



Left common trunkus pulmonary veins have genetic background and poorer rhythm outcome after paroxysmal atrial fibrillation catheter ablation



Sung Hwa Choi, MD*; Tae-Hoon Kim, MD; Myunghee Hong, PhD*; Oh-Seok Kwon, PhD; Daehoon Kim, MD; Je-Wook Park, MD; Hee Tae Yu, MD, PhD; Jae-Sun Uhm, MD, PhD; Boyoung Joung, MD, PhD; Moon-Hyoung Lee, MD, PhD; Chun Hwang, MD; Hui-Nam Pak, MD, PhD

Yonsei University Health System, Seoul, Republic of Korea

Korean Heart Rhythm Society

COI Disclosure

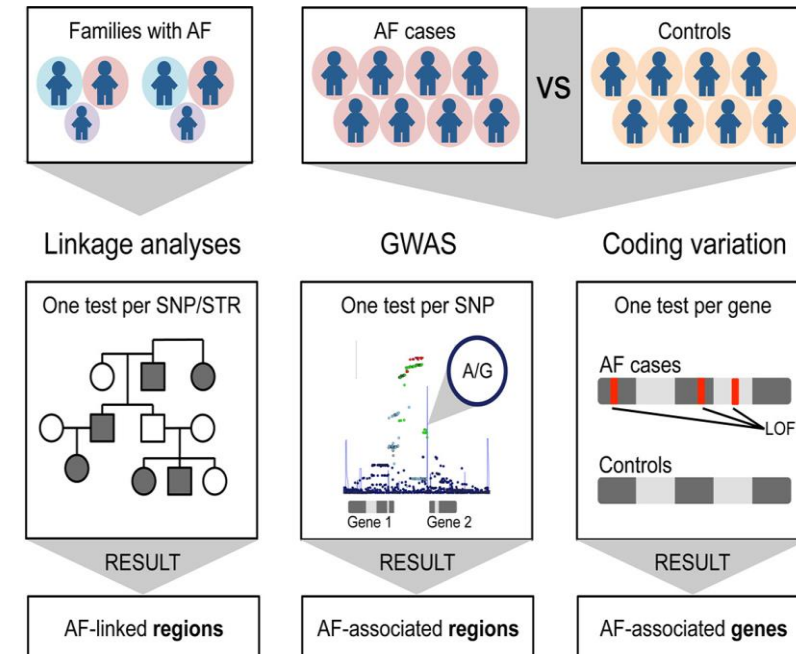
Sung Hwa Choi

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



Introduction

- Various risk factors for atrial fibrillation (AF) have been identified, recent studies have shown that **genetic factors** also play an important role in its development.
- Certain **pulmonary vein (PV) variants**, such as left common trunkus (LCT)-PV and accessory PV, are also associated with an increased risk of atrial fibrillation (AF).
- However, the **genetic trait of PV variations** and their **rhythm outcome** after AF catheter ablation (AFCA) is unclear.



Objective

- This study aimed to explore the **genetic and clinical characteristics of AF patients with LCT-PV or accessory PV** and their **rhythm outcomes after AFCA**



