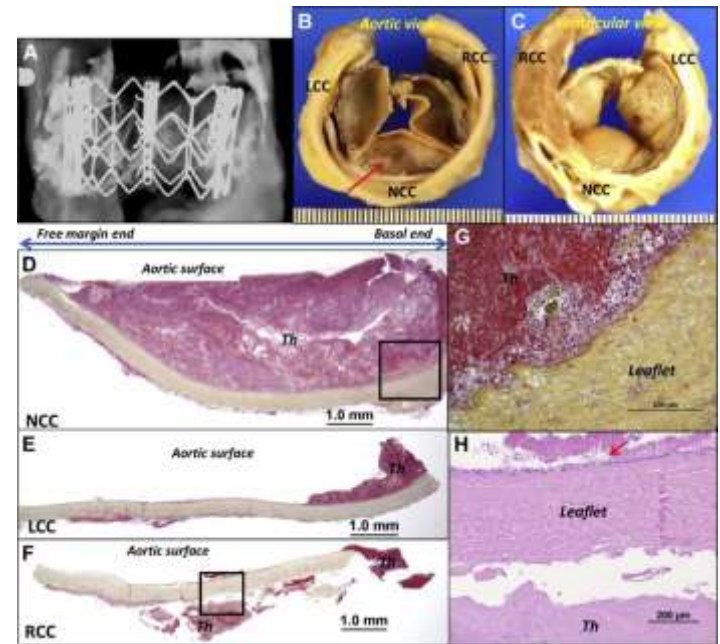


Valve thrombosis: clinical significance and treatment



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**Chief, Division of Cardiology, Heart Center,
Cheng-Hsin General Hospital, Taipei, Taiwan**

Incidence of Valve Thrombosis in Surgically Implanted Biological Valves in Aortic Position

	N	Incidence of thrombosis
Stented Porcine	1463	0.55%
St Jude Biocor (St Jude Medical)	318	1.26%
Medtronic Mosaic (Medtronic Inc)	541	0.37%
Medtronic Hancock (Medtronic Inc)	270	0.84%
Stented pericardial	3031	0%
Stentless	74	0%

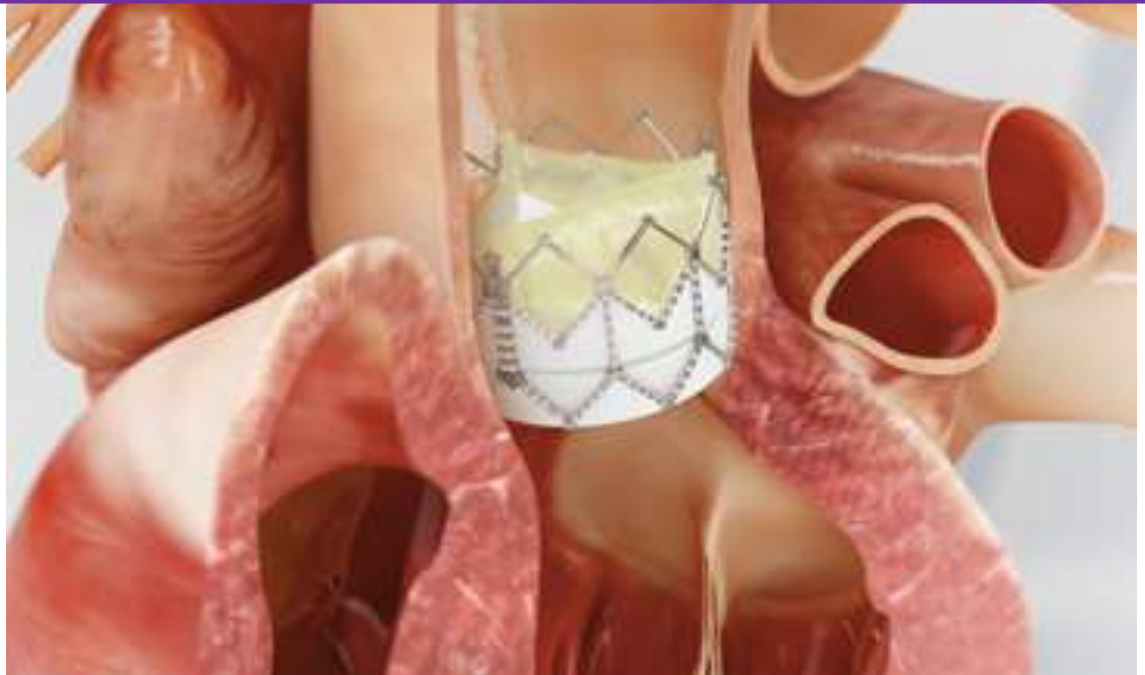
Aortic side **Ventricular side**



➤ Bioprosthetic surgical aortic valves rarely thrombose, with an estimated incidence of 0.01% to 1.26%.

Transcatheter aortic valve replacement

- Transcatheter valve replacement represents a safe and well-recognized alternative in inoperable and/or high-operative-risk patients.



- However, little is known of the occurrence of valve thrombosis following TAVR and how to manage it.

Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

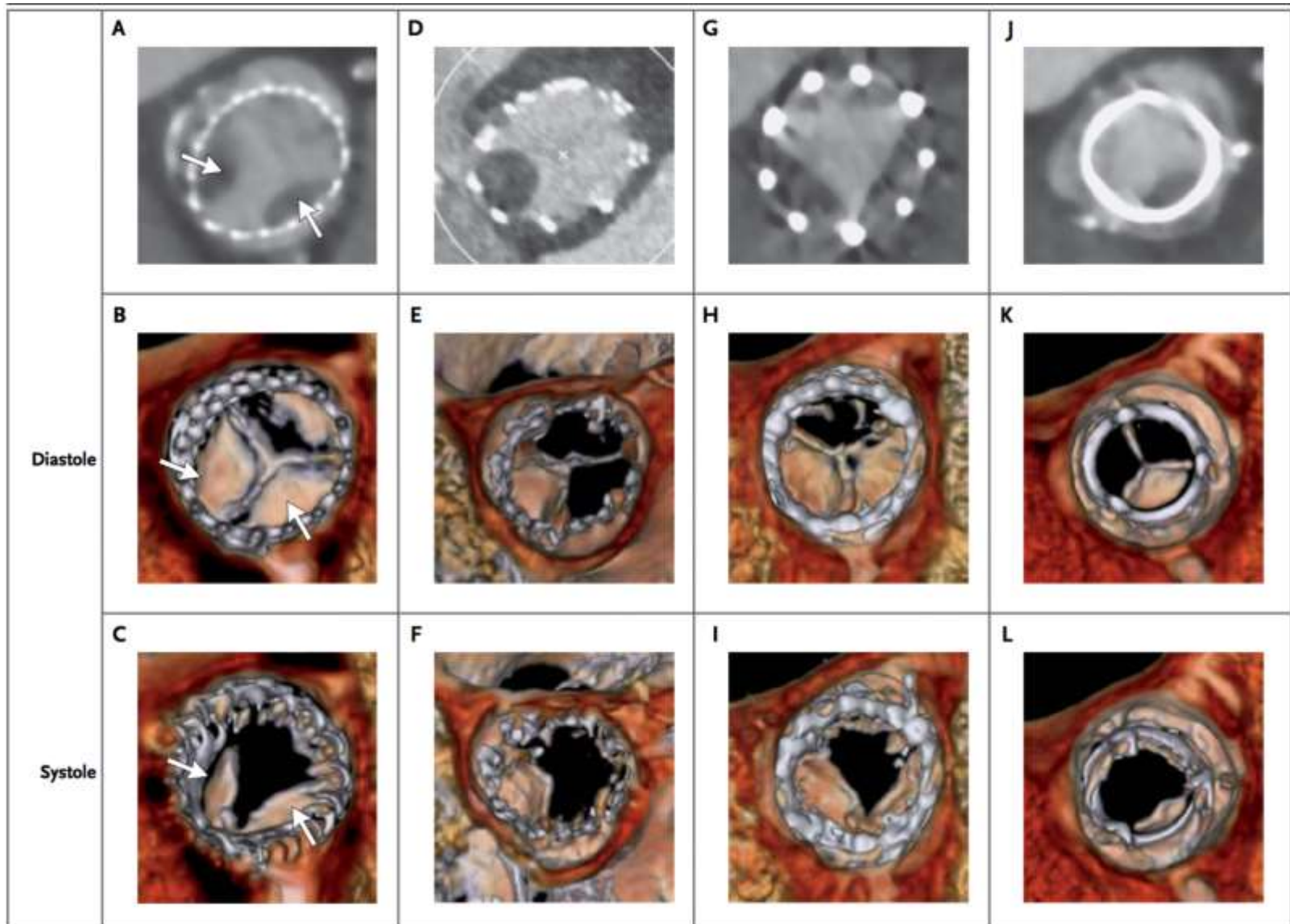


Figure 2. Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types.

Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

Azeem Latib, MD*; Toru Naganuma, MD*; Mohamed Abdel-Wahab, MD; Haim Danenberg, MD; Linda Cota, MD; Marco Barbanti, MD; Helmut Baumgartner, MD; Ariel Finkelstein, MD; Victor Legrand, MD; José Suárez de Lezo, MD; Joelle Kefer, MD;

- THV thrombosis was defined as follows
 - (1) THV dysfunction secondary to thrombosis **diagnosed based on response to anticoagulation therapy, imaging modality or histopathology findings**, or
 - (2) **mobile mass** detected on THV suspicious of thrombus, **irrespective of dysfunction** and **in absence of infection**.
- Between January 2008 and September 2013, 26/4266 **(0.61%)** THV thromboses were reported in patients undergoing TAVR in 12 centers (20 in the Edwards Sapien/Sapien XT cohort and 6 in the Medtronic CoreValve cohort).
- All THV thrombosis cases occurred **within 2 years from TAVR**.

Early Aortic Transcatheter Heart Valve Thrombosis

Diagnostic Value of Contrast-Enhanced Multidetector Computed Tomography

Tina Leetmaa, MD*; Nicolaj C. Hansson, MD*; Jonathon Leipsic, MD; Kaare Jensen, MD; Steen H. Poulsen, MD; Henning R. Andersen, MD; Jesper M. Jensen, MD; John Webb, MD; Philipp Blanke, MD; Mariann Tang, MD; Bjarne L. Nørgaard, MD

Background—Early stent valve thrombosis after transcatheter aortic valve implantation (TAVI) is a rare complication, which is diagnosed based on the appearance of clinical symptoms of heart failure and echocardiographic findings. After TAVI, transthoracic echocardiography is performed to assess transcatheter heart valve (THV) function. However, preliminary reports indicate the potential additive clinical value of multidetector computed tomography (MDCT) for the diagnosis of THV thrombosis. We sought to determine the value of MDCT for the diagnosis of THV thrombosis and the frequency of this complication after balloon-expandable TAVI.

Methods and Results—MDCT was performed in 140 patients within 1 to 3 months after TAVI with the Edwards Sapien XT THV to assess the presence of THV thrombosis and THV stent geometry. Post-TAVI MDCT identified THV thrombosis in 5 patients (4%). Of note, 4 of these patients were asymptomatic and had a normal transthoracic echocardiographic examination with a left ventricular ejection fraction of >50%. All patients were on dual-antiplatelet therapy. Neither

5/140 (4%) patients were identified with THV thrombosis. All of them were asymptomatic.

Conclusions—Post-TAVI MDCT is a valuable tool for the diagnosis of THV thrombosis, and this complication seems to be more common than previously anticipated. Larger studies are required to identify specific risk factors of THV thrombosis. (*Circ Cardiovasc Interv.* 2015;8:e001596. DOI: 10.1161/CIRCINTERVENTIONS.114.001596.)

