Prevalence and Clinical Characteristics of Cardiac Amyloidosis in Patients Undergoing Catheter Ablation for Atrial Fibrillation: Evidence from Atrial and Ventricular Biopsy

Toyokazu Otsubo[1], Takanori Yamaguchi[1], Yuya Takahashi[1], Kana Nakashima[1], Kodai Shinzato[1], Ryosuke Osako[1], Shigeki Shichida[1], Yuki Kawano[3], Akira Fukui[2], Kei Hirota[2], Naohiko Takahashi[2], Koichi Node[1]

[1] Department of Cardiovascular Medicine Saga University
[2] Department of Cardiology and Clinical Examination, Faculty of Medicine, Oita University
[3] Division of Cardiology, Saiseikai Futsukaichi Hospital

COI Disclosure

Name of Authors :Toyokazu Otsubo, Takanori Yamaguchi, Yuya Takahashi, Kana Nakashima, Kodai Shinzato, Ryosuke Osako, Shigeki Shichida, Yuki Kawano, Akira Fukui, Kei Hirota, Naohiko Takahashi, Koichi Node

- ✓ Takanori Yamaguchi received honoraria from Abbott Medical Japan and Medtronic Japan.
- ✓ Takanori Yamaguchi, Toyokazu Otsubo, Yuya Takahashi are affiliated with the Department of Advanced Management of Cardiac Arrhythmia, Saga University, sponsored by Abbott Medical Japan, Nihon Kohden Corporation, Japan Medtronic, Japan Lifeline, Boston Scientific Japan, and Fides-ONE Corporation.
- ✓ The other authors declare that they have no conflict of interest.
- ✓ This work was supported by JSPS KAKENHI Grant Number JP21K08056.

科研費
KAKENHI

Ethical Issues and Funding sources

- This study was approved by Ethics Committee Saga University Hospital.
- All patients gave written consent to participate in the study.
- The research conforms with the principle outlined in the Declaration of Helsinki.
- This work was supported by JSPS KAKENHI Grant Number JP21K08056

科研費
KAKENHI

Background

- ✓ Cardiac amyloidosis is reported to be associated with atrial fibrillation (AF).

van den Berg MP et al. Eur Heart J. 2019 Apr 21;40(16):1287-1293.

- ✓ However, the frequency and clinical characteristics of cardiac amyloidosis in patients undergoing AF ablation have not been reported.

Objective

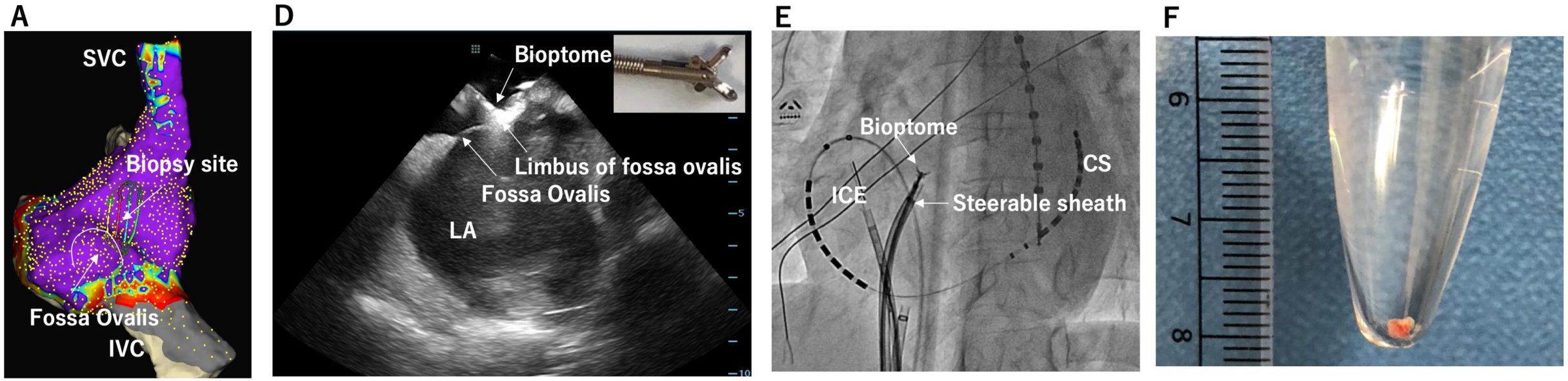
The purpose of this study was to evaluate the prevalence and clinical characteristics of cardiac amyloidosis in patients undergoing AF ablation.