Methods

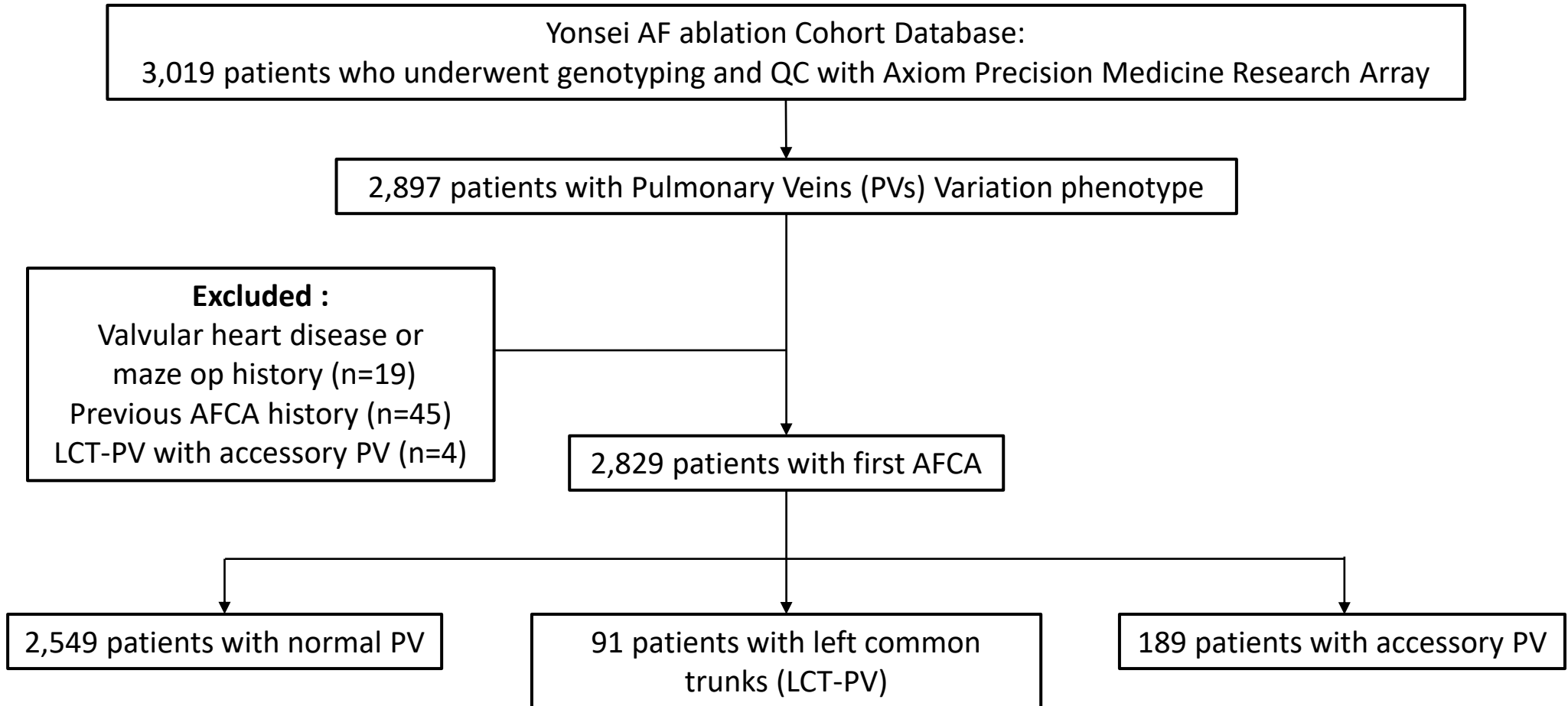


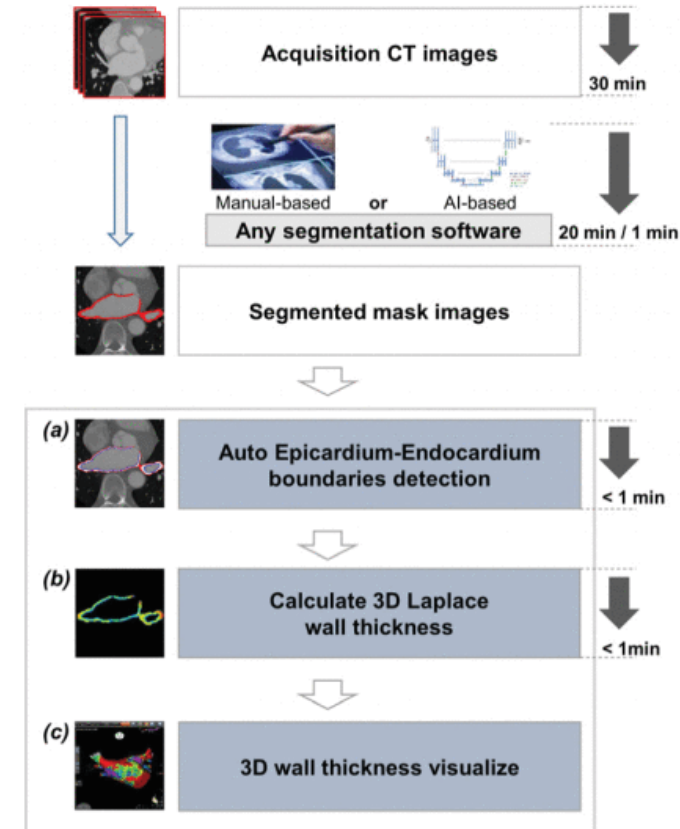
Figure 1. Flow chart of the study



Methods

3D spiral CT scans

- **LCT-PV** : the upper and lower PV separate at >10 mm distal to the left PV antrum margin
- **Accessory PV** : separate from the superior or inferior PVs with an independent drainage into the left atrium
- **Left atrial wall thickness (LAWT)**
 - Antral area, Rt, Lt – anterior, posterior, roof
 - Anterior wall, LA appendage, Posterior wall, Posterior inferior wall, Left lateral isthmus, Septum
 - AMBER software (Laonmed Inc., Seoul, Korea)



Methods

Selection of SNPs from 12 AF-associated genes

- AF-associated genes (DSP, GJA1, NEO1, KCNQ1, NPPA, PITX2, RYR2, SCN10A, SHOX2, ATP2A2, TBX3, and TBX5) that involved in the development of heart and PVs.

LCT-PV (91/2549)						Discovery (76/1550)			Validation (15/999)		
Gene	SNP	Chr.	Position (hg19)	Risk/non-risk allele	RAF (%)	OR	95% CI	p	OR	95% CI	p
SCN10A	rs9871453	3	38853962	A/G	26.2	1.520	1.068-2.162	0.020	2.206	1.052-4.625	0.036
NEO1	rs1979409	15	73465477	A/G	14.1	1.707	1.129-2.581	0.011	2.316	1.084-4.949	0.030
Accessory PV (189/2549)						Discovery (142/1550)			Validation (47/999)		
Gene	SNP	Chr.	Position (hg19)	Risk/non-risk allele	RAF (%)	OR	95% CI	p	OR	95% CI	p
SCN10A	rs146775048	3	38800884	T/C	1.31	2.817	1.273-6.236	0.011	3.314	1.110-9.893	0.032