Early Aortic Transcatheter Heart Valve Thrombosis

Diagnostic Value of Contrast-Enhanced Multidetector Computed Tomography

- THV thrombosis after balloon-expandable TAVI seems to be **more common** than previously anticipated and is **commonly occult on TTE**.
- The role of **routine post-procedural MDCT** as a supplement to routine TTE and TOE for detection of THV thrombosis **in patients potentially at a heightened risk** of thrombus formation needs further investigation.
- Larger studies are required to identify **specific risk factors** of THV thrombosis.

Given the low rates of clinically apparent THV thrombosis, routine post-implantation CT is hardly justifiable in the asymptomatic patient.

Transcatheter Aortic Valve Replacement Failure

Déjà vu ou Jamais vu?

Darren Mylotte, MB BCh, MD; Nicolo Piazza, MD, PhD

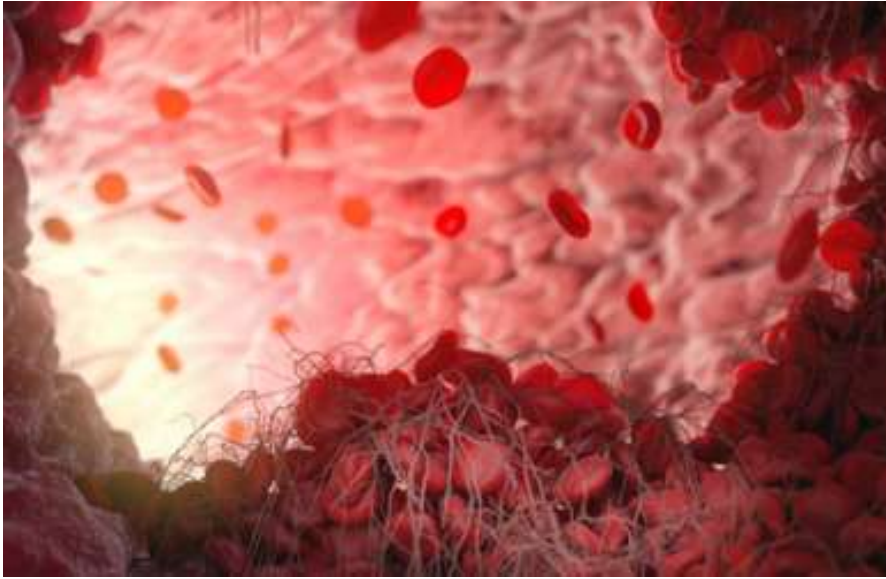
Several theoretical reasons that TAVR thrombosis could be observed more frequently than in historical surgical series:

- (1) TAVR patients may be more likely to have **coexisting prothrombotic conditions** (eg, cancer),
- (2) a **metallic THV frame** could provide a nidus for thrombosis,
- (3) **incomplete THV expansion** creates leaflet folds and potential recesses for thrombus formation,
- (4) **incomplete THV apposition to the aorta** can delay endothelialization, and
- (5) **native leaflet overhang** and the **tall sealing skirts** can create areas of diminished blood flow and stagnation in either **the bioprosthetic valve cusps** or the **native sinuses**, respectively.

(Circ Cardiovasc Interv. 2015;8:e002531.

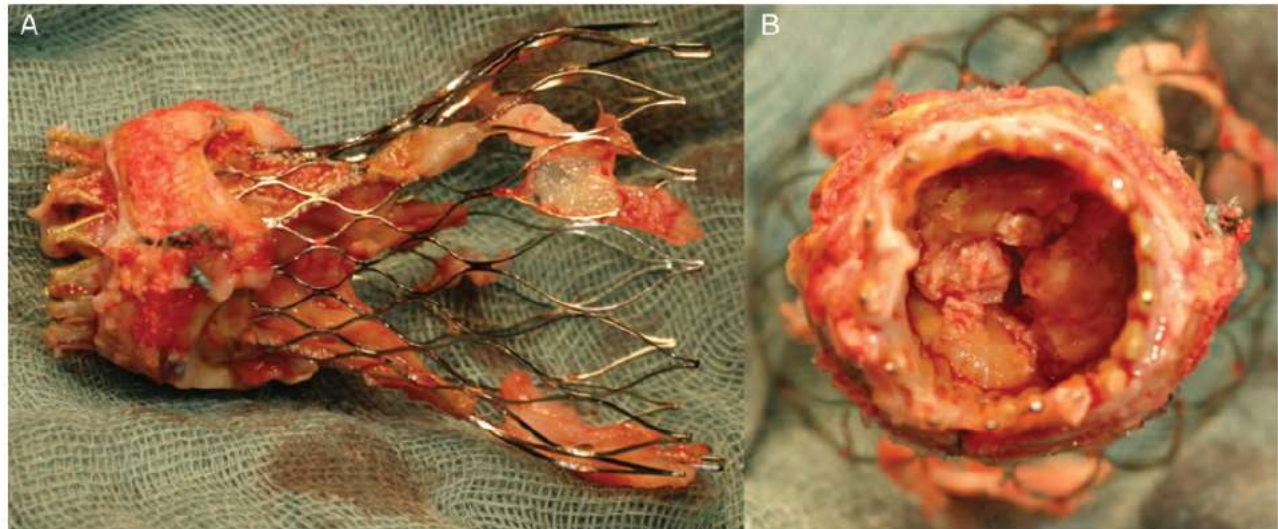
DOI: 10.1161/CIRCINTERVENTIONS.115.002531.)

Possible mechanisms of valve thrombosis



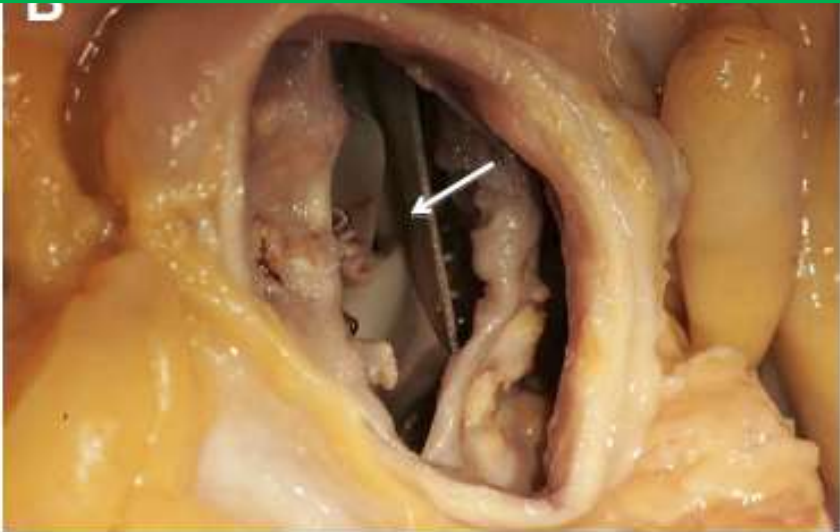
Coagulation disorders or prothrombotic conditions that predispose patients to thrombus formation

Previous infective endocarditis



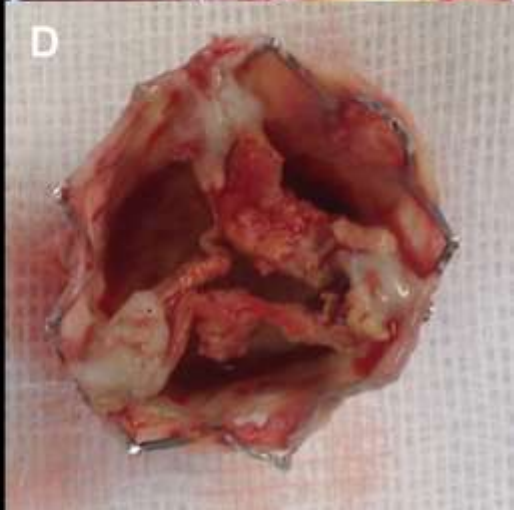
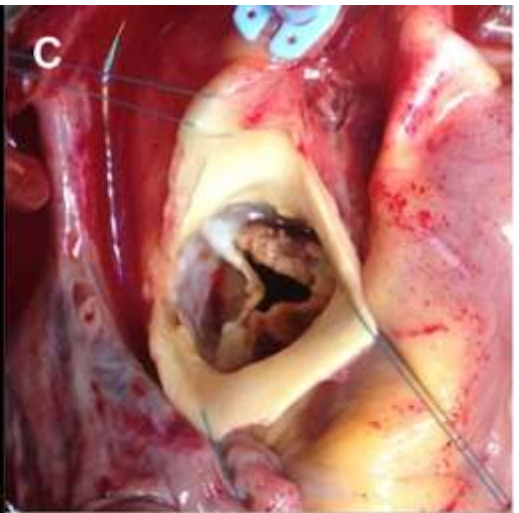
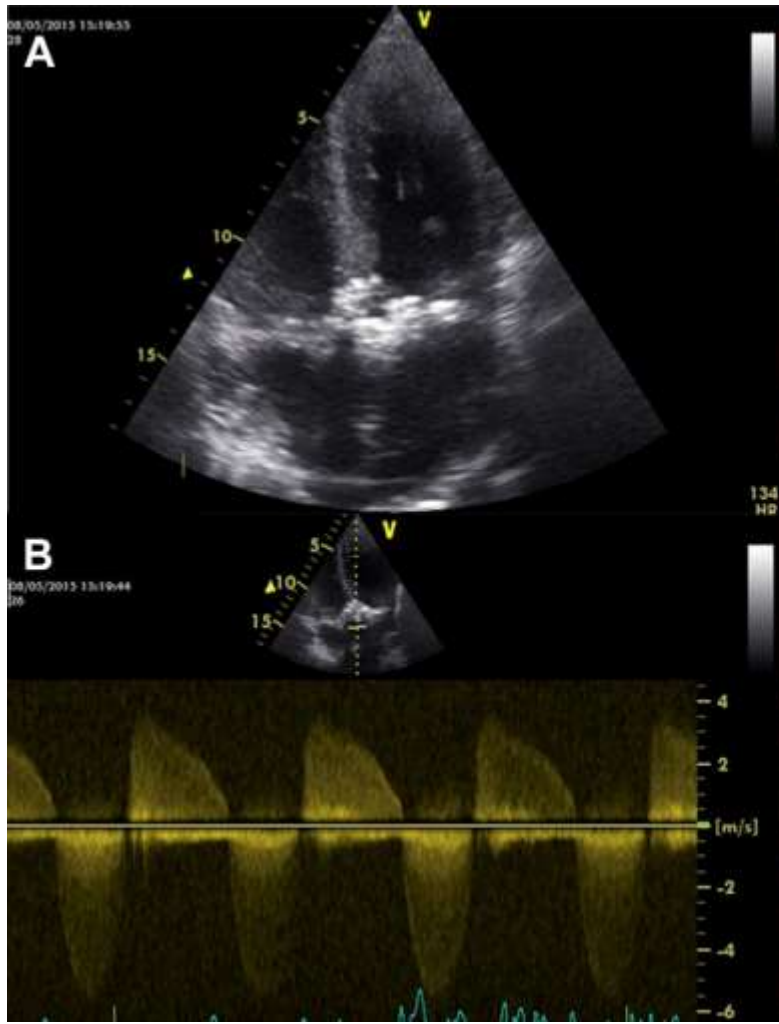
Possible mechanisms of valve thrombosis

