出國報告（出國類別：開會）

2025 年美國心律年會

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摘　要

本次赴美參與 2025 年 Heart Rhythm Society 年會，旨在發表本人關於 SGLT2 抑制劑對糖尿病合併心房顫動患者之癌症風險影響之研究，並觀摩國際間在心律疾病與自主神經、腦部結構、基因風險分型等領域的最新成果。會議中多項研究運用多元資料整合與機器學習方法（如二階段分群分析、風險預測模型）對心房顫動進行病人分型與預後預測，並強調心腦交互機轉與臨床應用潛力。本人目前亦正進行相關之心腦交互作用研究，內容聚焦於自主神經變化與腦部灰質萎縮在心律異常病患中的表現與意義。透過此次會議交流，進一步確認本研究方向與國際趨勢接軌，並反思本院在多元資料應用、AI 分析訓練、跨領域研究整合等面向的發展機會，提出具體可行之改進建議以強化研究品質與執行效率。

關鍵字：（至少一組）

心房顫動、SGLT2 抑制劑、心腦交互作用、機器學習、分群分析

目　次

一、 目的

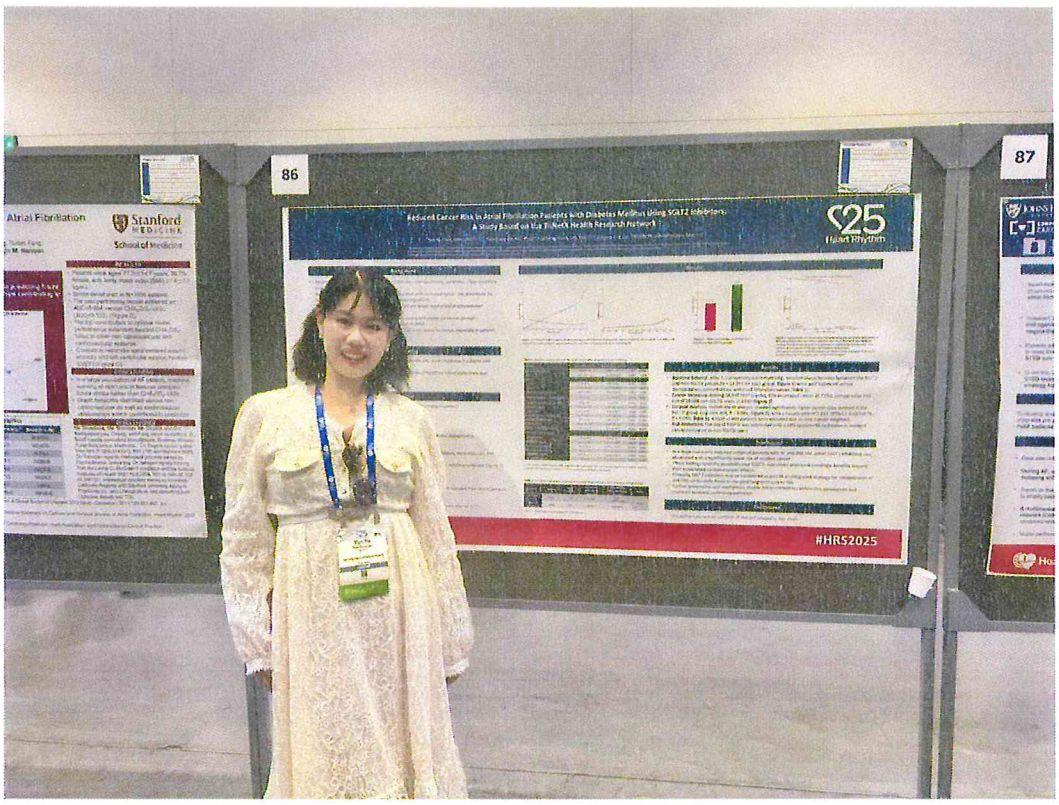
本次出國之主要目的為參加於美國聖地牙哥舉行之 2025 年 Heart Rhythm Society 年會，進行學術海報發表並觀摩國際最新心律疾病相關研究成果。本人於會中發表主題為「SGLT2 抑制劑對糖尿病合併心房顫動患者癌症風險之影響」。另亦希望藉此次會議交流，深入了解目前國際在心房顫動之異質性分群、風險預測模型、自主神經功能與腦部結構變化等跨系統研究進展，對本人目前進行中之「心腦交互作用與心律異常關聯性研究」進行比對與發展延伸方向，進而提升研究品質與臨床應用價值。

