], Benny Wei-Yun Hsu PhD[2], Vincent S. Tseng, PhD[2], Hsuan-Ming Tsao, MD[1,3], Ling Chen, PhD[4], Shih-Ann Chen MD[3,5,6,7], Wei-Shiang Lin MD[8], Wen-Yu Lin MD[8], Yuan Hung MD[8], Su-Shun Lo MD[3], Gau-Jun Tang MD[4]

[1] Division of Cardiology, Department of Internal Medicine, National Yang Ming Chiao Tung University Hospital, Yilan, Taiwan;
[2] Institute of Computer Science and Engineering, Department of Computer Science, National Yang Ming Chiao Tung University, Hsinchu, Taiwan
[3] School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan;
[4] Institute of Hospital & Health Care Administration, National Yang Ming Chiao Tung University, Taipei, Taiwan;
[5] Heart Rhythm Center, Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan
[6] Cardiovascular Center, Taichung Veterans General Hospital, Taichung, Taiwan
[7] Department of Post Baccalaureate Medicine, College of Medicine, National Chung Hsing University, Taichung, Taiwan
[8] Division of Cardiology, Department of Internal Medicine, Tri-service General Hospital, Taipei, Taiwan

Input

CIEDs



Patients

Two-lead intracardiac electrocardiograms

Feature Extractor

- Age
- Gender
- Height
- Weight
- Hypertension

….

Process

Data Preprocessing and Cleaning

AHRE Sustainability Prediction Framework

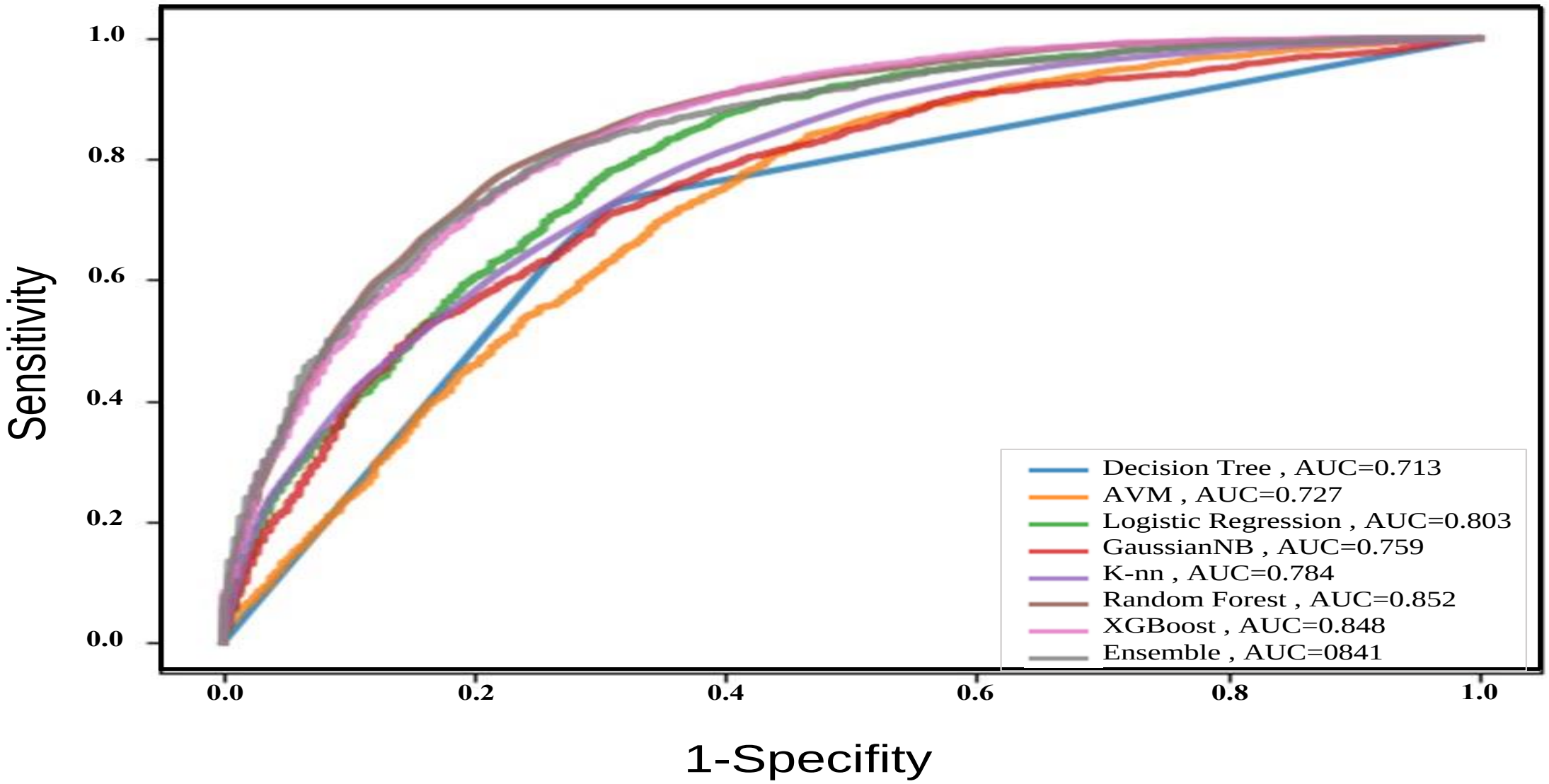
Output

Prediction Model Results

Does the AHRE last for more than six minutes ?