valve malposition and incomplete expansion



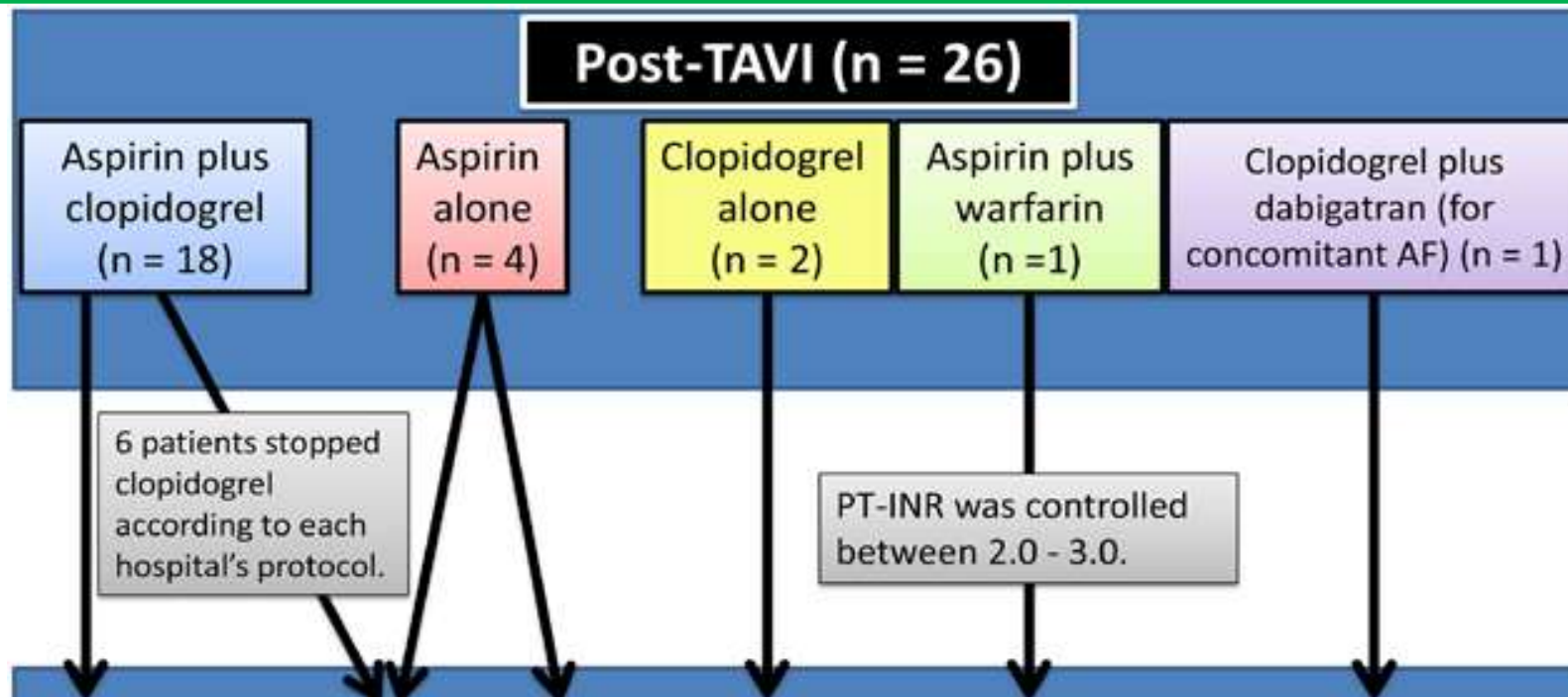
Possible mechanisms of valve thrombosis

Valve degeneration due to leaflet injury/fracture during crimping or implantation



Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

pertinent antithrombotic treatment as a possible mechanism??



The THV thrombosis was **not associated with discontinuation of antiplatelet/ antithrombotic therapy** or **with an underlying thrombogenic diathesis**, i.e., **THV thrombosis can occur, despite patients' drug compliance.**

Valve Thrombosis Following Transcatheter Aortic Valve Implantation: A Systematic Review

Juan G. Córdoba-Soriano, Rishi Puri, Ignacio Amat-Santos, Henrique B. Ribeiro, Omar Abdul-Jawad Altisent, María del Trigo, Jean-Michel Paradis, Eric Dumont, Marina Urena, and Josep Rodés-Cabau*

Clinical presentations

Echocardiographic Data

Diagnostics techniques					Echocardiographic data					
TTE	TEE	CT	Angio	ICE	LVEF	AR post-TAVI	Valve thickness	MG post-TAVI	MG at diagnosis	MG post-treatment
Yes	Yes	—	Yes	—	—	No	Yes	—	—	—
2 ¹¹	Yes	—	—	—	NSTEMI	—	Yes	—	—	—

➤ **Most patients experienced progressive dyspnea or refractory HF.**



—	—	—	7	34	9
59%	No	Yes	5	43	28
—	Trivial	Yes	—	41	—
—	—	Yes	—	9	—
60%	—	Yes	8	53	10
—	—	Yes	8	50	9
—	—	Yes	—	48	6
—	—	Yes	—	—	—
—	—	Yes	—	—	—
cases					
—	No	Yes	—	—	—
—	—	—	—	—	—

* LVEF, left ventricular ejection fraction; MG, mean gradient; NSTEMI, non-ST-segment elevation myocardial infarction; TAVI, transcatheter aortic valve implantation; TTE, transthoracic echocardiography; TEE, transesophageal

Diagnosis – Echocardiography

➤ increased valve thickness or restricted leaflet mobility or direct visualization of thrombus

➤ increase from baseline in transvalvular gradient

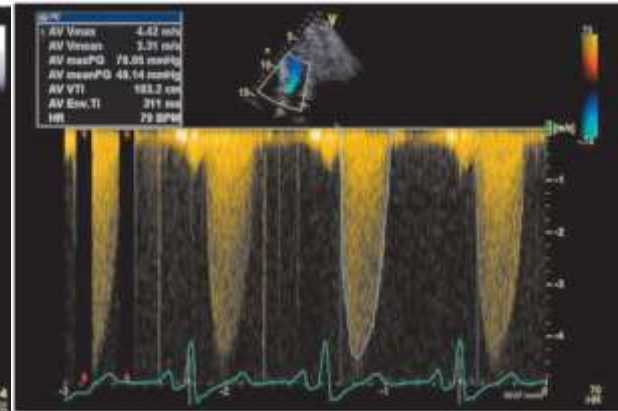
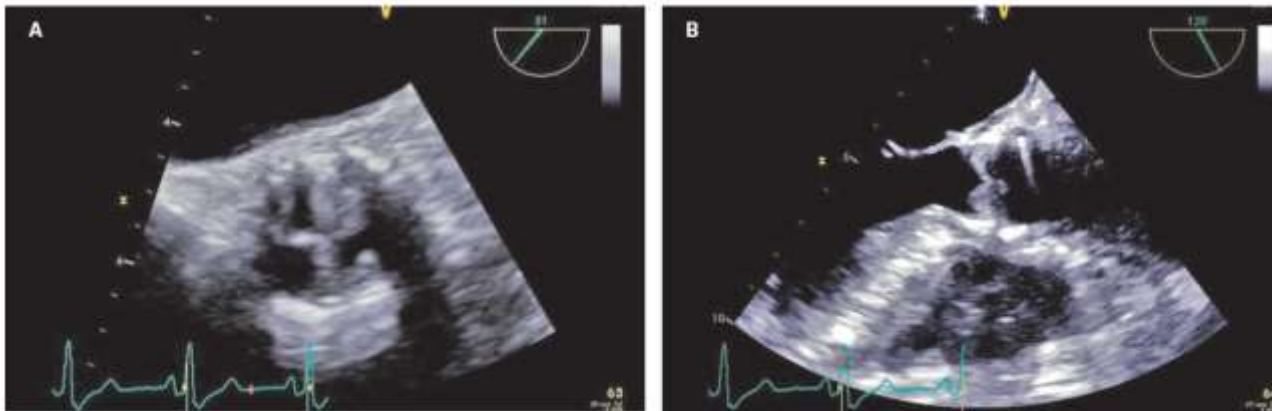


Figure 1: Transoesophageal echocardiography views of the prosthetic aortic valve before starting anticoagulation (short axis [A] and long axis [B]).

Figure 2: Continuous-wave Doppler of the prosthetic aortic valve before starting anticoagulation.

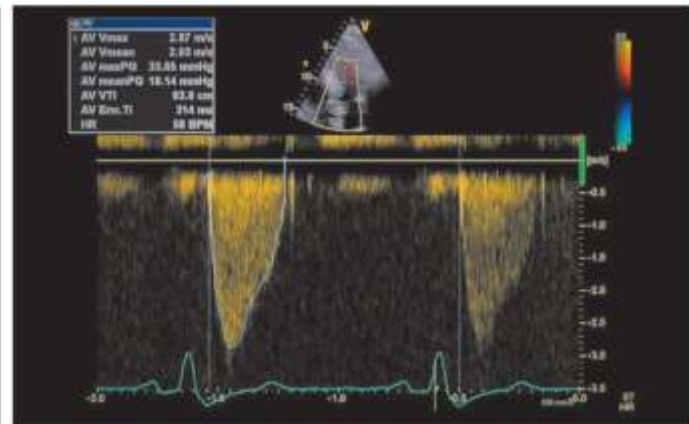
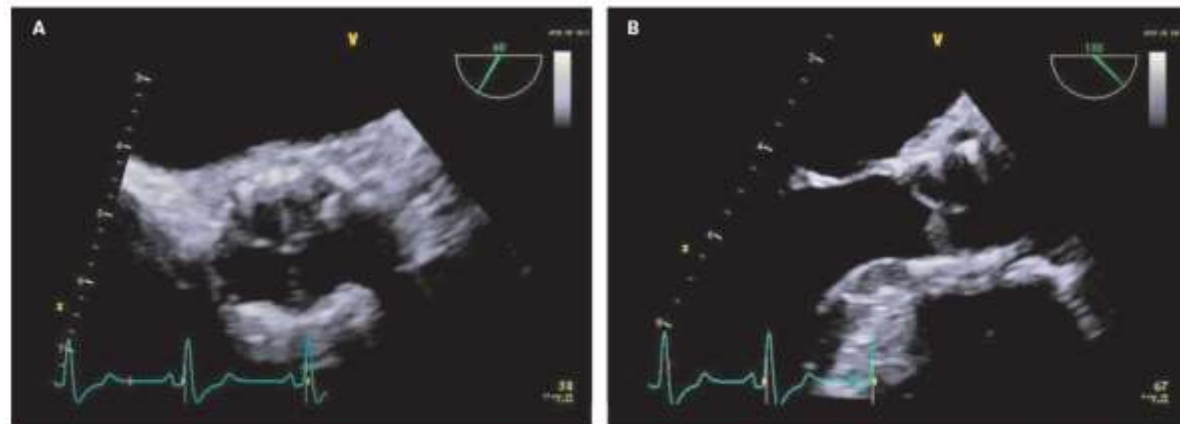