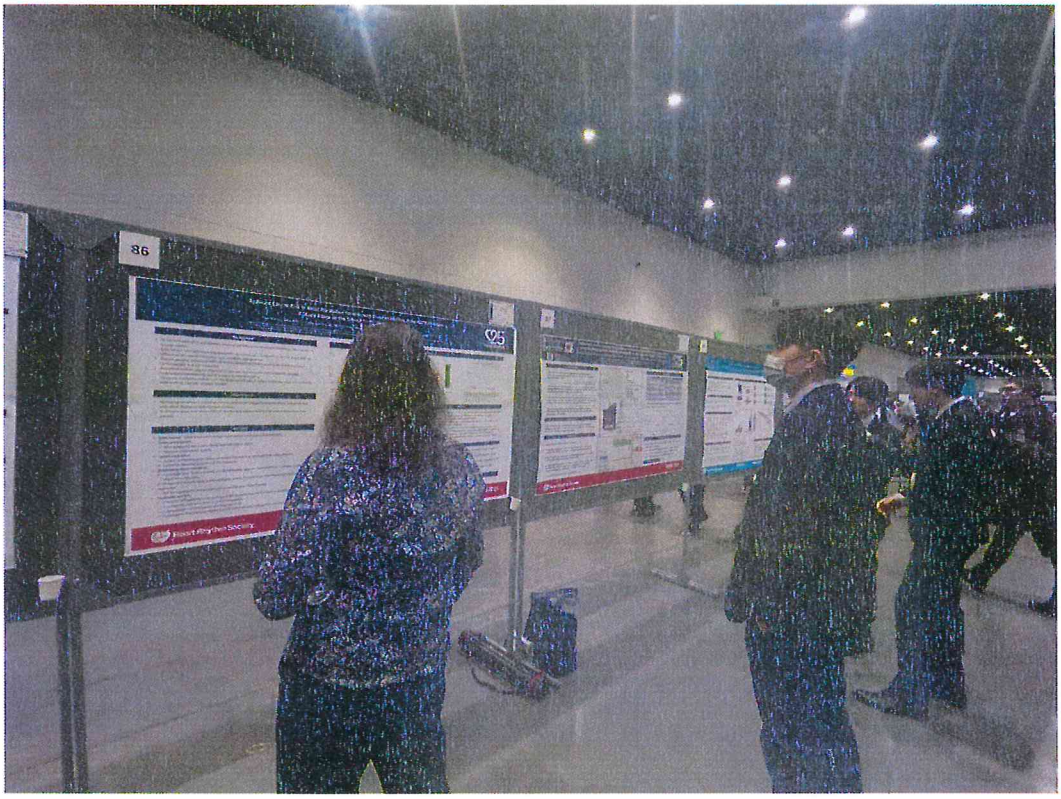
二、 過程

4 月 23 日：自台北搭乘班機經舊金山轉機至聖地牙哥，因班機延誤 8 小時，當日晚間 22:30 抵達下榻飯店（The Bristol Hotel - San Diego）。

4 月 24 日：上午參加 PFA（Pulsed Field Ablation）專題講座，瞭解其作為非熱能心肌電燒方式的最新應用與優勢。晚上參與 EP reunion dinner，與來自全球的電生理專家建立聯繫。

4 月 25 日：本人發表研究海報，主題為：「SGLT2 抑制劑對糖尿病合併心房顫動患者癌症風險之影響」。現場獲得多位專家肯定，並進行深入討論。





4 月 26 日：參觀其他參展者的海報與展區，汲取國際最新研究方向；下午至中途島航空母艦博物館參訪，並於館內餐廳用餐。

4 月 27 日-4 月 28 日：自聖地牙哥返回台北，途經舊金山轉機。

三、 心得

此次參與 Heart Rhythm Society 年會，不僅讓我有機會發表研究成果，也能第一線觀察國際心房顫動（Atrial Fibrillation, AF）研究趨勢，特別是在疾病分型、風險預測與多重共病管理等方面的前沿進展，收穫豐碩。

本人所發表之研究主題為「SGLT2 抑制劑於糖尿病合併心房顫動患者中對癌症風險的影響」，使用美國 TriNetX 多中心臨床資料庫進行回溯性分析。研究結果顯示，在調整相關共變數後，使用 SGLT2 抑制劑的患者其癌症發生風險顯著較低，提示該類藥物除既有的心腎保護作用外，可能亦具備影響癌症發生的潛在生物學效應。此結果有助於支持其作為整合慢性病治療策略之一的可行性，並於會議現場引發與多位學者針對其抗氧化、細胞增殖調控等可能機轉之深入討論。

在其他海報觀摩中，有幾點特別值得一提：

(1) **自主神經與大腦功能影像分型研究（UCLA 團隊）**

該研究首度以 中樞自主神經結構（Central Autonomic Network, CAN）影像指標對 AF 患者進行未監督式分群，發現不同群體間在中風與憂鬱症風險（包括 CHADS-VASc 與抑鬱量表）上具顯著差異。這不僅擴展了傳統以心臟結構與功能為基礎的風險模型，更強化腦心軸在 AF 臨床異質性分析中的角色。

(2) **多基因風險分數（Polygenic Risk Scores, PRS）與臨床風險模型整合（澳洲團隊）**

在 UK Biobank 資料中，研究者將 PRS 與 HARMS-AF 及 CHARGE-AF 等臨床模型結合，提升對 AF 發生的預測精度。此方法展現 群體預防與個體化醫療 的雙重價值，未來若能在亞洲人群中複製並優化演算法，有望應用於健康檢查與早期介入。

(3) **AF 與腦萎縮與認知功能關聯研究（日本千葉大學）**

該研究基於 24 個月的追蹤報告，提出腦部灰質體積在 AF 患者中顯著減少，但是灰質萎縮未必直接對應認知衰退，提醒我們在評估心房顫動的認知併發症時，須同時考量微血管病變、炎症及氧化壓力等多重因素。