Method

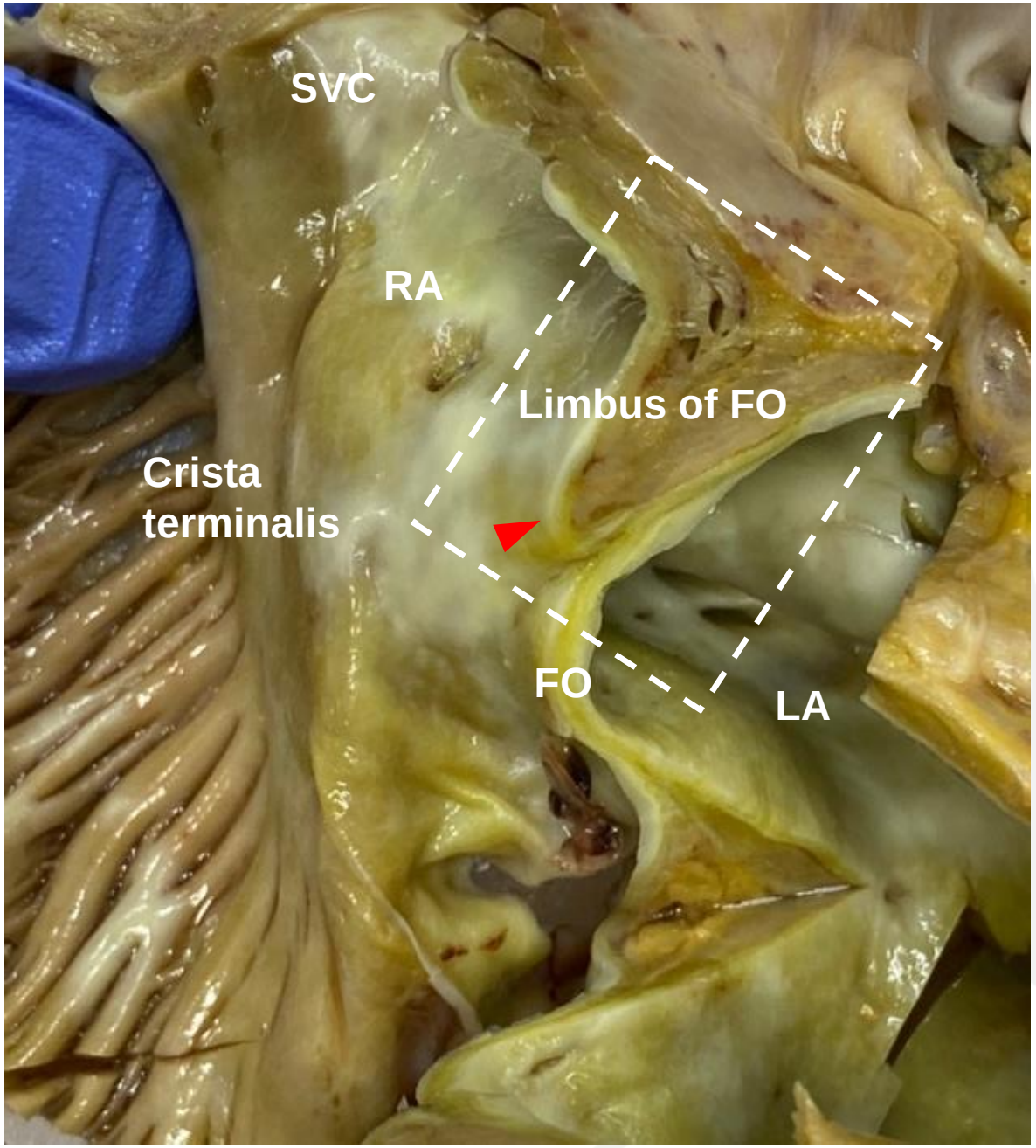
- ✓We performed both endocardial right atrial (RA) and right ventricular (RV) biopsies in 402 patients who underwent AF catheter ablation.
- ✓No patients were diagnosed with cardiac amyloidosis before the procedures.