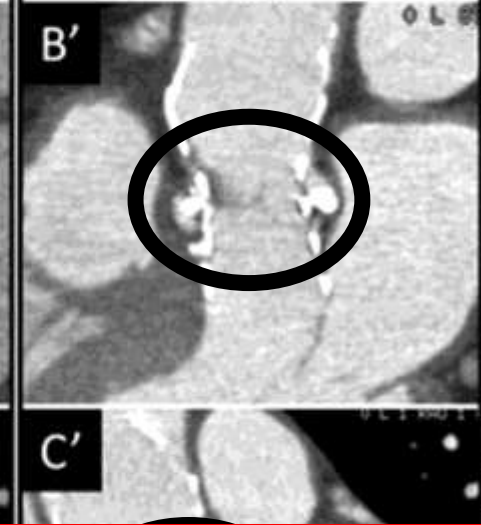
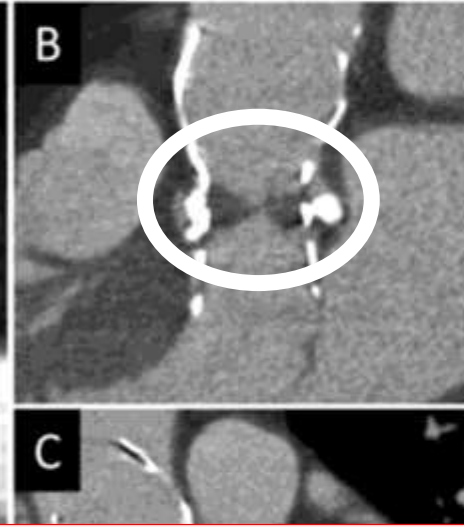
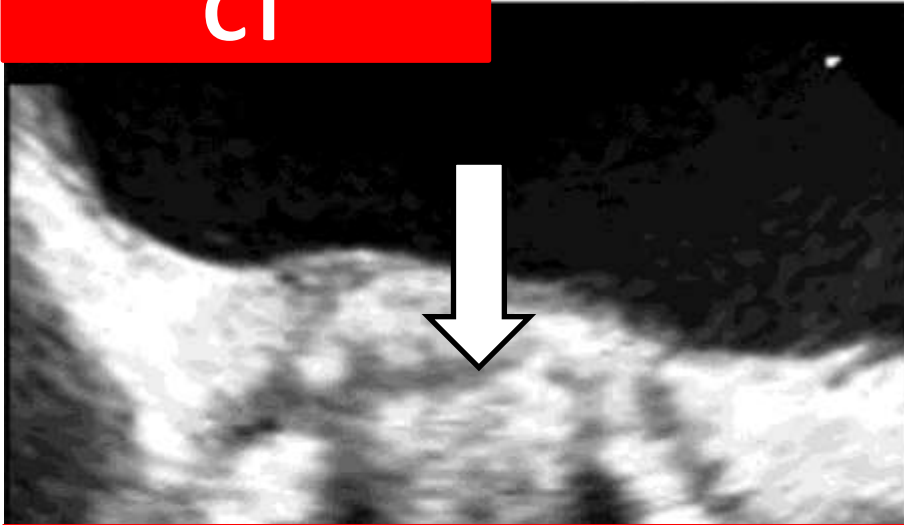
Figure 3: Transoesophageal echocardiography views of the prosthetic aortic valve after starting anticoagulation (short axis [A] and long axis [B]).

Figure 4: Continuous-wave Doppler of the prosthetic aortic valve after starting anticoagulation.

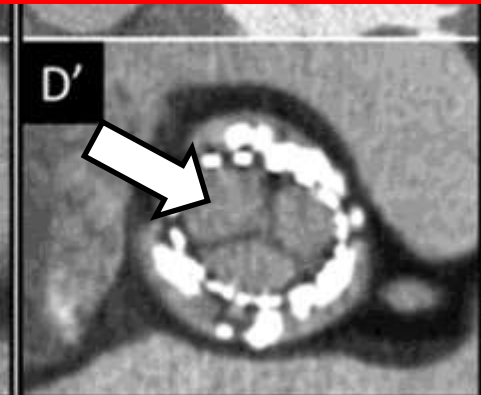
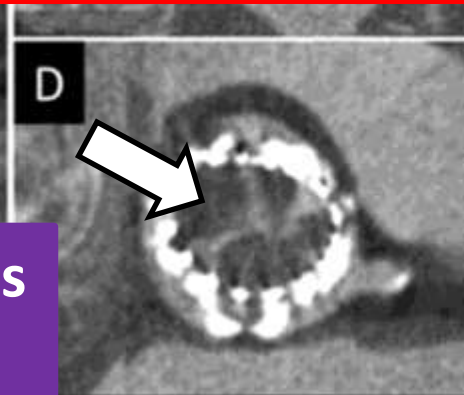
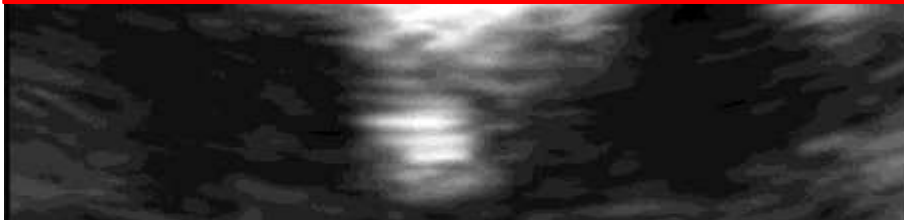
Diagnosis
CT

Diagnosis of THV thrombosis

8-months after
anti-coagulation



CT should be considered in patients with echo evidence of THV dysfunction or where cardiac embolism is suspected, irrespective of the echo findings.



CT revealed hypodense structures compatible with thrombus.

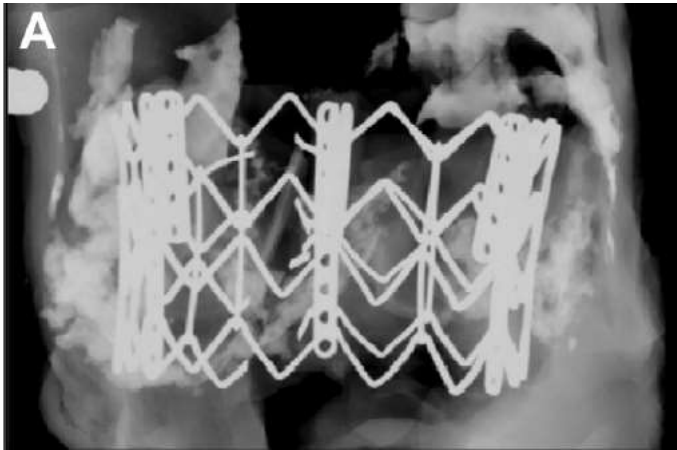
Thrombus Formation Following

(J Am Coll Cardiol Intv 2015;8:728-39)

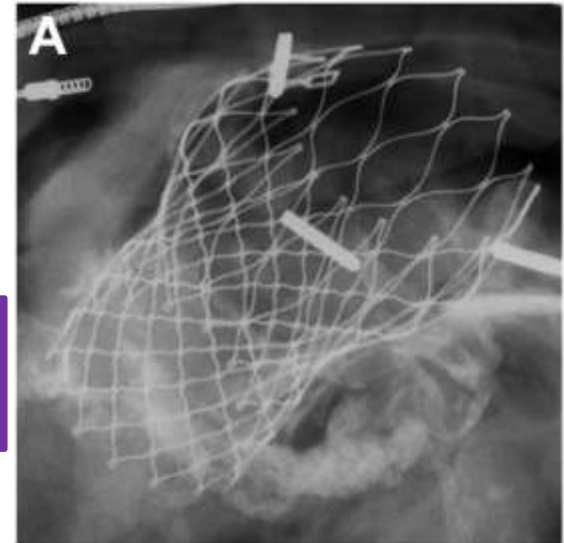
Transcatheter Aortic Valve Replacement

Diagnosis Pathology

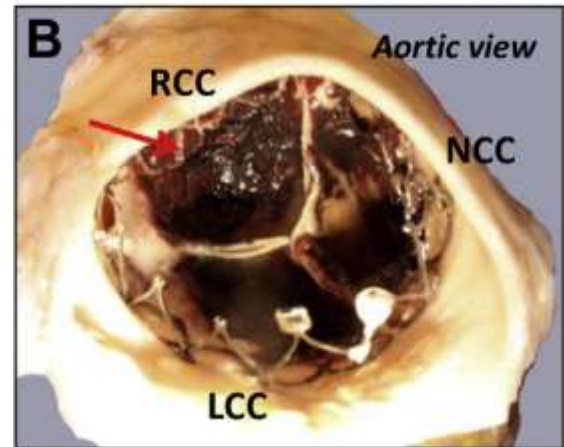
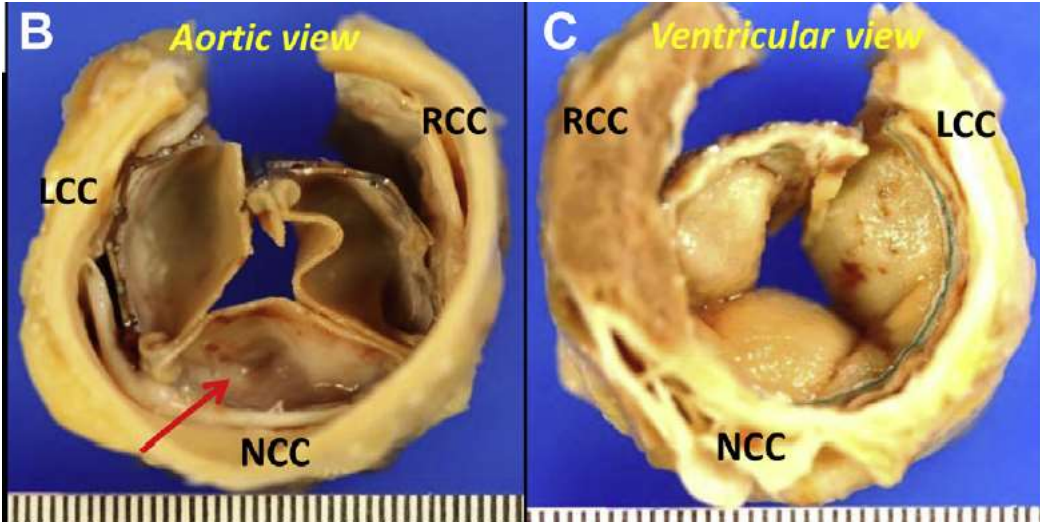
MD,* Sydney Pomenti, BS,* Christian Marin y Kall, MD,*
ID,† Elena Ladich, MD,† Robert Kutys, MS,† Yaar Aga, BS,*
Michael E. Ring, MD,|| Renu Virmani, MD†



Sapien



CoreValve



Valve Thrombosis Following Transcatheter Aortic Valve Implantation: A Systematic Review



Management and outcomes

Antos, Henrique B. Ribeiro, Omar Abdul-Jawad Altisent, Marina Urena, and Josep Rodés-Cabau*

Thrombosis management and clinical outcomes

Patient	Management of thrombosis						Treatment at discharge			Time to success, months	Hystopathologic confirmation
	ASA	Clopidogrel	VKA	UFH	LMWH	Surgery	ASA	Clopidogrel	VKA		
1 ¹⁰	-	-	-	-	-	Yes	-	-	-	-	Yes
2 ¹¹	-	-	Yes	Yes	-	No	-	-	Yes	1	No
3 ¹³	Yes	Yes	Yes	-	-	No	Yes	Yes	Yes	2	No
4 ¹³	Yes	No	Yes	-	-	No	Yes	No	Yes	2	No
5 ¹³	-	-	Yes	-	-	No	-	-	-	2	No
6 ¹⁴	-	-	Yes	-	-	No	-	-	Yes	3	No
7 ¹⁴	-	-	Yes	-	-	No	-	-	Yes	2	No
8 ¹⁴	-	-	Yes	-	-	No	-	-	-	2	No
9 ¹⁵	-	-	-	-	-	Sí	Yes	No	Yes	-	Yes
10 ¹⁶	-	-	-	-	-	Sí	-	-	-	-	Yes
11 ¹⁷	-	-	Yes	-	-	No	-	-	Yes	2.5	No
12 ¹⁸	-	-	Yes	-	Yes	No	-	-	Yes	10	No
13 ¹⁹	Yes	No	Yes	Yes	No	No	Yes	No	Yes	1	No
14 ²¹	Yes	Yes	Yes	-	-	No	Yes	Yes	Yes	3	No
15 ²²	-	-	-	-	-	No	-	-	-	-	Yes
16 ²²	-	-	-	-	-	No	-	-	-	-	Yes
Acute thrombosis cases											
17 ¹²	-	-	-	Yes	-	No	-	-	-	-	Yes
18 ²⁰	Yes	Yes	No	Yes	No	No	-	-	-	-	Yes