Methods

High polygenic risk score (PRS)

- LCT-PV : those with two or more risk alleles, indicating a higher genetic risk
- Accessory PV patients : presence or absence of the risk allele (rs146775048)



Results

- Baseline characteristics

	Normal PV (N=2549)	LCT-PV (N=91, 3.2%)	Accessory PV (N=189, 6.7%)	p value
Polygenic risk score	0.81 ± 0.79	1.18 ± 0.90	0.81 ± 0.83	<0.001 ^a
High PRS	441 (17.3)	30 (33.0)	12 (6.3)	<0.001
Age	59.0 ± 10.7	61.9 ± 10.5	58.3 ± 10.3	0.025
Male, n (%)	1902 (74.6)	59 (64.8)	132 (69.8)	0.046
Paroxysmal AF, n (%)	1695 (66.5)	59 (64.8)	120 (63.5)	0.665
AF duration, months	34.1 ± 39.8	37.2 ± 42.2	39.2 ± 46.5	0.517
Body mass index, kg/m²	25.0 ± 3.0	24.6 ± 2.8	24.6 ± 3.0	0.084
CHA₂DS₂VASc	1.7 ± 1.4	2.0 ± 1.6	1.6 ± 1.3	0.026
Hypertension	1228 (48.2)	41 (45.1)	82 (43.4)	0.388
Diabetes	385 (15.1)	13 (14.3)	23 (12.2)	0.534
Stroke/TIA	270 (10.6)	15 (16.5)	20 (10.6)	0.204
Heart failure	294 (11.5)	14 (15.4)	31 (16.4)	0.083
Vascular disease	256 (10.0)	10 (11.1)	13 (6.9)	0.347
LA diameter	41.2 ± 6.1	41.4 ± 6.2	41.4 ± 6.7	0.899
LVEF	63.4 ± 8.1	63.9 ± 8.5	63.4 ± 8.6	0.857
E/e'	10.1 ± 4.1	11.5 ± 4.4	10.7 ± 5.0	0.002
LAWT, mm	1.91 ± 0.34	1.90 ± 0.33	1.90 ± 0.33	0.943
LA voltage, mV (n=1,775)	1.42 ± 0.69	1.27 ± 0.68	1.24 ± 0.69	0.007 ^b
EAT of Atria	45.59 ± 20.20	41.82 ± 17.23	44.44 ± 21.60	0.175
CPVI	2549 (100.0)	91 (100.0)	189 (100.0)	
Empirical extra-PV LA ablation	727 (28.6)	36 (39.6)	67 (35.6)	0.012
Extra-PV foci trigger (n=1,821)	182 (11.0)	6 (10.2)	21 (18.4)	0.054
Follow up duration, months	39.2 ± 34.2	43.5 ± 37.3	45.3 ± 39.7	0.037