(4) **遺傳性心肌病風險預測模型（荷蘭 PLN Arg14del 研究）**

以聯合模型整合心電圖與心臟超音波數據，發展心衰風險預測模型，其 C-index 高達 0.93，展現動態模型於 高遺傳風險族群 中精準預測的能力。此方向對於基因治療興起的背景下，尤具臨床應用潛力。

整體而言，此次年會突顯「跨領域整合與精準醫療」之趨勢：從腦-心-基因-代謝的角度重新定義 AF 的風險與治療；從臨床大數據出發建立可操作的 AI 輔助工具；並逐步朝向個別化、前瞻性的疾病預防策略邁進。作為研究者，我亦更具信心持續推進本地資料的挖掘與國際鏈接，尋求臨床與科學的交匯突破。

四、 建議事項

（一） 設立多元臨床資料支援機制，強化研究資料可及性

為回應國際研究日益重視的資料整合趨勢，建議醫院建立研究導向的多元資料支援機制，例如：統一格式的資料申請範本、變項對照表與查詢諮詢窗口。此作法能協助研究者有效應用診斷碼、藥物紀錄、檢驗數據、心電圖與影像等異質資料，提升研究深度與效率。

（二） 推動 AI 分群與預測模型訓練，導入監督與非監督式學習概念

建議醫院定期開設機器學習入門課程，說明常用方法，包括：

監督式學習（Supervised Learning）：以已知結果（如是否中風）訓練模型，常用於風險預測（如邏輯回歸、XGBoost）。

非監督式學習（Unsupervised Learning）：無需標籤，透過演算法自動分群，例如：

K-means、階層式聚類（Hierarchical Clustering）

Two-stage clustering（二階段分群）：先以簡單模型初步分群，再用進階統計方法確認分群的穩定性與代表性。此方法特別適用於臨床混合型資料，已被廣泛應用於 AF 與多重共病病人分類研究中。

（三） 深化心腦交互研究，支持資料串接與分析模型建構

本次會議強調中樞自主神經、腦部結構與心律異常之潛在交互關聯，亦呼應本人目前正在進行的心腦交互研究。建議醫院可在倫理與技術支援層面，進一步協助既有心電圖、自律神經參數、腦部影像（如 MRI 報告）與認知量表資料的串接與清理，利於建立早期預警模型，提升慢性病整合照護價值。

（四） 簡化跨單位資料申請流程，提升跨領域研究效率

跨單位研究常需調用多系統資料（如心臟影像與用藥紀錄），建議醫院制定「研究資料整合申請指引」，設立單一窗口，由相關部門協助統整流程與初步資料可行性評估，使研究者能清楚掌握各單位資料格式、授權流程與倫理需求，降低合作障礙。

五、 附錄

Reduced Cancer Risk in Atrial Fibrillation Patients with Diabetes Mellitus Using SGLT2 Inhibitors: A Study Based on the TriNetX Health Research Network

Yun-Yu Chen, MPH, PhD[1,2,3,4,5]; Yenn-Jiang Lin, MD, PhD[3,4]; Yu-Cheng Hsieh, MD, PhD[1,2,4]; Gregory Y. H. Lip, MD, FRCP[5]; Shih-Ann Chen, MD[1,2,3,4]

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Background

- Atrial fibrillation (AF) and diabetes mellitus (DM) are common chronic conditions, often coexisting in older adults.
- Both AF and DM have been independently associated with increased cancer risk, potentially via inflammation, insulin resistance, and metabolic dysregulation.
- Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are widely used in DM and have shown cardiovascular and renal benefits.
- Preclinical studies suggest that SGLT2i may also possess anti-cancer properties through mechanisms like reducing insulin levels and oxidative stress.
- However, real-world evidence on the impact of SGLT2i on cancer incidence, especially in patients with both AF and DM, remains limited.

Objective(s)

- To investigate whether SGLT2i use is associated with reduced cancer incidence in patients with both atrial fibrillation and diabetes mellitus.
- To utilize a large, real-world multi-institutional database (TriNetX) for robust population-level analysis.

Method

- **Data source:** TriNetX Research Network (81 global healthcare organizations).
- **Study population:**
  - ✓ Adults aged 55–85 with both AF and DM (2016–2023).
  - ✓ Minimum follow-up: 1 year.
- **Cohort definition:**
  - ✓ Cohort A: Patients with documented SGLT2i use (e.g., empagliflozin, dapagliflozin).
  - ✓ Cohort B: Patients with no SGLT2i exposure.
- **Propensity-Score Matching:**
  - ✓ 1:1 propensity score matching (PSM) to balance age, sex, comorbidities, medication use, and healthcare utilization.
  - ✓ Probability density plots were applied to assess if it is balance after marching technique (Figure 1).
- **Outcome:**
  - ✓ Primary endpoint: new-onset cancer identified via ICD-10 codes.
- **Statistical analysis:**
  - ✓ A total of 266 patients in Cohort 1 and 403 patients in Cohort 2 were excluded from results because they had the outcome prior to the time window.
  - ✓ Kaplan-Meier survival curves and log-rank tests.
  - ✓ Cox proportional hazards model: hazard ratio (HR with 95% confidence interval [CI]).