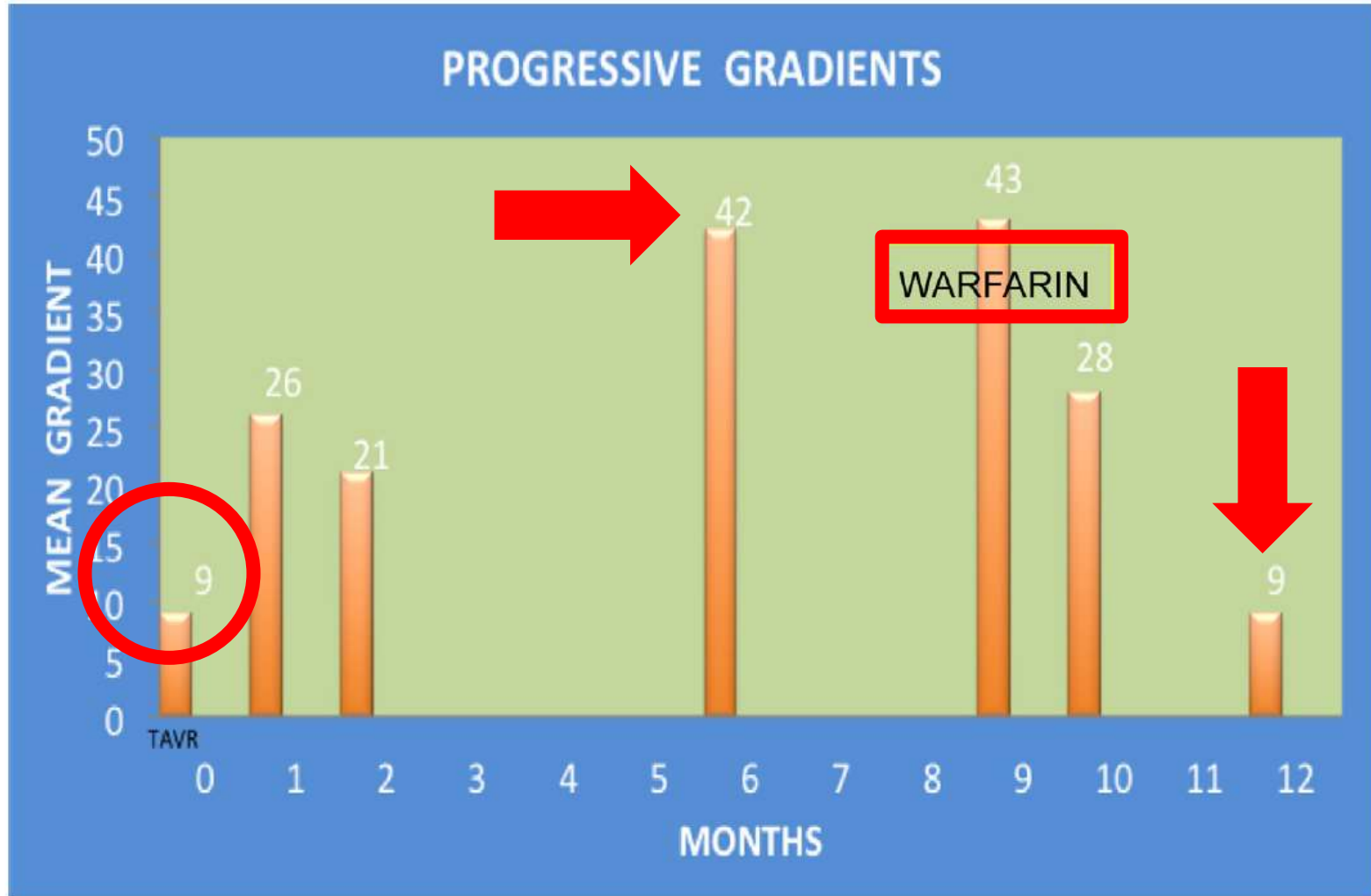
ASA, acetylsalicylic acid; LMWH, low molecular weight heparin; UFH, unfractionated heparin; VKA, vitamin K antagonist.

Treatment for valve thrombosis

- There were **no guidelines** to base a proper treatment for valve dysfunction secondary to thrombosis.
- **The most commonly** used treatment regimen for THV thrombosis was **anticoagulation, which proved to be extremely efficacious.**
- Anticoagulation was effective **even for chronic and organized thrombi.**
- This highlights the importance of **anticoagulation as soon as valve thrombosis is suspected**, not only in cases with visible thrombotic mass on valve leaflets but also in cases with THV

Valve in valve or surgery may be needed for those who anticoagulation is ineffective or contra-indicated.

Post-TAVR progressive PG over time



An increase is noted in the first 2 months with a marked increase at 6 and 9 months post-transcatheter aortic valve replacement (TAVR). Three months after initiation of anticoagulation therapy, mean pressure gradients (P_{mean}) normalized.

Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

- **23/26 (88%)** patients were treated with medical therapy, such as oral VKA with/without bridging heparin (n=21); heparin without subsequent oral because of high bleeding risk or patient refusal (n=2).
- **Anticoagulation was effective** and resulted in significant decrease of the AVPG or disappearance of the thrombotic mass in all 23 patients

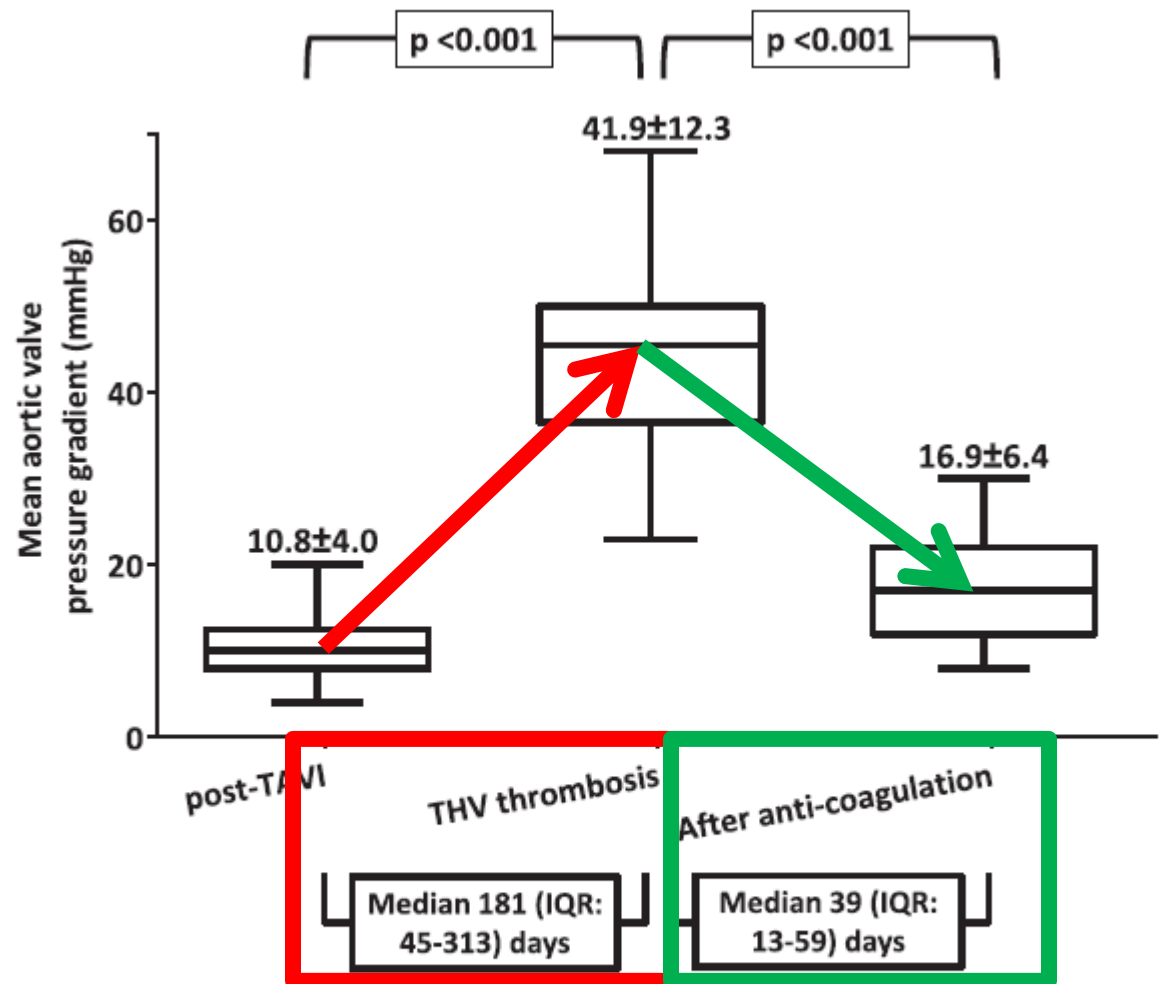


Figure 2. Significant decrease in mean aortic valve pressure gradient after treatment with anticoagulation. IQR indicates interquartile range; TAVI, transcatheter aortic valve implantation; and THV, transcatheter heart valve.

Prevention of thromboembolism in TAVR

- The main justification for use of antiplatelet and antithrombotic treatments post-TAVI is the **prevention of ischemic events, mainly cerebrovascular ones.**
- The antithrombotic therapy in the setting of TAVR has been **empirically determined**, with the most commonly recommended treatment consisting of **unfractionated heparin during the procedure** followed by (1) **aspirin** should be used indefinitely, (2) **concomitant clopidogrel for 3 to 6 months**, and (3) if **vitamin K antagonists** is indicated, no concomitant clopidogrel, based on experiences from coronary stents and surgical bioprosthesis.

Risk versus Benefit

Patients treated with TAVR are usually aging people and more fragile as compared with those who undergo surgical AVR

Prevention of
valve thrombosis and
other ischemic events



The low valve thrombosis incidence rates and the risks of anticoagulation-related bleeding may not allow recommendation of routine use of anticoagulants after TAVR.

Prevention of thromboembolism in TAVR

- In practice, actual use of antithrombotics/anticoagulation following TAVR is highly variable and should be **individualized**.