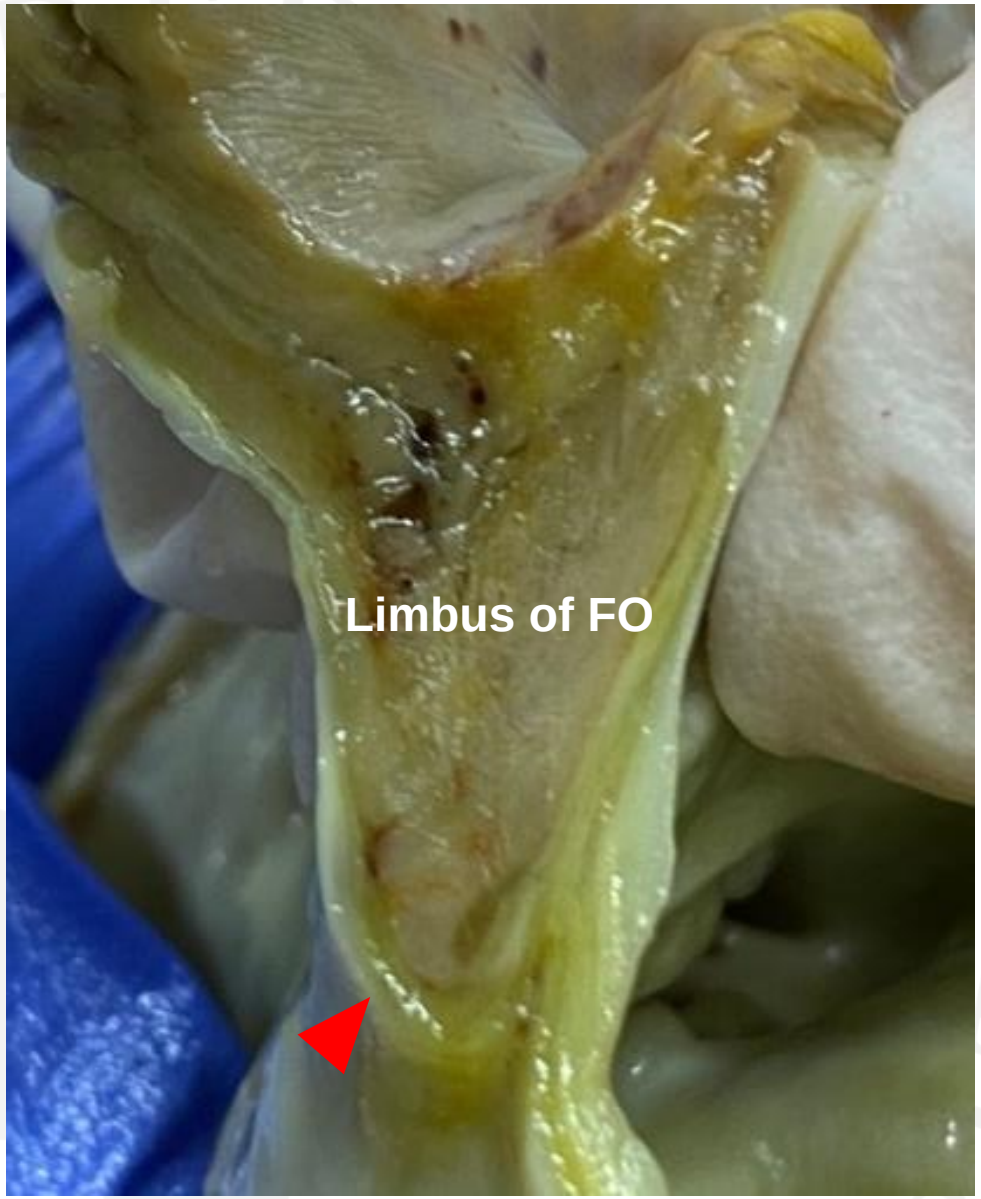
Method; Atrial Biopsy

- After electroanatomical mapping, all patients underwent right atrial septum biopsies from the limbus of Fossa Ovalis under intracardiac echography (ICE) and fluoroscopy.