Results

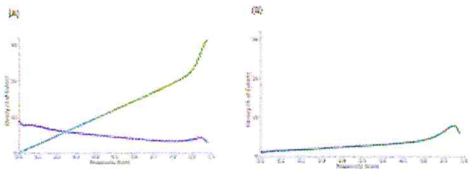

Figure 1. Probability density plots demonstrating the distribution of propensity scores in SGLT2i users (cohort 1, purple) and non-SGLT2i users (cohort 2, green) before (A) and after 1:1 propensity score matching (B).

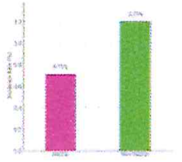

Figure 2. Cancer cumulative incidence rate in SGLT2i and Non-SGLT2i groups.

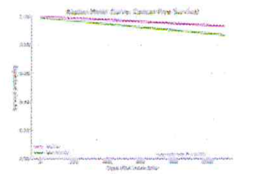

Figure 3. Kaplan-Meier survival analysis demonstrating the cumulative probability of remaining cancer-free over time in patients with atrial fibrillation and diabetes mellitus. The SGLT2i group (pink line) exhibited a significantly higher cancer-free survival rate compared to the non-SGLT2i group (green line). (The patients in Cohort 1 and 403 patients in Cohort 2 were excluded from results because they had the outcome prior to the time window.)

Table 1. Baseline characteristics of the study cohort after propensity score matching

Variables	SGLT2i (N=17011)	Non-SGLT2i (N=17011)	P-value	SMD
Age at baseline (years)	[illegible]	[illegible]	[illegible]	[illegible]
Male, n (%)	[illegible]	[illegible]	0.982	[illegible]
Race (%)				
- Asian	[illegible]	[illegible]	[illegible]	[illegible]
- White	[illegible]	[illegible]	[illegible]	[illegible]
- Black or African American	[illegible]	[illegible]	[illegible]	[illegible]
- Native Hawaiian or Pacific Islander	[illegible]	[illegible]	[illegible]	[illegible]
- American Indian or Alaska Native	[illegible]	[illegible]	[illegible]	[illegible]
- Unknown Race	[illegible]	[illegible]	[illegible]	[illegible]
- Other Race	[illegible]	[illegible]	[illegible]	[illegible]
Essential (primary) Hypertension	[illegible]	[illegible]	[illegible]	[illegible]
Secondary Hypertension	[illegible]	[illegible]	[illegible]	[illegible]
Hyperlipidemia	[illegible]	[illegible]	[illegible]	[illegible]
Chronic Kidney Disease (CKD)	[illegible]	[illegible]	[illegible]	[illegible]
Laboratory Measurements				
Glucose (mg/dL)	[illegible]	[illegible]	<0.001	[illegible]
Cholesterol (mg/dL)	[illegible]	[illegible]	<0.001	[illegible]
LDL Cholesterol (mg/dL)	[illegible]	[illegible]	<0.001	[illegible]
HDL Cholesterol (mg/dL)	[illegible]	[illegible]	[illegible]	[illegible]
Triglyceride (mg/dL)	[illegible]	[illegible]	<0.001	[illegible]
Hemoglobin A1c (%)	[illegible]	[illegible]	<0.001	[illegible]

CKD, chronic kidney disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SGLT2i: Sodium-glucose cotransporter-2 inhibitors; SMD, standardized difference of means.

Table 2. Comparison of cancer incidence and hazard ratios between SGLT2i and Non-SGLT2i groups.

Cohort	Number	Event number	Hazard Ratio (95% confidence interval)	P-value
Group A: SGLT2i	16745	119	0.611 (0.487-0.767)	<0.001
Group B: Non-SGLT2i	16608	199	Reference	

SGLT2i: Sodium-glucose cotransporter-2 inhibitors.

Results

- **Baseline Balance:** After 1:1 propensity score matching, baseline characteristics between the SGLT2i and non-SGLT2i groups (N = 17,011 for each group; **Figure 1**) were well balanced across demographics, comorbidities, and most laboratory values (**Table 1**).
- **Cancer Incidence:** Among 16,745 SGLT2i users, 119 developed cancer (0.71%), compared to 199 out of 16,608 non-SGLT2i users (1.20%) (**Figure 2**).
- **Survival Analysis:** Kaplan-Meier analysis showed significantly higher cancer-free survival in the SGLT2i group (Log-rank test, P < 0.001; **Figure 3**), with a hazard ratio of 0.611 (95% CI: 0.487–0.767; P < 0.001; **Table 2**). A total of 669 patients were excluded due to prior cancer diagnosis.
- **Risk Reduction:** The use of SGLT2i was associated with a 39% relative risk reduction in incident cancer compared to non-SGLT2i users.

Conclusion

- In a large real-world matched cohort of patients with AF and DM, the use of SGLT2 inhibitors was associated with a significantly lower risk of incident cancer.
- These findings raise the possibility that SGLT2i may confer additional oncologic benefits beyond their established cardiometabolic effects.
- Clinically, SGLT2 inhibitors may be considered as part of an integrated strategy for patients with AF and DM, particularly those at elevated long-term cancer risk.
- Further prospective and mechanistic studies are warranted to confirm this association and elucidate potential underlying pathways.