YES/NO

Manuscript in preparation


Sensitivity
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.2
0.4
0.6
0.8
1.0
1-Specifity
Decision Tree , AUC=0.713
AVM , AUC=0.727
Logistic Regression , AUC=0.803
GaussianNB , AUC=0.759
K-nn , AUC=0.784
Random Forest , AUC=0.852
XGBoost , AUC=0.848
Ensemble , AUC=0841

Random Forest

Time domain HRV	Patient profiles	Amplitude	Frequency	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)	AUROC
V				68.99%	68.64%	74.11%	71.22%	0.76
	V			74.24%	74.09%	77.36%	75.67%	0.823
		V		65.0%	65.7%	68.74%	66.93%	0.726
			V	72.69%	70.43%	81.6%	75.59%	0.787
V	V			77.51%	78.11%	78.61%	78.34%	0.849
V		V		71.86%	71.09%	77.01%	73.9%	0.789
V			V	73.45%	72.16%	79.44%	75.59%	0.802
	V	V		74.69%	75.34%	76.15%	75.7%	0.815
	V		V	77.89%	77.88%	80.13%	78.96%	0.853
		V	V	74.3%	72.85%	80.43%	76.43%	0.815
V	V	V		77.31%	77.87%	78.53%	78.18%	0.846
V	V		V	78.48%	78.09%	81.26%	79.63%	0.855
V		V	V	74.89%	73.72%	80.09%	76.75%	0.816
	V	V	V	77.87%	78.03%	79.83%	78.9%	0.854
V	V	V	V	78.0%	78.01%	80.17%	79.06%	0.852

Ensemble

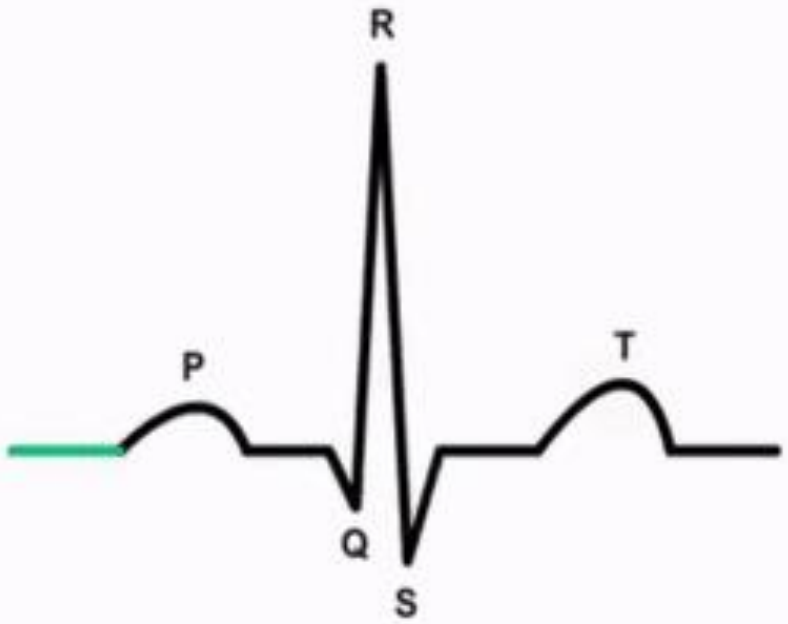
Time domain HRV	Patient profiles	Amplitude	Frequency	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)	AUROC
V				69.6%	65.19%	88.79%	75.16%	0.761
	V			71.68%	68.98%	82.51%	75.11%	0.801
		V		63.52%	63.94%	68.66%	65.99%	0.702
			V	67.65%	63.09%	90.74%	74.41%	0.781
V	V			72.89%	68.43%	88.61%	77.2%	0.824
V		V		70.74%	66.12%	89.48%	76.02%	0.781
V			V	70.72%	66.04%	89.7%	76.05%	0.812
	V	V		71.52%	69.94%	79.0%	74.18%	0.795
	V		V	70.87%	66.57%	88.18%	75.83%	0.822
		V	V	70.2%	65.65%	89.22%	75.62%	0.791
V	V	V		73.74%	69.24%	88.87%	77.81%	0.828
V	V		V	72.85%	68.13%	89.52%	77.36%	0.84
V		V	V	71.68%	66.8%	90.3%	76.78%	0.82
	V	V	V	72.51%	68.51%	87.06%	76.62%	0.824
V	V	V	V	73.63%	68.84%	89.83%	77.93%	0.841

Conclusion

- With incremental characters identification, RF and EM achieved the AUROC scores of 0.84-0.85

- The best accuracy of the AHRE sustainability was 78% by Random Forest ML-model

- We presented a ML-enabled IEGM model for predicting AHRE sustainability in the future in CIEDs based on the early IEGM segment, that may further develop an alarm system to prevent SCAF associated with major cardiovascular events.



Thank you for your attention