Results

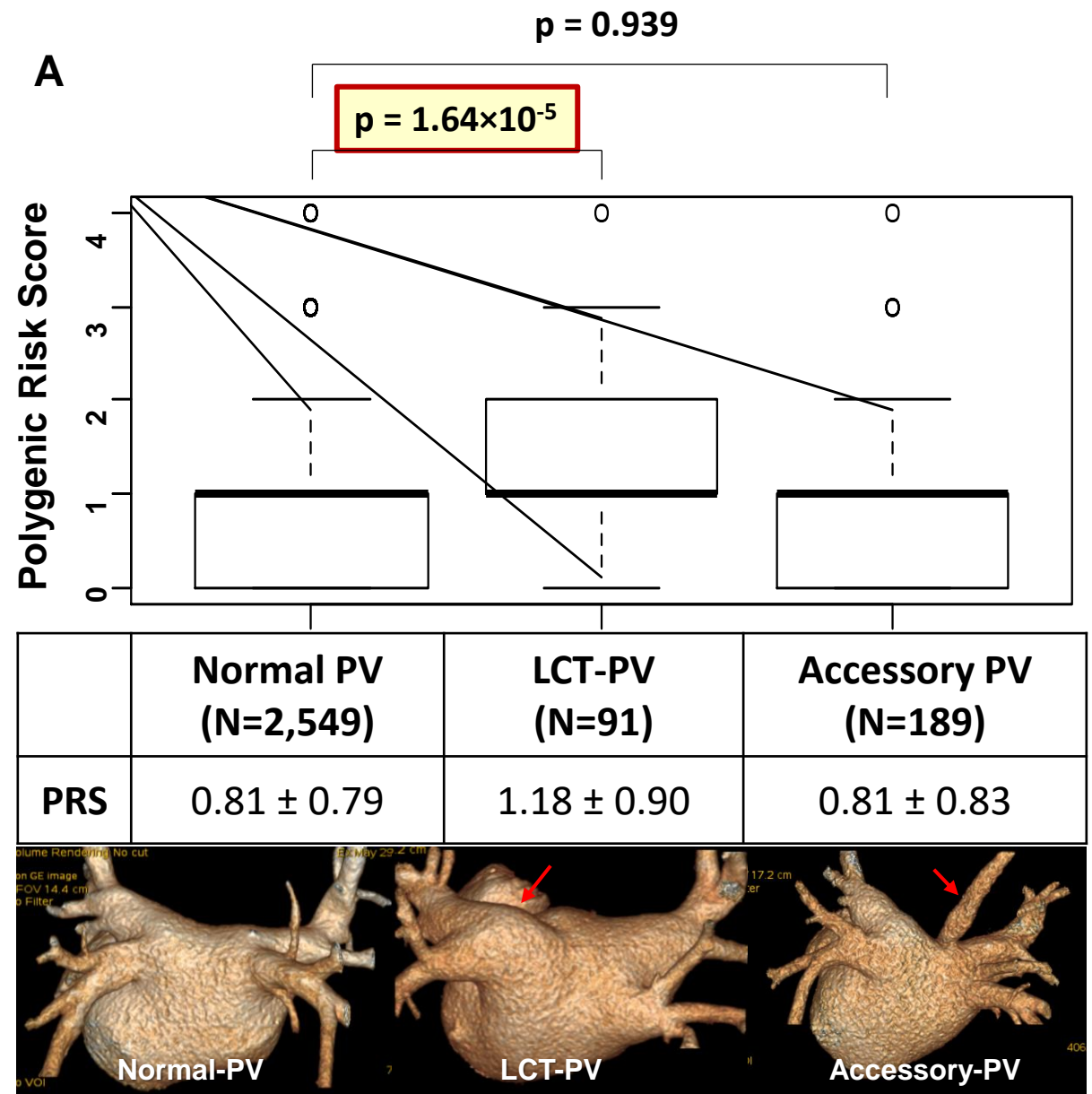


Figure 2(A) Comparison of PRS and the representative images of the LCT-PV and accessory PV



Results

- Predictors of AF recurrence on univariate and multivariate Cox regression analysis

	Univariate		Multivariate	
	HR (95% C.I.)	P value	HR (95% C.I.)	P value
Age, years	1.00 [1.00, 1.01]	0.250	0.98 [0.97, 1.00]	0.098
Male, n(%)	0.96 [0.85, 1.10]	0.556	0.87 [0.61, 1.25]	0.458
Paroxysmal AF, n(%)	0.56 [0.50, 0.63]	<0.001	0.91 [0.64, 1.30]	0.602
AF duration, months	1.00 [1.00, 1.00]	0.020	1.00 [1.00, 1.00]	0.432
Body mass index, kg/m ²	1.02 [1.00, 1.04]	0.118		
Hypertension	1.17 [1.04, 1.31]	0.009	1.15 [0.84, 1.56]	0.386
Diabetes	1.02 [0.87, 1.20]	0.780		
Stroke/TIA	1.24 [1.04, 1.47]	0.019	1.24 [0.76, 2.02]	0.381
Heart failure	1.33 [1.12, 1.57]	0.001	1.06 [0.67, 1.67]	0.806
Vascular disease	0.97 [0.81, 1.17]	0.761		
Early recurrence	2.80 [2.49, 3.15]	<0.001	2.02 [1.47, 2.79]	<0.001
Presence of LCT-PV	1.30 [0.96, 1.76]	0.093	2.12 [1.01, 4.42]	0.046
Presence of accessory PV	1.04 [0.84, 1.30]	0.704		
rs146775048 (SCN10A)	1.17 [0.82, 1.67]	0.399		
rs9871453 (SCN10A)	1.06 [0.97, 1.17]	0.211		
rs1979409 (NEO1)	1.03 [0.91, 1.15]	0.682		
Polygenic risk score	1.06 [0.98, 1.14]	0.140		
LA diameter (Echo)	1.04 [1.03, 1.05]	<0.001	1.02 [0.99, 1.05]	0.230
LV ejection fraction, %	0.99 [0.98, 0.99]	<0.001	0.99 [0.97, 1.01]	0.454
E/e'	1.01 [1.00, 1.03]	0.051	0.96 [0.91, 1.02]	0.203
LA wall stress	1.00 [1.00, 1.00]	<0.001	1.00 [1.00, 1.00]	0.788
EAT volume of atria (cm ³ , CT)	1.01 [1.00, 1.01]	<0.001	1.00 [0.99, 1.01]	0.501
LAWT, mean	1.05 [0.88-1.25]	0.605		
Mean LA voltage, mV (n=1,775)	0.60 [0.53, 0.68]	<0.001	0.64 [0.48, 0.85]	0.002
Extra-PV foci trigger (n=1,824)	1.87 [1.52, 2.28]	<0.001	1.71 [1.18, 2.50]	0.005