Yamaguchi et al. J Am Heart Assoc. 2022;11:e024521. DOI: 10.1161/JAHA.121.024521





Biopsy site

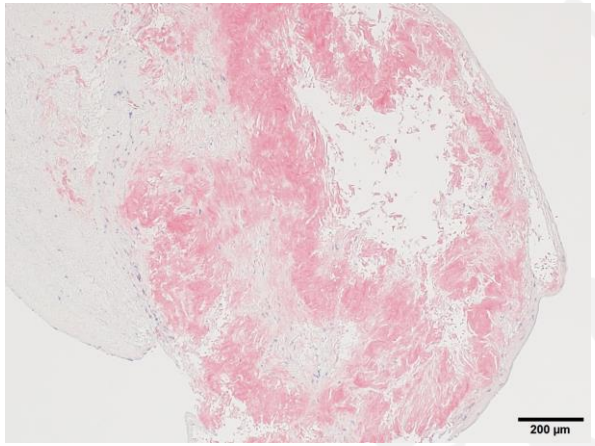
Manuscript in preparation

Method; Amyloid deposition

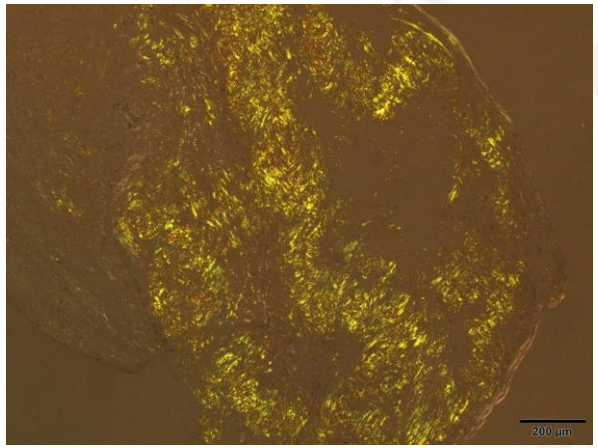
83yo female

Right atrium

Congo red staining

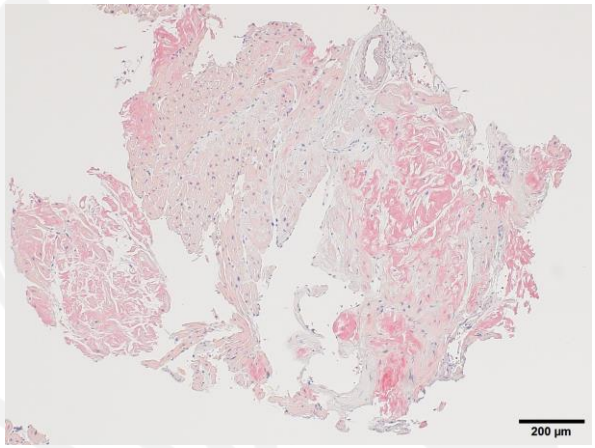


apple-green birefringence

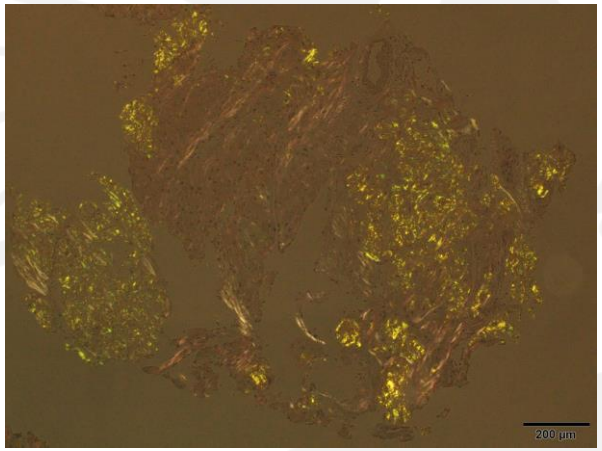


Right ventricle

Congo red staining



apple-green birefringence



- ✓ Amyloid deposition was assessed by Congo red staining and apple-green birefringence under polarizing microscope.
- ✓ Immunostaining was performed using the monoclonal antibodies in the Kumamoto amyloidosis center.

Result

- ✓ Amyloid deposition was identified both in the RA and RV samples in 14 patients (4%).
- ✓ One patient had amyloid only in the RA samples.
- ✓ Amyloid typing revealed ATTR type in 12 patients and AL type in 3 patients.