Disclosures

- The authors declare no conflicts of interest related to this study.

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Graph Networks of Clinical Features that Predict Stroke in Atrial Fibrillation Patients from Machine Learning Models

Stanford Cardiovascular Institute

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BACKGROUND

- Atrial fibrillation (AF) affects 5-10 million people in the U.S. is strongly associated with a risk for stroke[1,2].
- However, the CHA_2DS_2-VASc score is suboptimal, and the 2023/4 AF guidelines stress the need for improved predictors[3].
- As such, a critical unanswered question is: **Can we improve stroke prediction compared to CHA_2DS_2-VASc?**

HYPOTHESIS

- **We hypothesized that a machine learning model comprising >100 clinical features could predict subsequent stroke in AF patients better than the current CHA_2DS_2-VASc in a large registry.**
- **We further hypothesized that developing a graph network to the model would identify novel relationships between features.**

METHODS

- We studied N=7,498 patients diagnosed with AF at a large academic-community hospital network.
- We applied univariate statistics to identify the most relevant features, then applied Random Forest machine learning.
- We analyzed 104 time-dependent covariates to identify features associated with subsequent stroke, compared to the CHA_2DS_2-VASc score.
- We then utilized the correlation graph to identify feature relationships within the optimal model.

Major Finding

Machine learning leveraging rich clinical features outperformed CHA_2DS_2-VASc in predicting future stroke among AF patients. Graph network analysis further revealed key relationships contributing to prediction.

Figure B: Predicting Stroke

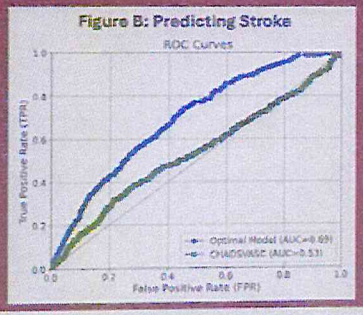

Figure C: Graph Network Linking AF & Stroke

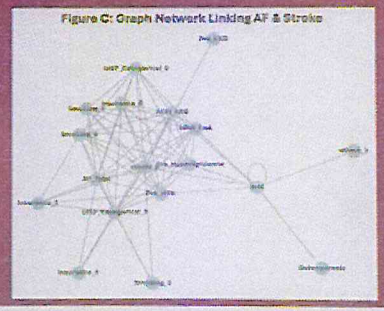

Figure A: Study Design

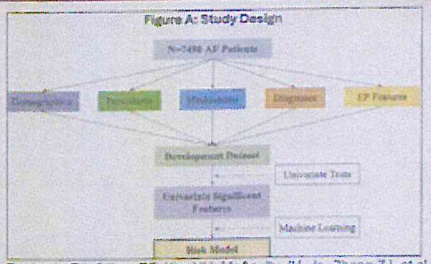

Table. Patient Demographics

Feature	Non-Stroke(N=6342)	Stroke (N=1156)
Age*	77.4±14.9	80.8±13.2
Female Gender, N (%)*	2481 (39.0)	493 (42.6)
BMI*	27.5±6.6	26.7±6.4
Racial Category = White, N (%)	4004 (63.1)	750 (64.9)
Congestive Heart Failure, N (%)	977 (15.4)	200 (17.3)
Chronic Kidney Disease, N (%)*	717 (11.3)	164 (14.2)
CHA2DS2-VASc*	2.6±1.2	2.8±1.5
Hypertension, N (%)*	2572 (40.6)	560 (48.4)

RESULTS

- Patients were aged 77.9±14.7 years, 39.7% female, with body mass index (BMI) 27.4±7.0 kg/m2.
- Stroke developed in N=1156 patients.
- The best performing model achieved an AUC=0.694 versus CHA_2DS_2-VASc (AUC=0.533) (Figure B).
- The top contributors to optimal model performance extended beyond CHA_2DS_2-VASc to other non-cardiovascular and cardiovascular features.
- Correlation networks were centered around ethnicity and left ventricular ejection fraction (LVEF) (Figure C).

CONCLUSIONS

- In a large population of AF patients, machine learning of rich clinical features predicted future stroke better than CHA_2DS_2-VASc.
- Graph networks identified various non-cardiovascular as well as cardiovascular relationships which contributed to prediction.

DISCLOSURES

Mr. Srivastava, Ms. Brennan, Mr. Clopton, and Drs. Bandyopadhyay, Chang, and Feng report no conflicts. Dr. Brodt reports consulting from Atricure, Biosense Webster, Pulse Bioscience, Medtronic. Dr. Rogers reports grants from NIH (F32HL144101), NIH LRP, and Stanford SSPS. Dr. Ganesan reports intellectual property owned by Florida Atlantic University. Dr Narayan reports funding from the Laurie C. McGrath Foundation and the National Institutes of Health (R01 HL83359, R01 HL149134, T32 HL166155), intellectual property owned by University California Regents and Stanford University, equity in PhysCade Inc. and Lifesignals.ai, and consulting from Uptodate, Abbott and TDK.