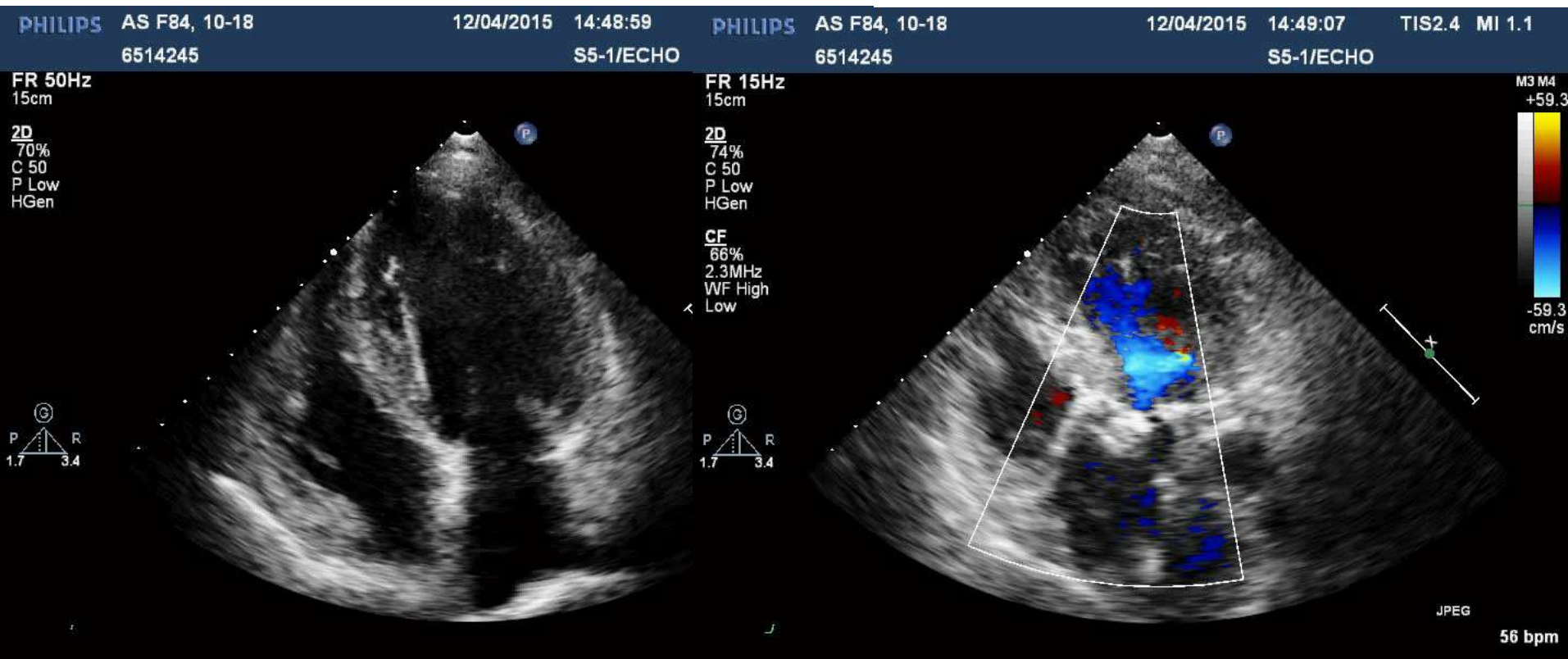
	PARTNER Trial (17,18)	ACC/STS Recommendations (58)	CCS Statement (59)
Pre-procedural	Aspirin 80 mg Clopidogrel 300 mg	—	—
Procedural	Unfractionated heparin Goal ACT: 250 s Reversal with protamine optional Bivalirudin—not allowed?	Unfractionated heparin Goal ACT: 300 s Reversal with protamine recommended Bivalirudin—not mentioned	—
Post-procedural (first 30 days)	Aspirin 81 mg/day indefinitely + Clopidogrel 75 mg/day × 90 days	Aspirin 81 mg/day indefinitely + Clopidogrel 75 mg/day × 3–6 months If warfarin indicated (AF), then no clopidogrel	Indefinite low-dose aspirin generally recommended + Thienopyridine × 1–3 months If oral anticoagulant indicated (AF), avoid triple therapy unless definite indication exists

ACC = American College of Cardiology; ACT = activated clotting time; AF = atrial fibrillation; CCS = Canadian Cardiovascular Society; STS = The Society for Thoracic Surgeons; TAVI = transcatheter aortic valve implantation.

- **Randomized trials** are the best path forward to determine the balance between the efficacy and risks of antithrombotic treatment in this high risk population.

TAVI case

F85, admitted for Fc IV heart failure,
70 mmHg MPG, 111 mmHg PPG, AVA= 0.6cm².

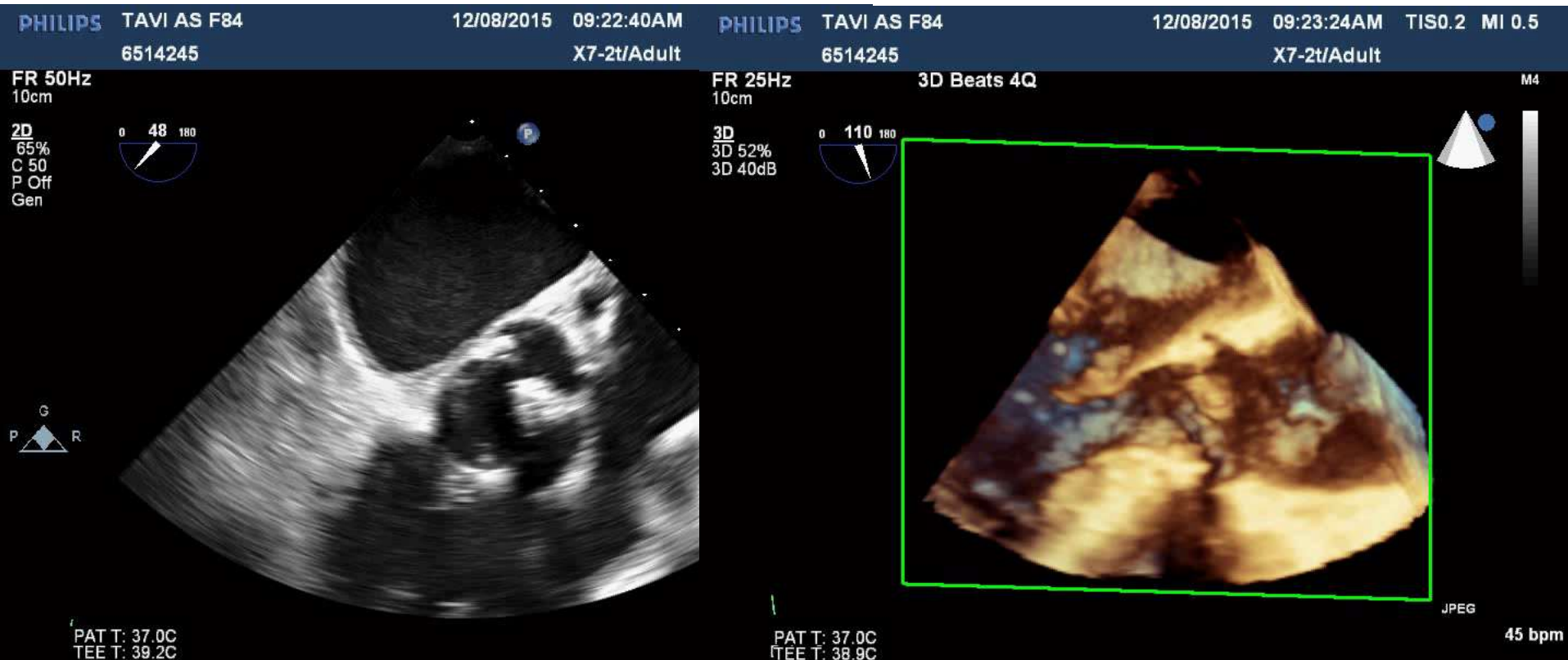


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TAVI case

F85, admitted for Fc IV heart failure,
Heavily calcified annulus and leaflets

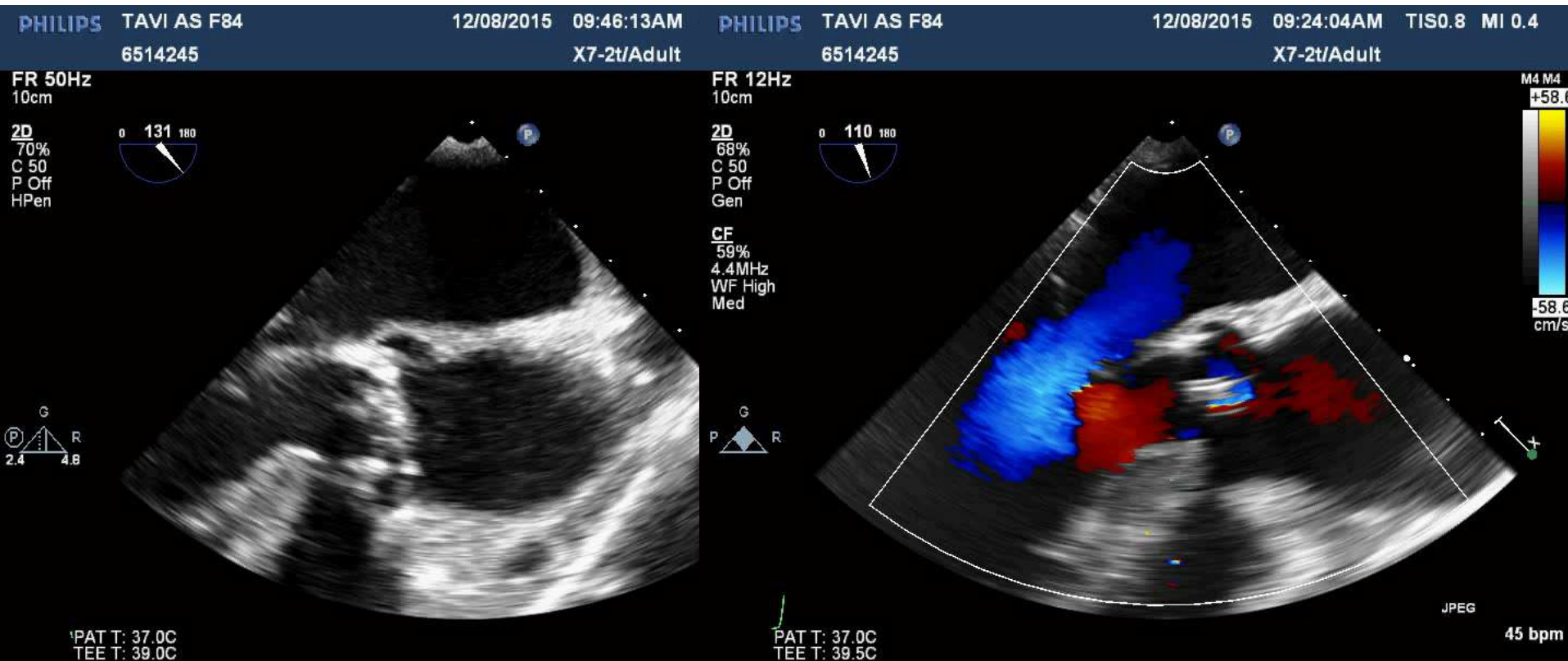


1015_20151208 OR T

1016_20151208 OR T

TAVI case

F85, admitted for Fc IV heart failure,
Heavily calcified annulus and leaflets w/ AS and AR