Results

B. LAWT 3D-reconstruction

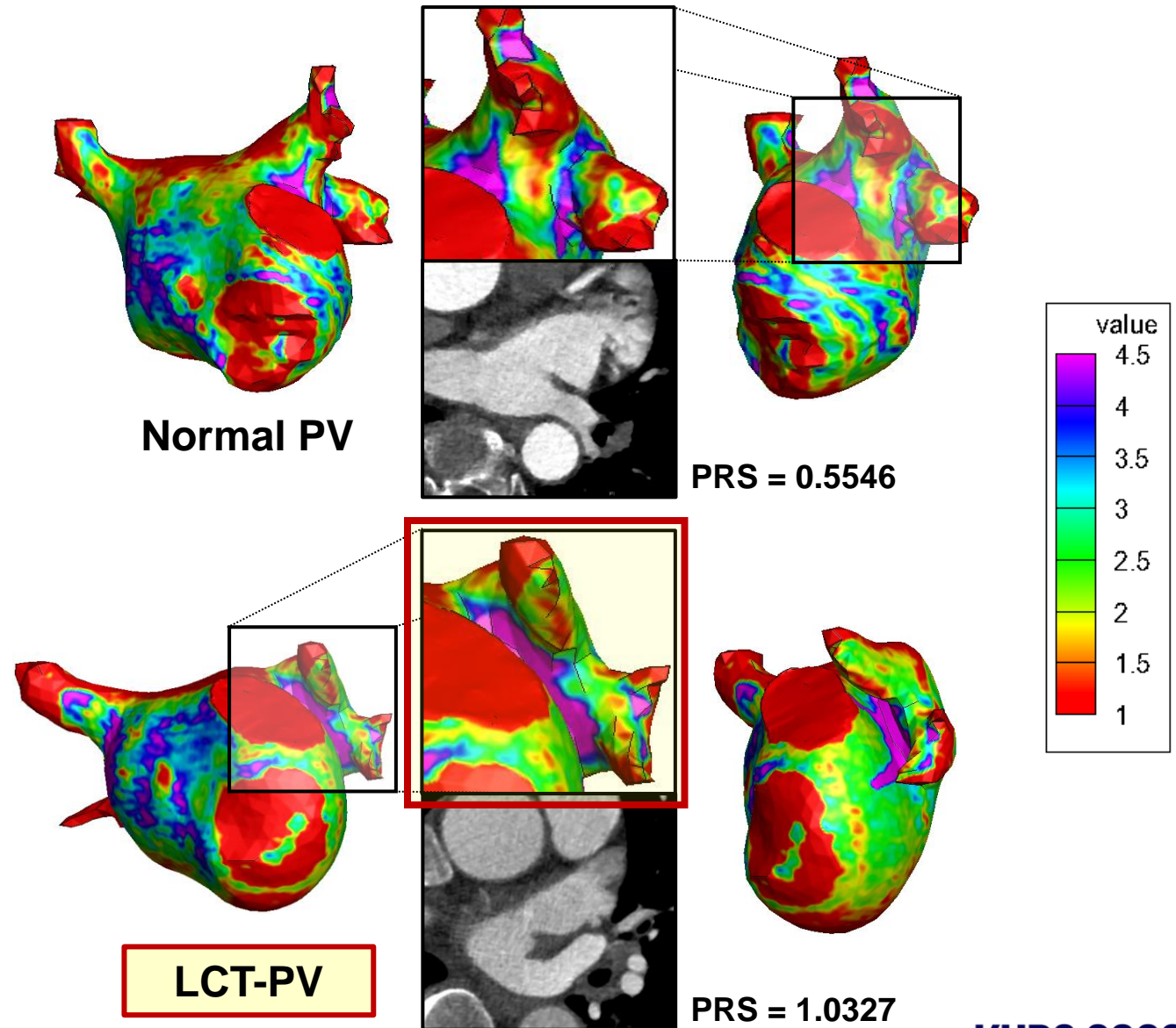


Figure 2(B) LAWT 3D-reconstruction CT images of a patient with LCT-PV and a patient with normal PV



Results

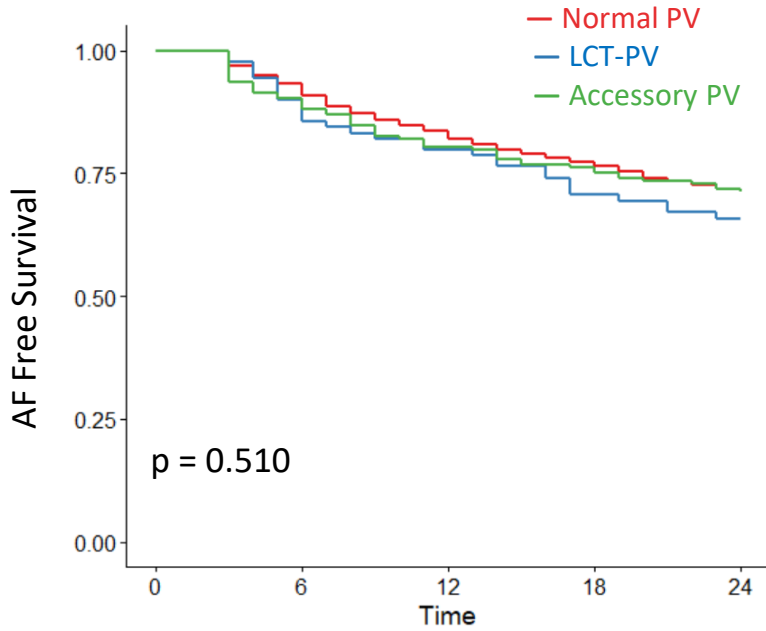
- LAWT according to PV variants with genetic risk