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A Novel Risk Score For The Identification of Heart Failure with Preserved Ejection Fraction in Patients with Atrial Fibrillation: The $LOAD_2$ score

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Background

- Heart failure with preserved ejection fraction (HFpEF) commonly co-exists in patients with atrial fibrillation (AF).
- Diagnosis is challenging and often overlooked or delayed due to the symptom similarities between AF and HFpEF.
- The gold standard for diagnosing HFpEF requires invasive right heart catheterization.
- In the broader population, non-invasive scoring systems have been developed to identify patients with a high probability of HFpEF, however these have shown limited utility in the AF population.
- With emerging therapeutic options for the treatment of HFpEF, early identification may assist with improving patient quality of life and outcomes.

Objective: Develop a non-invasive bedside scoring system to improve early identification of HFpEF in patients with atrial fibrillation.

Method

Consecutive symptomatic patients with paroxysmal or persistent AF scheduled for an AF ablation were included. Individuals undertook non-invasive clinical investigations in the 4 weeks prior to their AF ablation procedure. Invasive measurement of mean left atrial pressure was undertaken following transseptal puncture for AF ablation. HFpEF defined as left atrial pressure > 15mmHg at rest.

Non-invasive

Clinical data and exercise testing undertaken prior to ablation procedure.

Invasive

Pressure data collected at time of ablation procedure.

- Clinical and echocardiographic variables were assessed for their ability to predict HFpEF.
- For continuous variables, Receiver Operating Characteristic Analysis was performed, and Youden's Index was calculated to determine optimal cut-off values.
- Categorical variables were assessed using odds ratios.
- Logistic regression was used to assess the association between predictor variables and invasive evidence of HFpEF with stepwise backward selection applied to refine the model.
- Model performance was evaluated using Receiver Operating Characteristic Analysis.
- The sensitivity and specificity of the model were compared against two existing models, H$_2$FpEF and HFA-PEFF.

Results

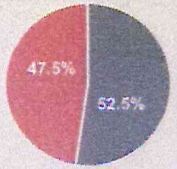
Baseline characteristics	No HFpEF (n=63)	HFpEF (n=57)	p-value
Age (years)	62.1±10.4	65.7±11.8	0.082
Female n (%)	16 (25%)	20 (35%)	0.333
BMI (kg/m^2)	27.6±4.4	30.2±4.9	0.003
Paroxysmal AF n (%)	32 (51%)	27 (47%)	0.799
Hypertension n (%)	37 (59%)	47 (82%)	0.121
Diabetes n (%)	3 (5%)	12 (21%)	0.012
Sleep Apnoea n (%)	20 (32%)	14 (25%)	0.460
Stroke n (%)	5 (8%)	4 (7%)	0.864
CAD n (%)	4 (6%)	6 (11%)	0.429
Previous Ablation n (%)	24 (38%)	23 (40%)	0.844
Global longitudinal strain	16.2±2.8	12.5±2.7	0.017
E/e'	8.4±2.6	10.7±3.4	<0.001

Multivariable analysis identified the following variables for the final prediction model:

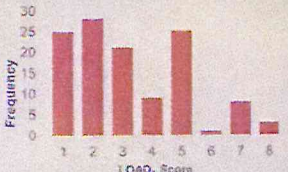
		Definition	Score
L	Left ventricular dysfunction	GLS<16%	1
O	Obesity	BMI> 30kg/m^2	2
A	AF duration	AF duration>10 years	2
D_2	Diabetes	Type 2 Diabetes	2
	Diastolic dysfunction	E/e' >10	3

Variables considered in logistic regression not included in final model: Hypertension, Age, Pacemaker, NT-proBNP, Aerobic Capacity (VO_{2peak}) and Left Atrial Reservoir Strain.

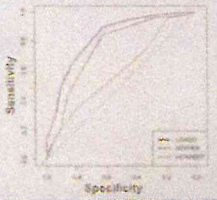
Prevalence of HFpEF



Distribution of $LOAD_2$ Scores



$LOAD_2$ Performance



- The $LOAD_2$ score demonstrated good discrimination, with an AUC of 0.87.
- Each 1-point increase was associated with an odds ratio of 2.8 (95% CI: 1.6-2.7) for HFpEF.
- A score of 3 had 89% sensitivity and 62% specificity (Youden .51).
- A score of 6 or higher provided >90% specificity.
- The $LOAD_2$ score outperformed existing HFpEF scores: H2FPEF (0.756, p=0.05) and HFA-PEFF (0.596, p<0.01)

Conclusion

The $LOAD_2$ score is a simple, non-invasive tool to improve identification of HFpEF in patients with atrial fibrillation.

$LOAD_2$ The University of Adelaide Royal Adelaide Hospital

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Comparative Outcomes of GLP1-RA and SGLT2i on AF Recurrence After Catheter Ablation in Patients with Type 2 Diabetes: A Population-Based Cohort Study

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Nuvance Health

HRS25 Heart Rhythm

Background

- Glucagon-like peptide-1 receptor agonists (GLP-1 RA) and sodium glucose co-transporter 2 inhibitors (SGLT2i) are well established to reduce major cardiovascular outcomes, with recent data revealing reduction in post-ablation atrial fibrillation (AF) recurrence individually.