Results; Comparison of Patient characteristics between amyloid and non-amyloid group

Variables	Total n = 402		Amyloid n = 15		Non-Amyloid n = 387	P value
Age, years	67 ± 11		77 ± 7		67 ± 11	**0.001***
Female, n (%)	123 (31)		4 (27)		119 (31)	0.736
BMI (kg/m^2)	25 ± 4		23 ± 3		25 ± 4	0.117
AF type						
Paroxysmal AF, n (%)	163 (41)		6 (40)		157 (41)	0.965
Non-paroxysmal AF, n (%)	239 (59)		9 (60)		230 (59)	
Hypertension, n (%)	236 (59)		10 (67)		226 (59)	0.531
Diabetes mellitus, n (%)	73 (18)		4 (27)		69 (18)	0.387
Sick sinus syndrome, n (%)	28 (7)		4 (27)		24 (6)	**0.002***
History of congestive heart failure, n (%)	115 (29)		11 (73)		104 (27)	**<.001***
NYHA functional class, n (%)						**0.001***
Ⅰ	247 (65)		7 (54)		240 (65)	
Ⅱ	119 (31)		3 (23)		116 (31)	
Ⅲ	13 (3)		3 (23)		10 (3)	
Ⅳ	2 (1)		0 (0)		2 (1)	
Kumamoto criteria	0[0-1]		1 [0-2]		0 [0-1]	**0.031***

Results; Comparison of Patient characteristics between amyloid and non-amyloid group

Variables(Laboratory parameters)	Total n = 402		Amyloid n = 15		Non-Amyloid n = 387	P value
hs-cTnT, pg/mL	16 [9-49]		16 [9-48]		40 [26-51]	0.708
NT-proBNP, pg/mL	602 [225-1244]		1701 [768-2887]		574 [205-1184]	0.161
Alubmin, g/dL	4.1 ± 0.3		3.9 ± 0.4		4.1 ± 0.3	0.195
Hb, mg/dL	14 ± 2		13 ± 2		14 ± 2	0.166
eGFR, ml/min/1.73m^2	62 ± 17		51 ± 12		61 ± 18	**0.024***

- ✓ High-sensitivity troponin T was no different between the two groups.
- ✓ The amyloid group had lower renal function than the non-amyloid group.

Results; Comparison of Patient characteristics between amyloid and non-amyloid group

Variables(ECG parameters)	Total n = 402		Amyloid n = 15		Non-Amyloid n = 387	P value
Heart rate, beat/min	82 ± 22		84 ± 24		82 ± 22	0.707
PR duration, ms	174 ± 35		193 ± 43		174 ± 34	0.273
QRS duration, ms	105 ± 30		102 ± 18		105 ± 34	0.746
Wide QRS more than 120ms, n (%)	52 (13)		1 (7)		51 (13)	0.507
CLBBB, n (%)	6 (1)		0 (0)		6 (2)	0.627
CRBBB, n (%)	28 (7)		0 (0)		28 (7)	0.280
QTc duration, ms	441 ± 29		454 ± 25		440 ± 29	0.069
Low QRS voltage in limb leads, n (%)	26 (64)		6 (40)		20 (5)	**<.001***
Poor R-wave progression in precordial leads, n (%)	35 (9)		6 (40)		29 (7)	**<.001***
Right axis deviation, n (%)	39 (10)		0 (0)		4 (1)	0.702
Left axis deviation, n (%)	4 (1)		2 (14)		37 (10)	0.560

- ✓ the amyloid group had more low QRS voltage in limb leads and poor r progression in precordial leads than the non amyloid group.

Results; Comparison of Patient characteristics between amyloid and non-amyloid group