	Normal PV		LCT-PV		Accessory PV		p value
	Low PRS (N=2108)	High PRS (N=441)	Low PRS (N=61)	High PRS (N=30)	Low PRS (N=177)	High PRS (N=12)	
LAWT, mean	1.91 ± 0.34	1.90 ± 0.35	1.85 ± 0.33	1.99 ± 0.30	1.90 ± 0.33	1.92 ± 0.38	0.648
RSPV anterior	2.16 ± 0.58	2.15 ± 0.59	2.06 ± 0.48	2.17 ± 0.61	2.23 ± 0.60	1.96 ± 0.62	0.415
RSPV posterior	1.65 ± 0.41	1.66 ± 0.42	1.69 ± 0.40	1.75 ± 0.42	1.60 ± 0.40	1.54 ± 0.37	0.289
RSPV roof	1.76 ± 0.55	1.77 ± 0.55	1.54 ± 0.51	1.83 ± 0.55	1.78 ± 0.60	1.68 ± 0.56	0.091
RIPV anterior	2.03 ± 0.57	2.02 ± 0.57	1.96 ± 0.56	1.94 ± 0.63	1.87 ± 0.51	1.88 ± 0.61	0.014
RIPV posterior	1.61 ± 0.42	1.61 ± 0.42	1.65 ± 0.39	1.70 ± 0.40	1.61 ± 0.39	1.42 ± 0.43	0.583
LSPV anterior	3.32 ± 1.11	3.22 ± 1.01			3.46 ± 1.16	3.54 ± 0.95	0.011 ^a
LSPV posterior	1.53 ± 0.40	1.53 ± 0.38			1.51 ± 0.38	1.50 ± 0.38	0.003 ^a
LSPV roof	1.56 ± 0.53	1.52 ± 0.52			1.59 ± 0.56	1.50 ± 0.52	0.164 ^a
LIPV anterior	2.83 ± 0.90	2.74 ± 0.79			2.89 ± 0.97	2.63 ± 0.65	0.230 ^a
LIPV posterior	1.76 ± 0.47	1.75 ± 0.44			1.76 ± 0.41	1.77 ± 0.38	0.653 ^a
Lt.PV anterior^b	3.07 ± 0.90	2.98 ± 0.79	3.41 ± 1.27	3.87 ± 1.41	3.17 ± 0.95	3.08 ± 0.65	<0.001
Lt.PV posterior^b	1.64 ± 0.40	1.64 ± 0.38	1.31 ± 0.32	1.50 ± 0.48	1.63 ± 0.36	1.64 ± 0.34	<0.001
Lt.PV roof^c	1.56 ± 0.53	1.52 ± 0.52	1.44 ± 0.42	1.39 ± 0.43	1.59 ± 0.56	1.50 ± 0.52	0.164
Anterior wall	1.99 ± 0.44	1.98 ± 0.44	1.88 ± 0.46	2.02 ± 0.31	1.98 ± 0.40	1.98 ± 0.59	0.602
LA appendage	2.20 ± 0.40	2.16 ± 0.40	2.13 ± 0.43	2.29 ± 0.35	2.15 ± 0.42	2.22 ± 0.46	0.212
Posterior wall	1.89 ± 0.49	1.89 ± 0.49	1.84 ± 0.45	2.03 ± 0.44	1.86 ± 0.40	1.85 ± 0.49	0.563
Posterior inferior wall	1.66 ± 0.41	1.66 ± 0.41	1.62 ± 0.40	1.78 ± 0.32	1.65 ± 0.40	1.69 ± 0.48	0.616
Left lateral isthmus	2.40 ± 0.58	2.38 ± 0.59	2.36 ± 0.53	2.55 ± 0.57	2.34 ± 0.55	2.41 ± 0.72	0.446
Septum	2.43 ± 0.57	2.39 ± 0.56	2.25 ± 0.54	2.54 ± 0.47	2.40 ± 0.53	2.48 ± 0.75	0.110