Objectives

- This study aims to investigate the comparative effects of GLP-1 RA users to SGLT2i users upon recurrent atrial fibrillation (AF) post ablation in patients with type 2 diabetes.

Methods

- Using the TriNetX database, we included adults (≥18 years) with type 2 diabetes and diagnosis of AF or AFL who received catheter ablation of AF or AFL between 01/01/2010 and 12/31/2023.
- Patients were categorized into 2 groups:
  - Those treated with GLP-RA after ablation
  - Those treated with SGLT2i after ablation
- Propensity score matching balanced demographics, biomarkers (BNP), clinical characteristics, and medications (including insulin, metformin, diuretics, antiarrhythmics and antithrombotics).
- Kaplan-Meier analysis and hazard ratios (HR) with 95% confidence intervals (CIs) compared composite cardioversion, anti-arrhythmic therapy, or recurrent atrial fibrillation ablation outcomes, heart failure exacerbations, all-cause hospitalizations, ischemic stroke and all-cause death.

Disclosures

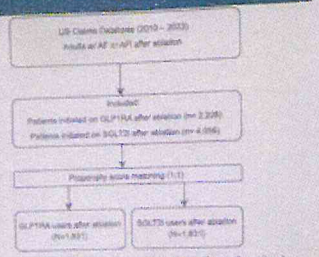
No Disclosure.

Results

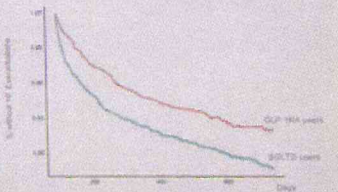
A total of 1,831 matched pairs of GLP1-RA users to SGLT2i users were included (mean age 66.7 years, males 59.5%).

Compared to SGLT2i users, GLP1-RA users demonstrated
- Significantly lower risk of heart failure exacerbations compared to SGLT2i users (HR=0.707, 95% CI=0.592-0.845, p<0.0001)

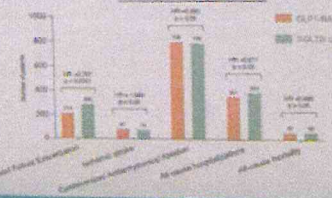
There was no significant difference between groups in
- Composite cardioversion, anti-arrhythmic therapy, or recurrent atrial fibrillation ablation outcomes (HR=0.96, 95% CI=0.888-1.081, p=0.686)
- Ischemic stroke (HR=1.065, 95% CI=0.777-1.46, p=0.693)
- All-cause hospitalizations (HR=0.877, 95% CI=0.759-1.014, p=0.075)
- All-cause death (HR=0.985, 95% CI=0.685-1.411, p=0.935)



Heart Failure Exacerbation-Free Survival



Hazard Ratio Outcomes



Conclusion

- These findings suggest that post-procedural use of GLP1-RA may further reduce heart failure exacerbations compared to SGLT2i, although there are no significant differences in recurrent AF or other related AF adverse outcomes. Further prospective investigations are warranted to confirm these findings.

In patients with type 2 diabetes and AF/ AFL, post procedural use of GLP1-RA compared to SGLT2i may further reduce heart failure exacerbations.

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Title: A Dynamic Risk Prediction Model for Heart Failure in Phospholamban p.(Arg14del)-positive Individuals: A Step Towards Patient Selection for Future Genetic Therapies

Background

Future genetic therapies are emerging rapidly and could be lifesaving for patients with an **inherited cardiomyopathies.**

For phospholamban ***(PLN)*** **p.(Arg14del)-positive individuals**, accurate risk prediction is crucial to identify those who will benefit most, as this variant exhibits **reduced penetrance and a highly variable expression.**

Objective(s)

The aim of this study is **to identify *PLN* p.(Arg14del)-positive individuals at risk of heart failure** using a dynamic heart failure risk model.

Method

- Data were collected of **330 *PLN* p.(Arg14del)-positive individuals**, median age 42 (IQR 30-55), 45% male.
- The median follow-up period was **7.1 years** (IQR 3.6-11.6) after first cardiological investigation.
- **35 (~11%)** individuals developed the heart failure endpoint.
- **Combined heart failure endpoint:** heart failure hospitalization, left- or biventricular assist device implantation, heart transplantation or heart failure-related death.
- The **LVEF (%)** was derived from echocardiography, and the **QRS amplitude (lead aVR)** was derived from standard 12-lead ECG using Modular ECG Analysis System (MEANS).

Results

JOINT MODEL

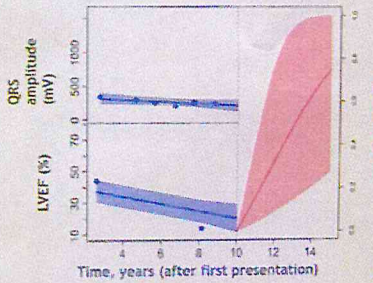
→LONGITUDINAL SUBMODEL

- LVEF (%)
  - mean (intercept) 53.49 (±0.58, *P* <0.001)
  - mean decrease of 0.50% points per year (±0.11, *P* <0.001)
- QRS amplitude (lead aVR)
  - mean (intercept) 555.85 (±15.5, *P* <0.001)
  - mean decrease of -13.0 mV per year (±1.61, *P* <0.001)
  - sex (male) 59.38 (±19.41, *P* =0.002)

→SURVIVAL SUBMODEL

- Age at baseline HR 1.024 (95% CI 0.987-1.063, *P* = 0.206)
- Spatial QRS amplitude (lead aVR) HR 0.996 (95% CI 0.992 - 0.999, *P* = 0.008)
- LVEF HR 0.867 (95% CI 0.817-0.913, *P* = <0.001)

Figure 1.
Example individual trajectory and heart failure risk prediction using Joint Model.