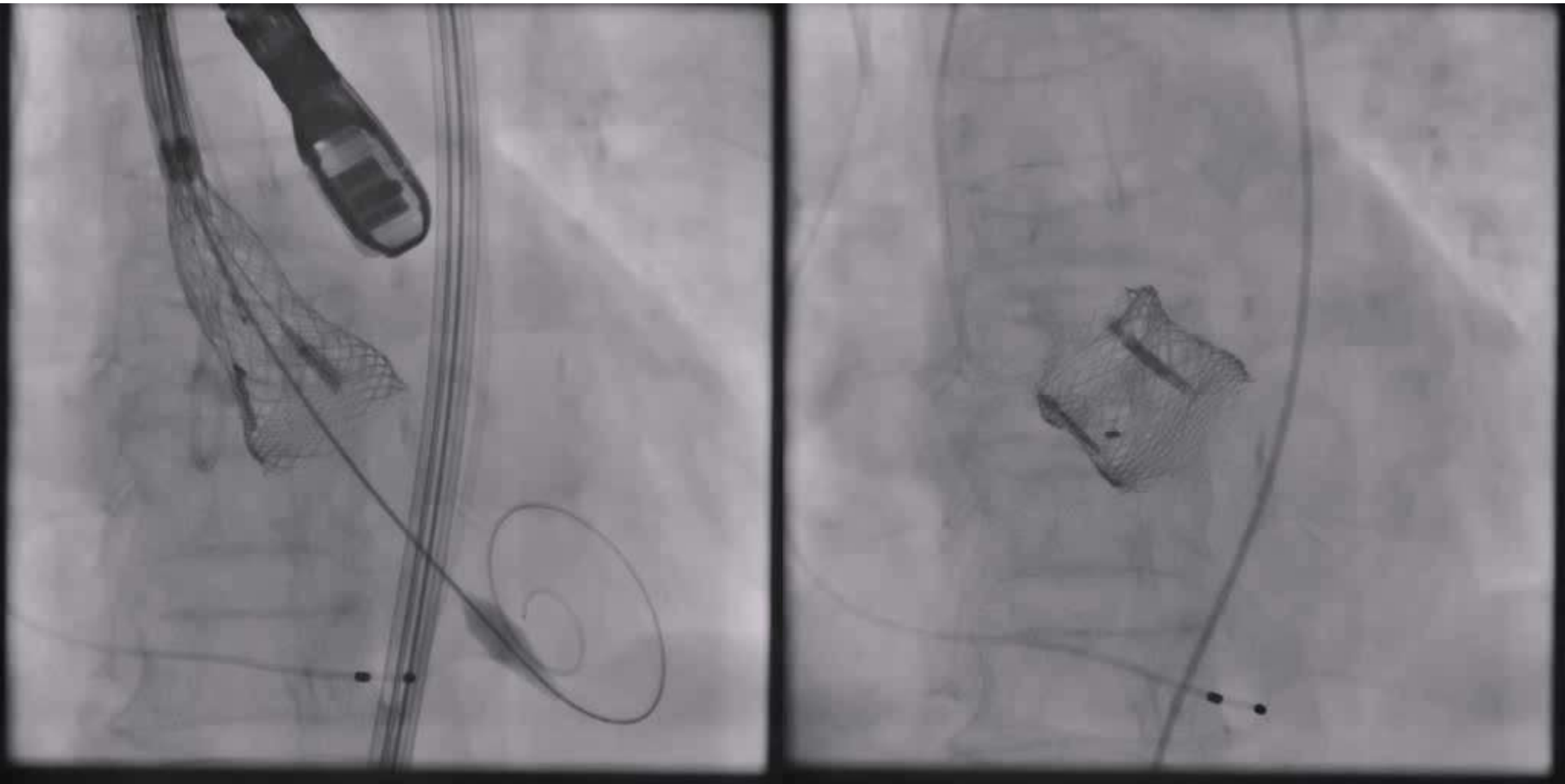


1027_20151208 OR T

1019_20151208 OR T

TAVI case

F85, admitted for Fc IV heart failure,
A 27mm Lotus valve was deployed



TAVI case

F85, admitted for Fc IV heart failure improved to Fc II,
Good prosthesis function but mild to moderate PVL
due to big annular calcium

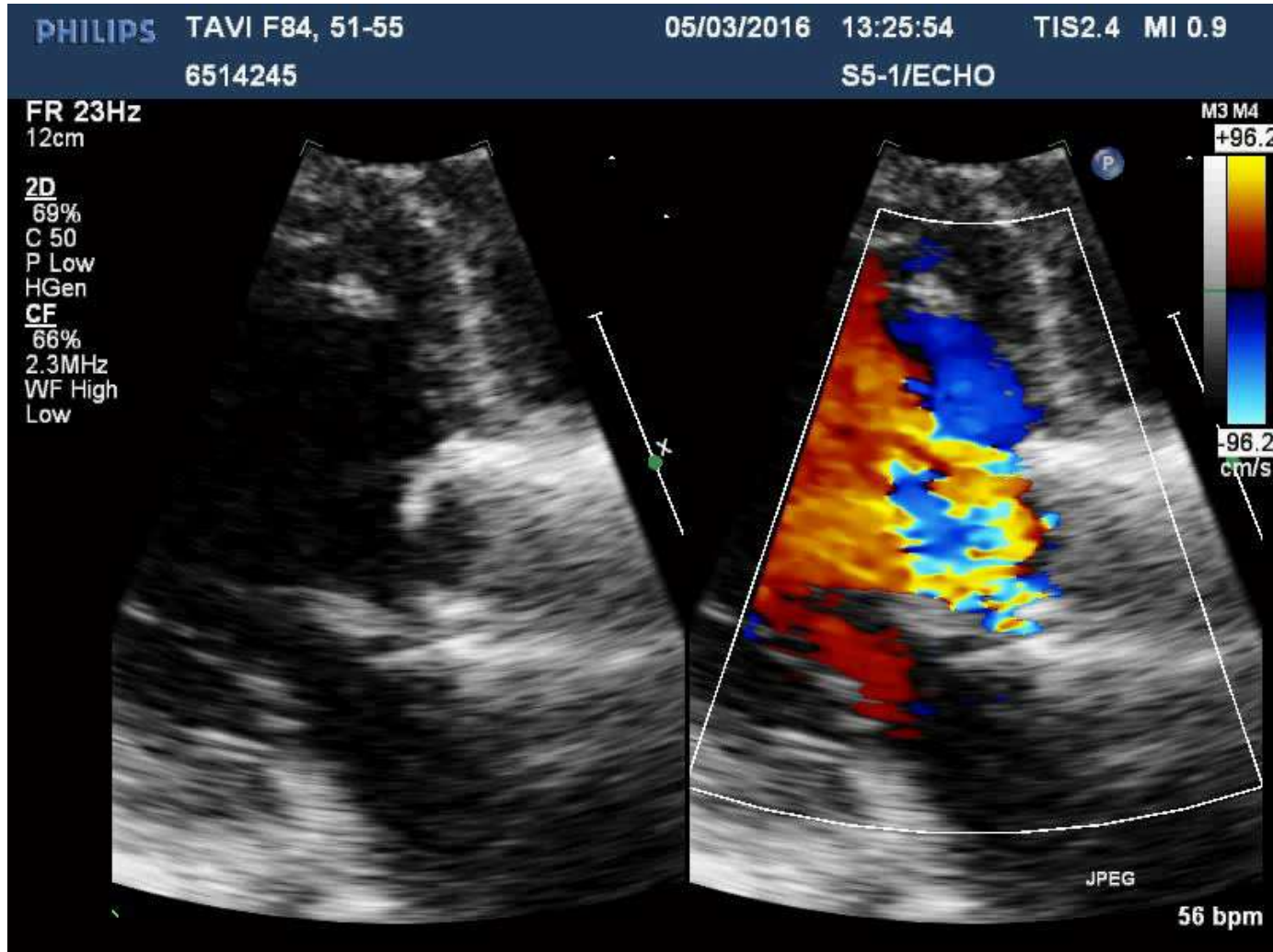


1093_20151208 OR T

1101_20151208 OR T

6 months later

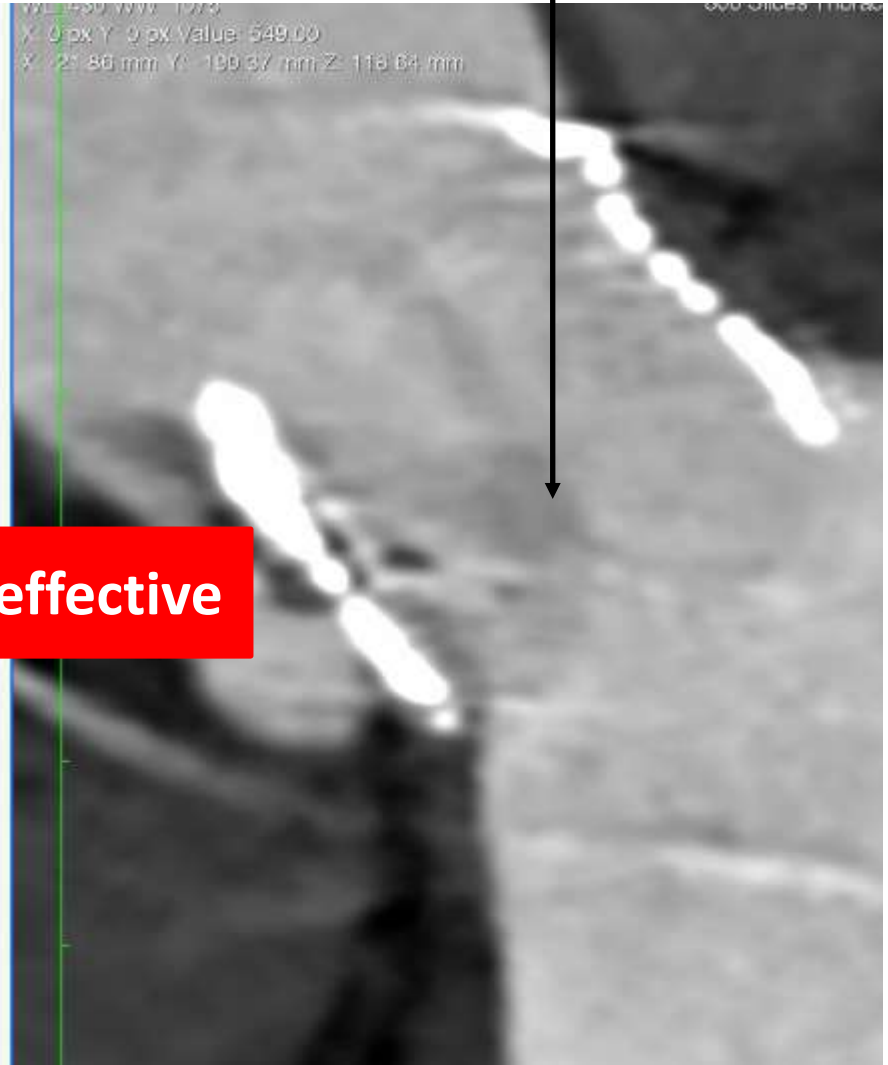
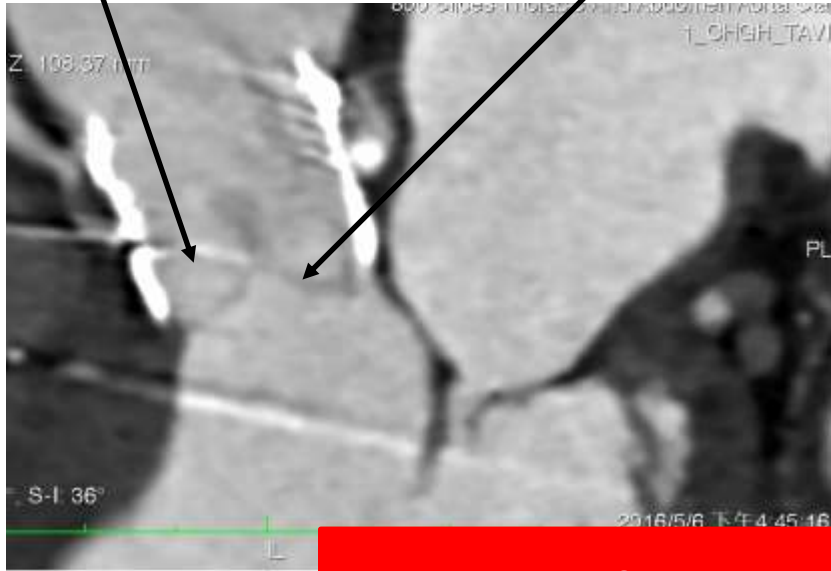
Progressive severe AR with Fc IV heart failure