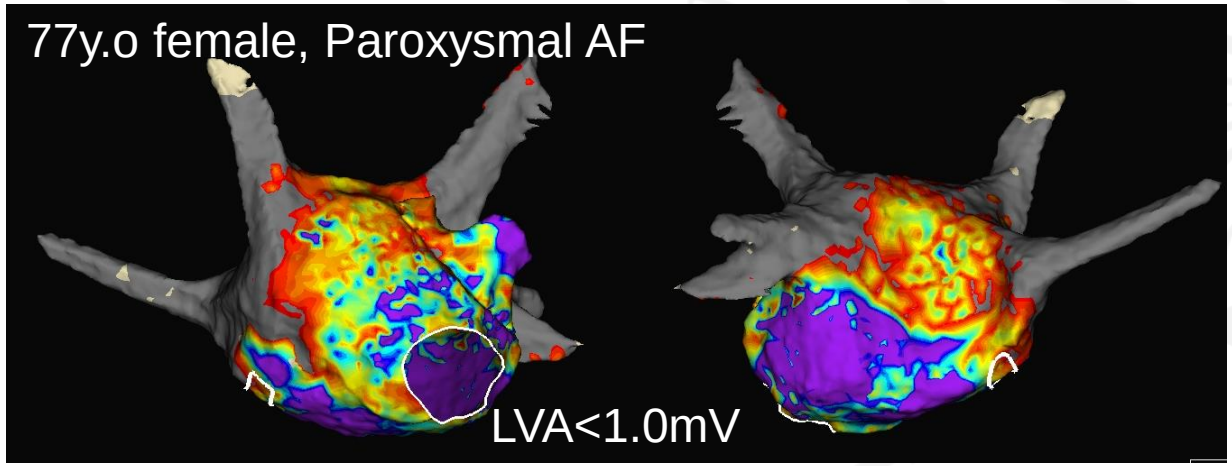
Variables(Echocardiographic parameters)	Total n = 402		Amyloid n = 15		Non-Amyloid n = 387	P value
LV ejection fraction, %	62 ± 12		61 ± 13		62 ± 12	0.651
LV end-diastolic diameter, mm	46 ± 6		41 ± 8		46 ± 6	**0.03***
LV end-systolic diameter, mm	30 ± 7		28 ± 7		30 ± 7	0.206
Interventricular septal thickness, mm	10 ± 2		12 ± 2		10 ± 2	**<.001***
LV posterior wall thickness, mm	10 ± 1		12 ± 2		10 ± 1	**<.001***
LA diameter, mm	41 ± 6		41 ± 5		41 ± 6	0.777
E-wave velocity, m/s	0.7 ± 0.2		0.8 ± 0.2		0.7 ± 0.2	0.231
A-wave velocity, m/s	0.6 ± 0.2		0.5 ± 0.2		0.6 ± 0.2	0.602
E/A ratio	1.2 ± 0.6		1.7 ± 0.8		1.2 ± 0.6	0.226
E/e' ratio	9.7 ± 4.5		17 ± 8		9 ± 5	**<.001***
Pericardial effusion, n(%)	21 (5)		5 (33)		16 (4)	**<.001***

- ✓ The amyloid group had thicker interventricular septum and LV posterior wall than the non amyloid group.
- ✓ The amyloid group had more E/e' ratio than the non amyloid group.
- ✓ Pericardial effusion was more frequently pointed out in the amyloid group than the non amyloid group.

Results; Comparison of Patient characteristics between amyloid and non-amyloid group

Parameters during ablation procedure

Variables	Total n = 402		Amyloid n = 15		Non-Amyloid n = 387	P value
mean LA voltage	5.7 ± 2.2		3.5 ± 1.9		5.7 ± 2.2	**<.001***
Presence of $LVA_{0.5}$, n (%)	34 (37)		10 (67)		110 (33)	**0.007***
Presence of LVA1.0, n (%)	62 (68)		13 (87)		207 (62)	**0.049***
The inducibility of LAMRT, n(%)	42 (10)		6 (40)		36 (9)	**<.001***



- ✓ The amyloid group had lower left atrial bipolar voltage and a higher rate of induction of atrial tachycardia after pulmonary vein isolation than the non-amyloid group.

Discussion

- ✓ There was no significant difference in troponin T values between the amyloid and non-amyloid groups, but all patients in the amyloid group had positive troponin T before the procedure.

- ✓ Troponin T could be a useful biomarker for diagnosis of exclusion in amyloidosis.

	TnThs < 14pg/ml	TnThs > 14pg/ml	Total
Amyloid	**0(0)**	**15(100)**	15
Non-amyloid	152(43)	200(57)	352
	152	215	367