DYNAMIC (3-YEAR) C-STATISTIC RANGING FROM 0.83 TO 0.93 DURING TEN YEARS OF FOLLOW-UP

Conclusion

This study presents a dynamic model incorporating longitudinal ECG and echocardiographic data to predict heart failure risk in *PLN* p.(Arg14del)-positive individuals, offering a foundation for optimizing patient selection for future genetic therapies.

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Combining Polygenic with Clinical Risk Scores in Atrial Fibrillation Risk Prediction: Implications for Population Screening

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Heart Rhythm 25

Background

AF development is determined by clinical risk factors and genetic predisposition. Few studies have explored integration of polygenic risk scores (AF-PRS) to enhance clinical risk prediction models.

Objective(s)

We evaluated the interaction between AF-PRS and the $HARMS_2$-AF and CHARGE-AF clinical risk scores on incident AF risk among the UK Biobank.

Method

AF-PRS was examined in those with and without incident AF based on ICD-10 coding (baseline AF was an exclusion) and divided into tertiles to create low, intermediate and high-risk categories.

Regression analysis examined the combined impact of AF PRS and the $HARMS_2$-AF and CHARGE-AF risk scores and incident AF risk.

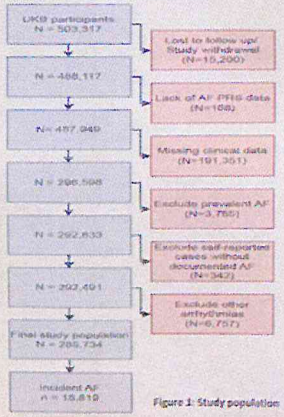


Figure 1: Study population

Results

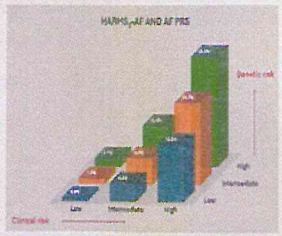
Among 285,734 participants with available whole genome sequencing data (52% female, age 57 years (IQR 50-63), 84.6% caucasian), AF incidence was 6.6% with a median time to AF 8.5 (IQR 5.0-11.2) over median 12.9 years follow up.

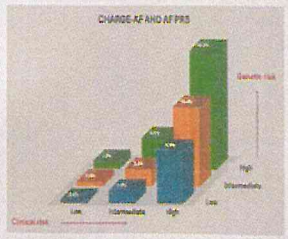
	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Hypertension	6.063 (5.855, 6.319)	<0.001	3.578 (3.434, 3.729)	<0.001
Age	1.101 (1.087, 1.126)	<0.001	1.099 (1.095, 1.102)	<0.001
Obesity (BMI >30kg/m^2)	1.864 (1.794, 1.936)	<0.001	1.370 (1.309, 1.435)	<0.001
Male sex	2.302 (2.218, 2.389)	<0.001	1.888 (1.811, 1.967)	<0.001
Sleep apnoea	3.632 (3.344, 3.945)	<0.001	2.115 (1.930, 2.318)	<0.001
Smoking	1.586 (1.531, 1.644)	<0.001	1.135 (1.092, 1.179)	<0.001
Alcohol >10 standard drinks/wk	1.239 (1.195, 1.284)	<0.001	1.044 (1.003, 1.086)	<0.001
Diabetes	2.332 (2.187, 2.486)	<0.001	0.562 (0.516, 1.053)	0.515
Physical inactivity	1.076 (1.028, 1.125)	0.001	1.010 (0.962, 1.060)	0.695
AF-PRS (high)	2.057 (1.985, 2.131)	<0.001	2.754 (2.523, 2.892)	<0.001

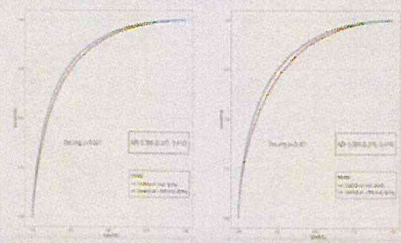
High AF-PRS tertile was independently associated with incident AF risk, after adjustment for clinical risk factors (HR 2.75, 95% CI 2.62-2.89, p<0.001).

AF-PRS enhanced AF risk prediction when combined with:

- $HARMS_2$-AF (AUC 0.839 (DeLong p<0.001, NRI 0.395 [0.377, 0.412])
- CHARGE-AF risk models (AUC 0.828 (DeLong p<0.001, NRI 0.394 [0.376, 0.414]).







Conclusion

Combining genetic and clinical risk using the $HARMS_2$-AF and CHARGE-AF risk scores significantly improved AF risk prediction. Incorporating polygenic to clinical risk scores may enhance poputation screening and promote targeted interventions to reduce the incidence of AF.

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