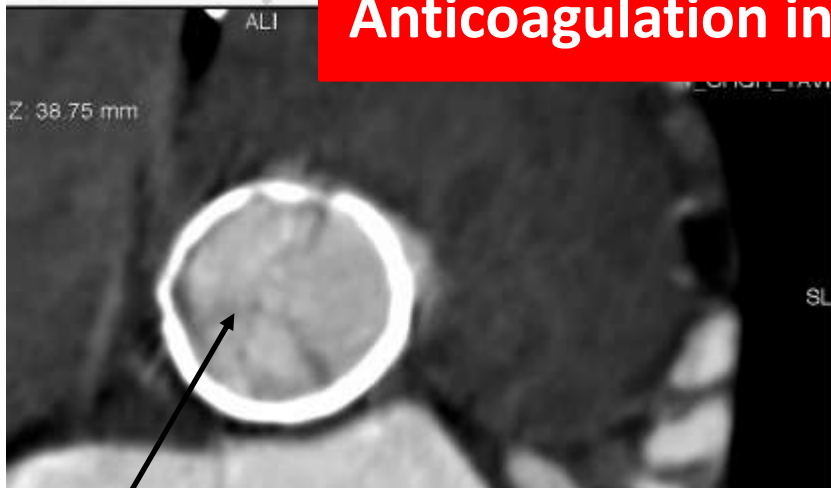
normal cups

Thickened cups

Thickened cups



Anticoagulation ineffective

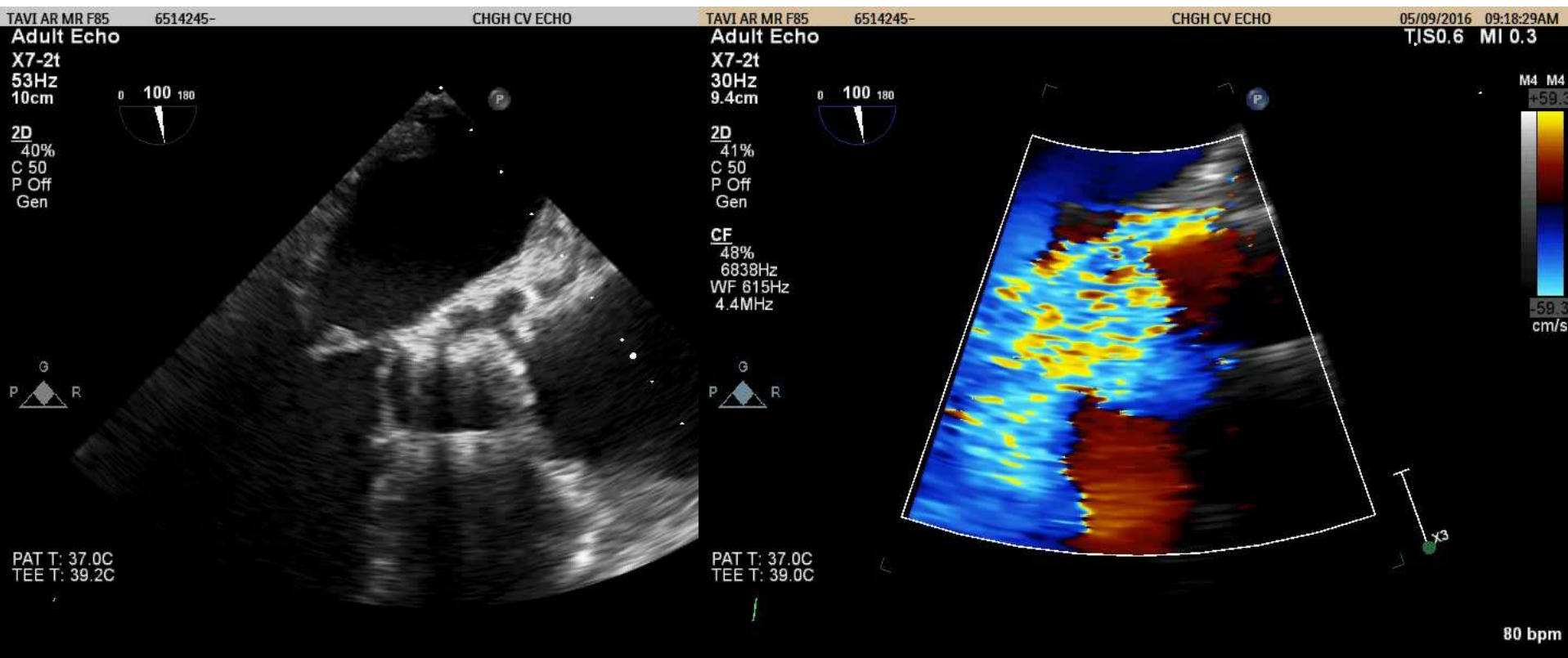


normal cups

Suspected valve thrombosis with prolapse

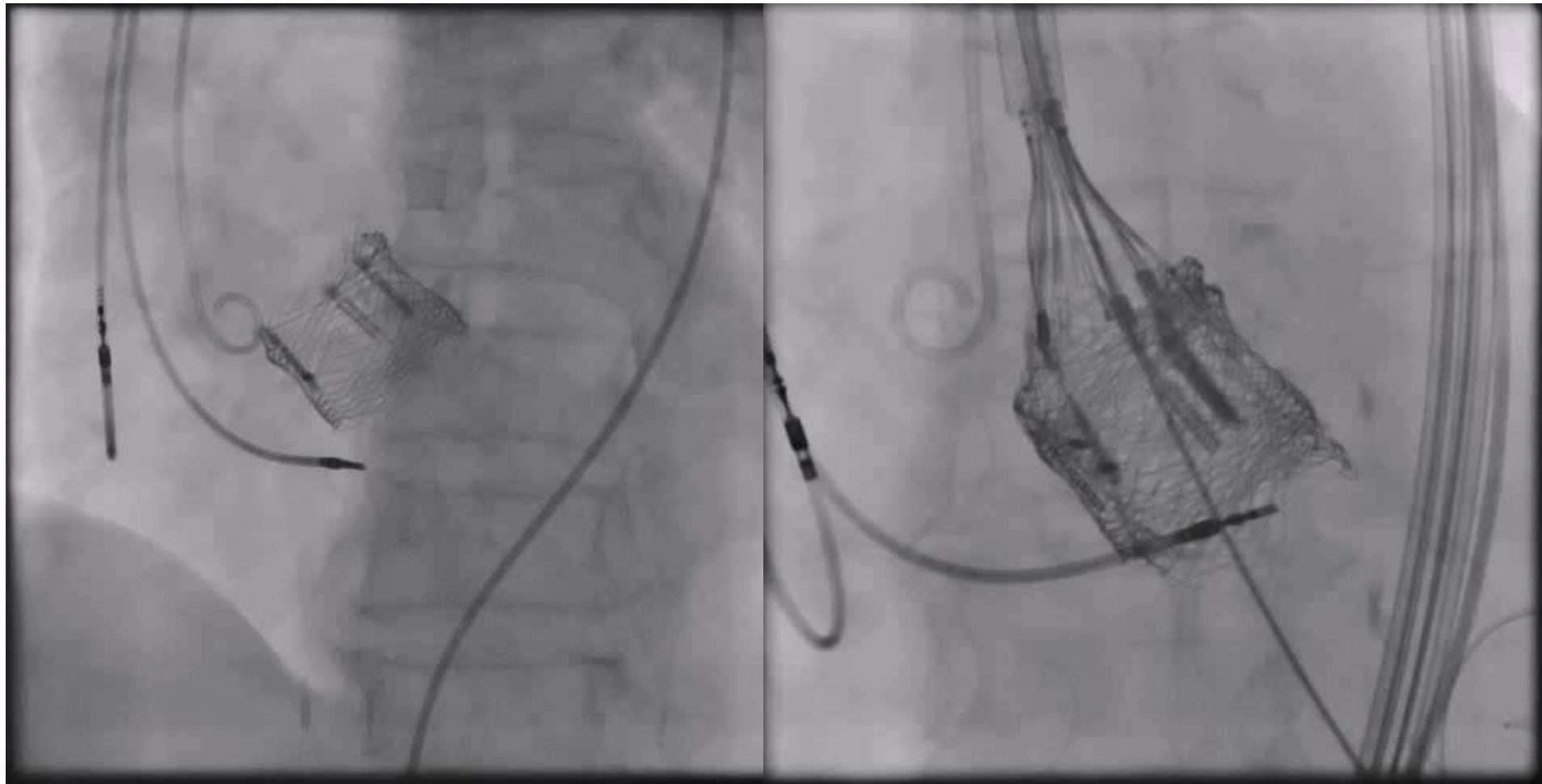
TAVI case

F85, admitted for Fc IV heart failure,
Prolapse of one leaflets with severe AR



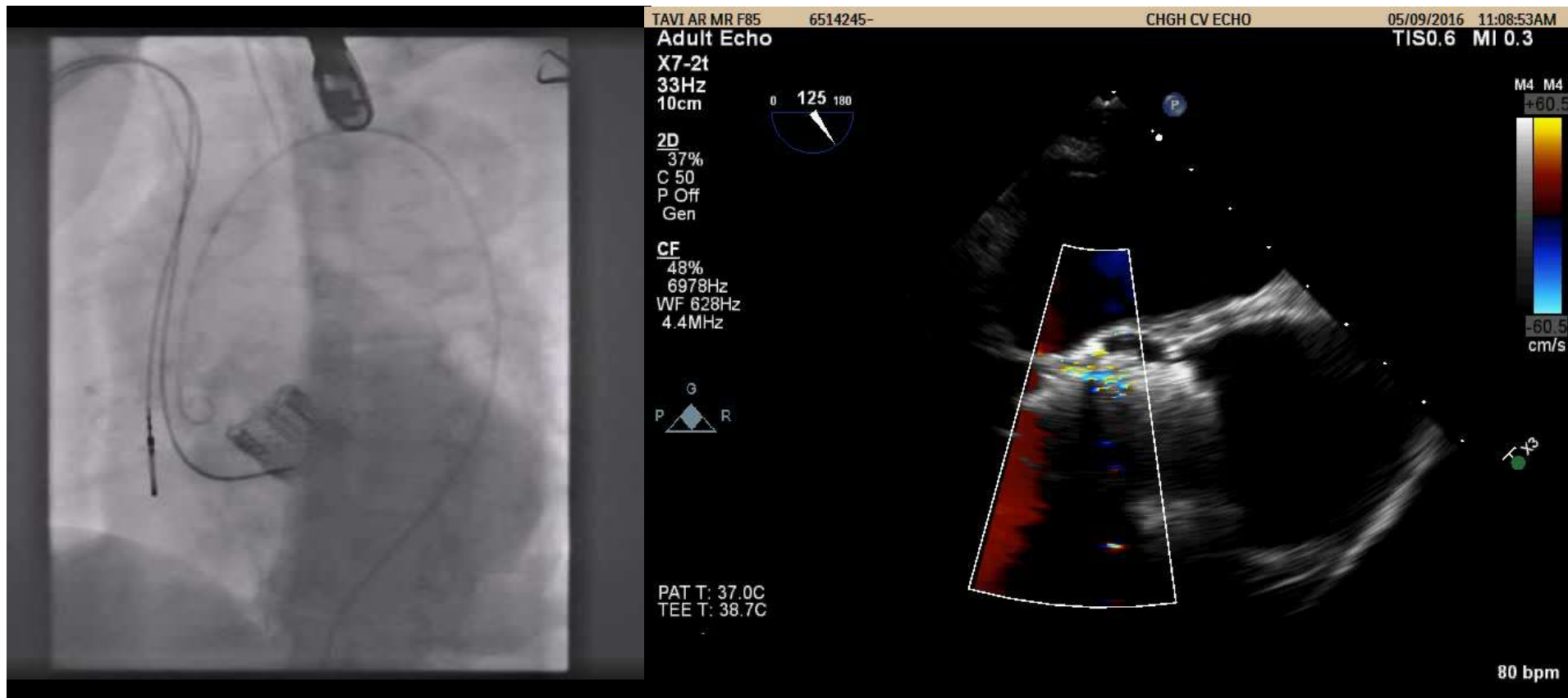
TAVI case

F85, admitted for Fc IV heart failure,
Another 27mm Lotus valve was deployed (Lotus-in-Lotus)



TAVI case

F85, admitted for Fc IV heart failure improved to Fc I-II,
After Lotus-in-Lotus treatment



Conclusions

- THV thrombosis is a rare phenomenon that was detected with in the **first 2 years after TAVI** and usually presented with **dyspnea and increased gradients**.
- Thrombosis should be suspected in cases of **premature THV dysfunction**, even if a thrombotic mass is not clearly detected.
- **Anticoagulation** resulted in restoration of normal THV function **within 2 months of treatment**, and should be considered the **treatment of choice** when THV thrombosis is suspected, **even in patients without visible thrombus** on echocardiography.
- **Valve in valve or surgery** may be needed for those who anticoagulation is ineffective or contra-indicated.



Thank You and Have a Nice Day!