Discussion

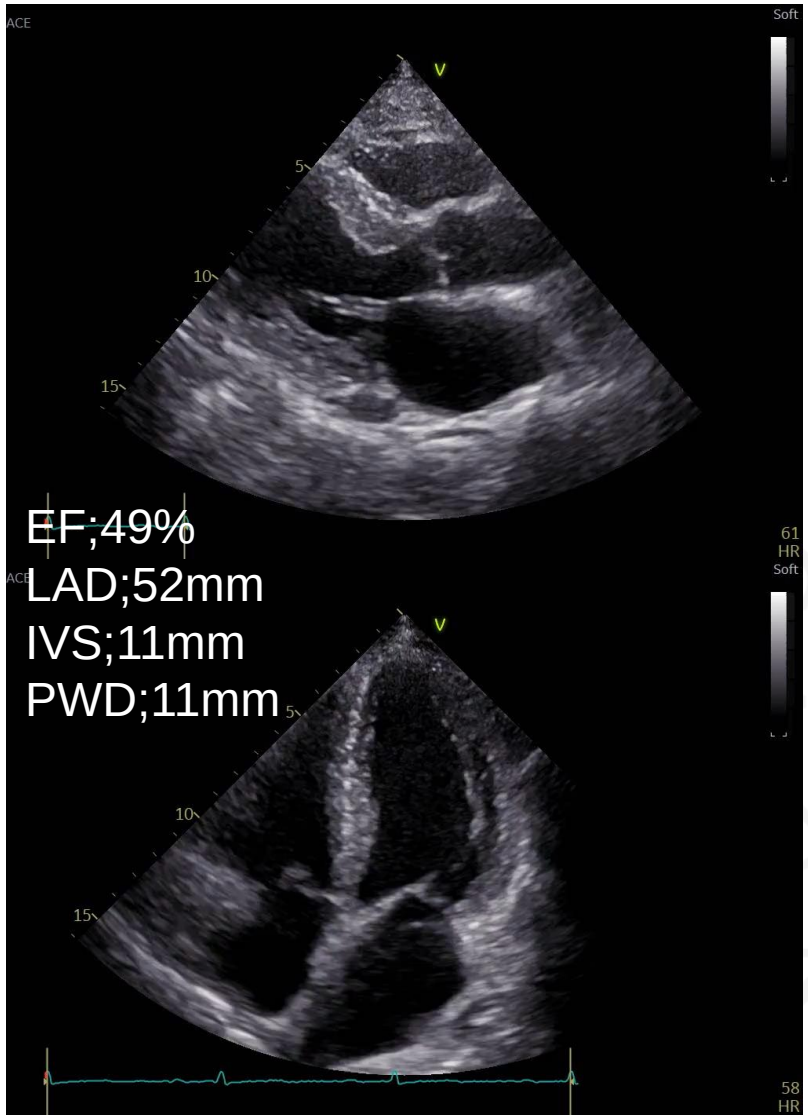
- ✓ As previous reported, amyloid patients had a thicker interventricular septum and posterior ventricular wall on echocardiography compared to the non-amyloid patients, but the difference was not so significant in this study.

Marume K, et al. Circ J. 2019 Jul 25;83(8):1698-1708.

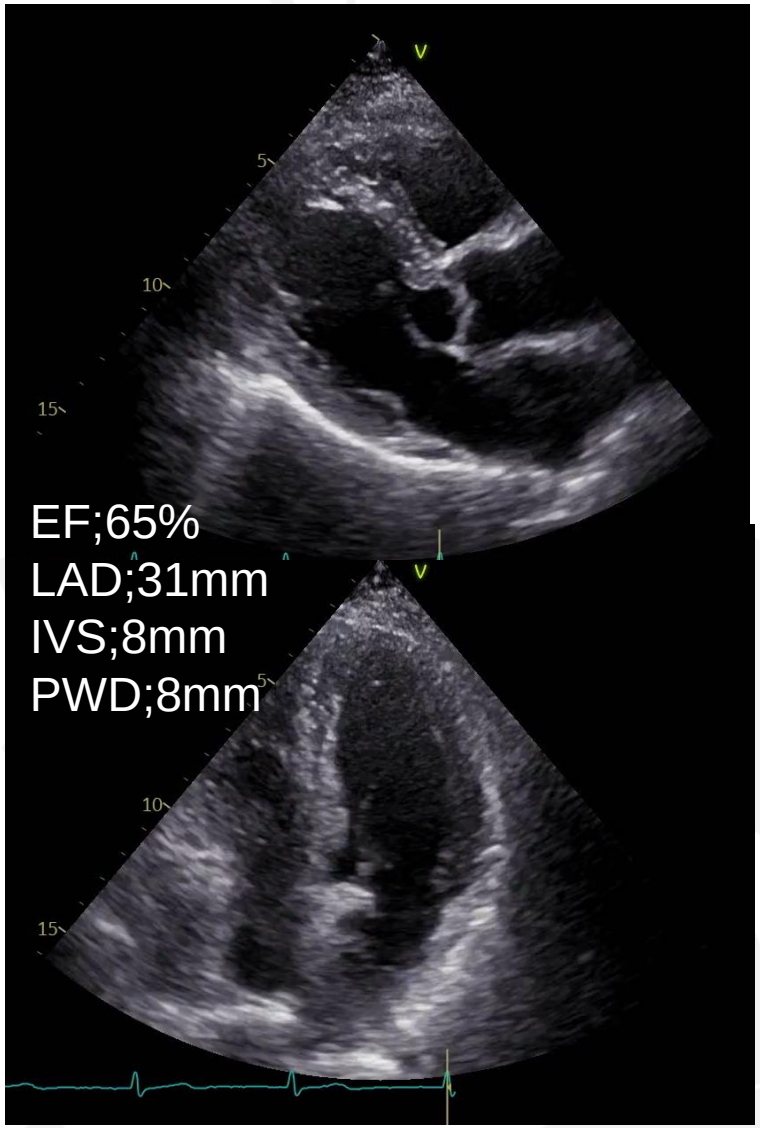
- ✓ Interestingly, there were not many cases in which cardiac amyloidosis was strongly suspected before biopsy.