Results

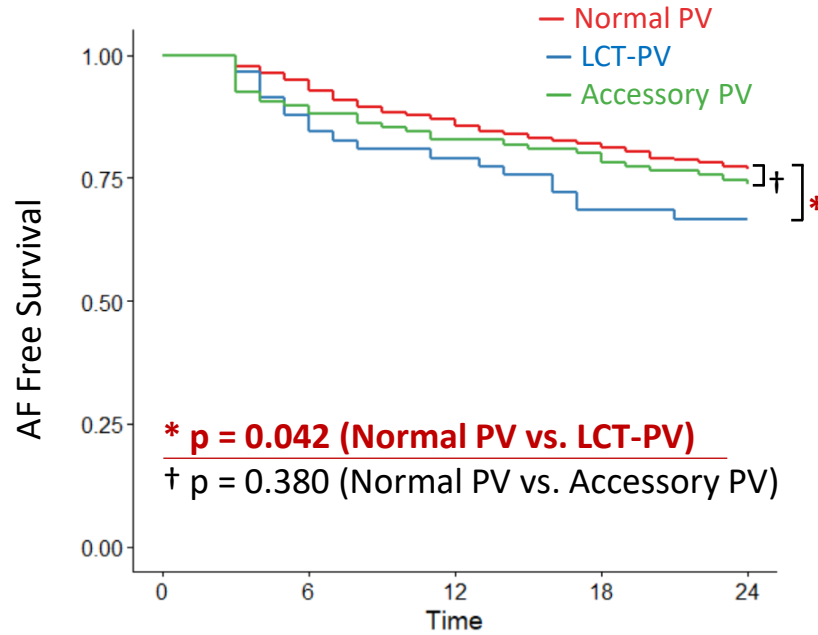
A. Overall



Number at risk

	0	6	12	18	24
Normal PV	2549	2309	2023	1798	1507
LCT-PV	91	80	70	60	53
Accessory PV	189	165	142	135	123

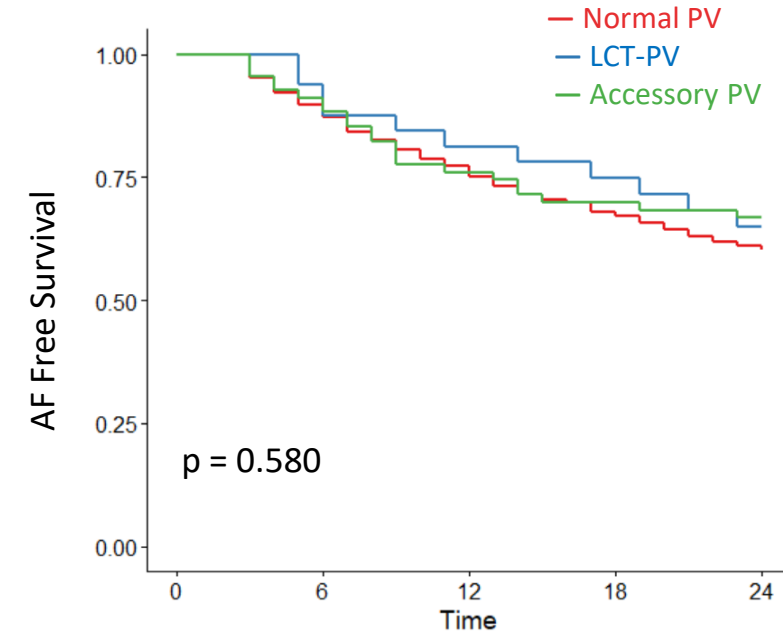
B. Paroxysmal AF



Number at risk

	0	6	12	18	24
Normal PV	1696	1559	1390	1258	1079
LCT-PV	59	50	45	37	33
Accessory PV	120	103	93	90	81

C. Persistent AF



Number at risk

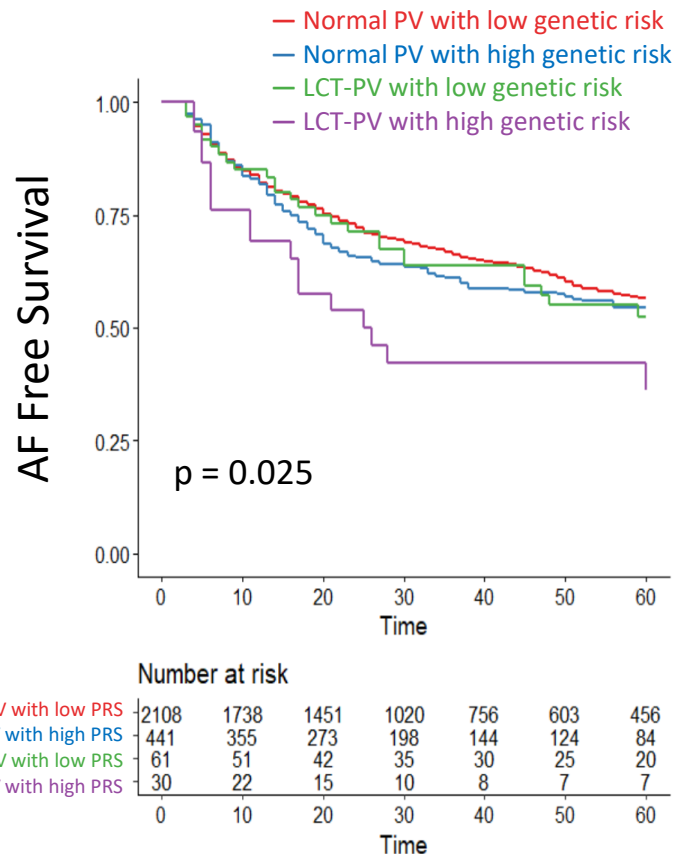
	0	6	12	18	24
Normal PV	853	750	633	540	428
LCT-PV	32	30	25	23	20
Accessory PV	69	62	49	45	42

Figure 3. Kaplan–Meier curves of AF relapse after RFCA categorized by the types of AF

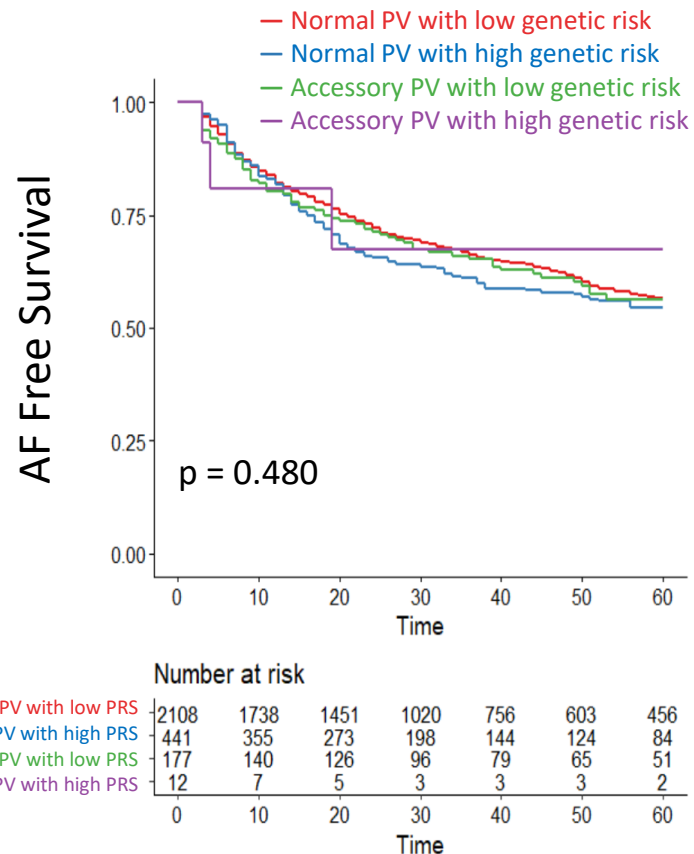


Results

A. Left Common Trunkus-PV



B. Accessory PV



C. Adjusted hazard ratio for AF recurrence associated with genetic risk

* Adjusted by age, sex, paroxysmal AF

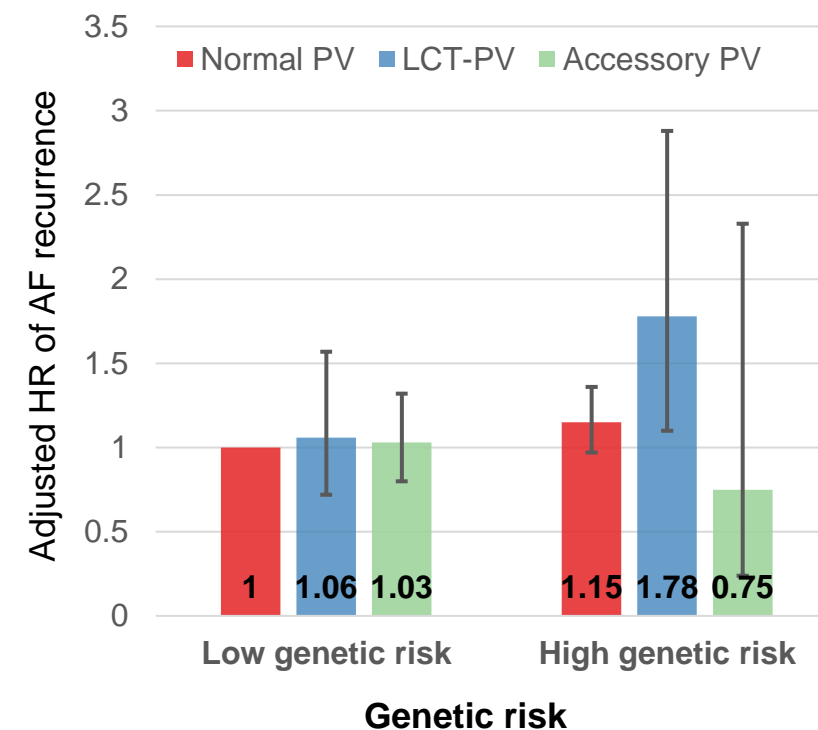


Figure 4. Kaplan–Meier curves of freedom from recurrence of atrial fibrillation after RFCA according to presence of LCT-PV with genetic risk (A) and the accessory PV with genetic risk (B), adjusted hazard ratio for AF recurrence associated with genetic risk (C)



Discussion

- We found that in **LCT-PV** patients **with high PRS**, thicker **anterior WT of the left PV** was confirmed, and **AF recurrence** was also found to occur more frequently after ablation.
- Previous study, the use of LAWT-guided PV antrum isolation demonstrated favorable outcomes.
- These results suggest that LCT-PV PRS can help predict prognosis and identify individuals who may benefit from a tailored procedure in AF.
- **Limitation**
 - Single center study
 - Only included patients who underwent catheter ablation
 - Limitation of the clinical utility of the PRS



Conclusion

- LCT-PV has a significant genetic background.
- Patients with AF and LCT-PV has higher PRS than other groups.
- The post-AFCA recurrence rate was significantly higher in patients with LCT-PV and high PRS, especially in paroxysmal AF.
- These findings suggest that understanding the impact of PV variations on AFCA outcomes, including genetic factors, could help inform personalized treatment approaches and ablation modalities for AF patients.



Thank you for your attention!