The three case of cardiac amyloidosis

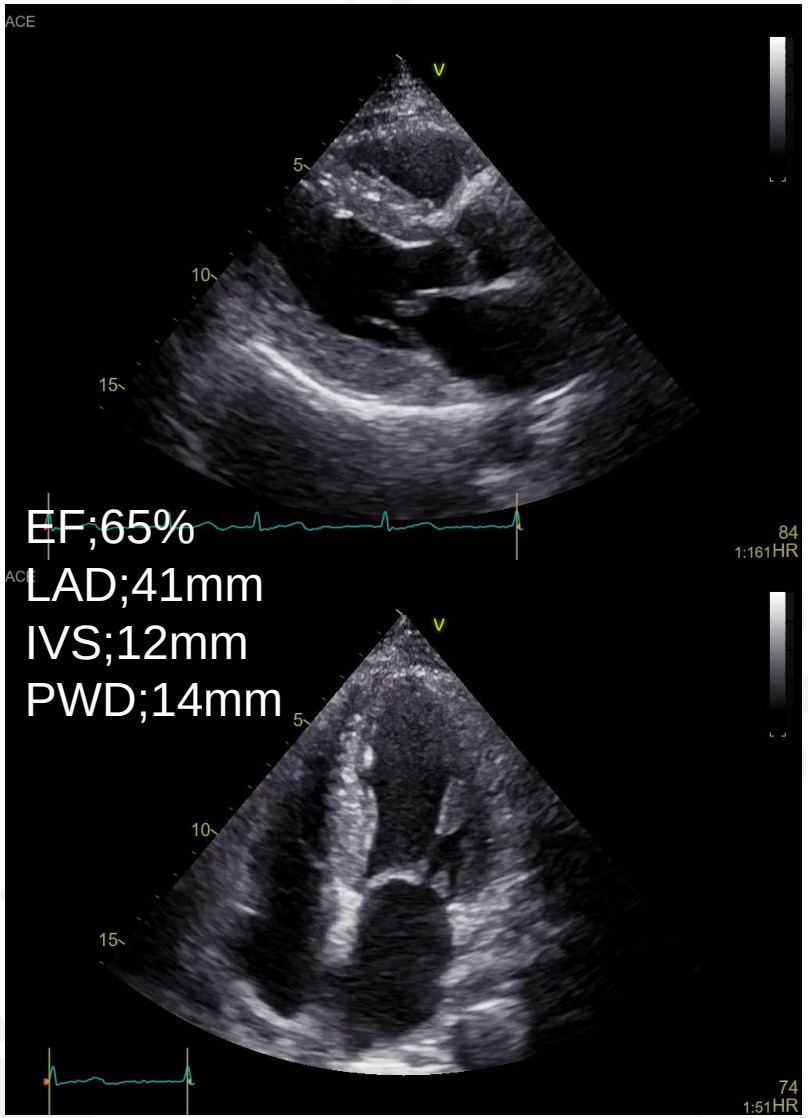
73y.o male, Persistent AF



78y.o male, Persistent AF



73y.o male, Persistent AF



amyloidosis was not strongly suspected on echocardiography before procedure.

Conclusion

- ✓Cardiac amyloidosis exists as an unexpected case among candidates for AF ablation.
- ✓Endomyocardial RA biopsy has equal or better diagnostic power for cardiac amyloidosis than RV biopsy and may be useful for early detection of amyloidosis.