Device based stroke prevention: Update on data, technologies and indications for LAA and PFO closure in EP patients

Thorsten Lewalter

Dept. of Cardiology and Intensive Care
Hospital Munich South
Peter Osypka Heart Centre
AFNET e.V. Deutschland







I2th Expert Meeting Berlin
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Consultant / Advisor / Speaker:

Medtronic, St. Jude, Biotronik, Boston Scientific, Cardiofocus, Bayer, Osypka, Boehringer,
Daiichi Sankyo, BMS, Pfizer, Novartis, Atricure, Toray, Abbott

Device based stroke prevention: Update on data, technologies and indications for LAA and PFO closure in EP patients

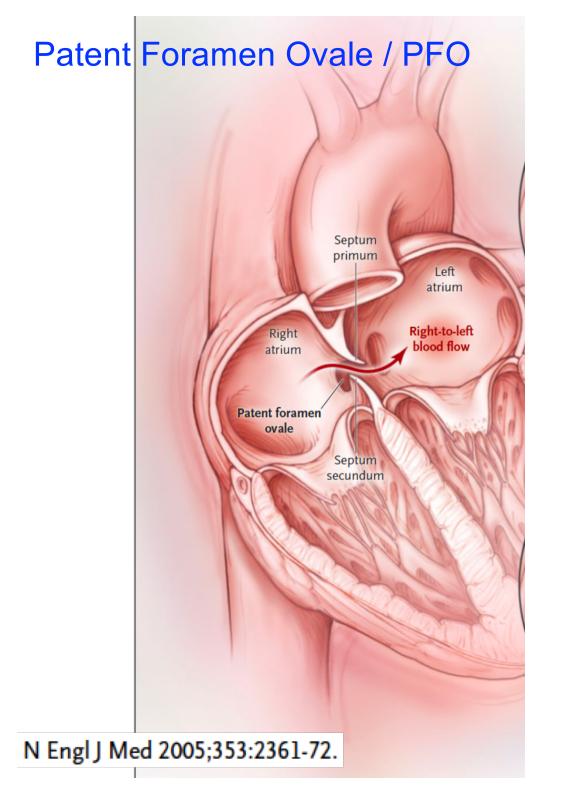
I. concept and device implantation (,,how")

2. clinical data ("why")

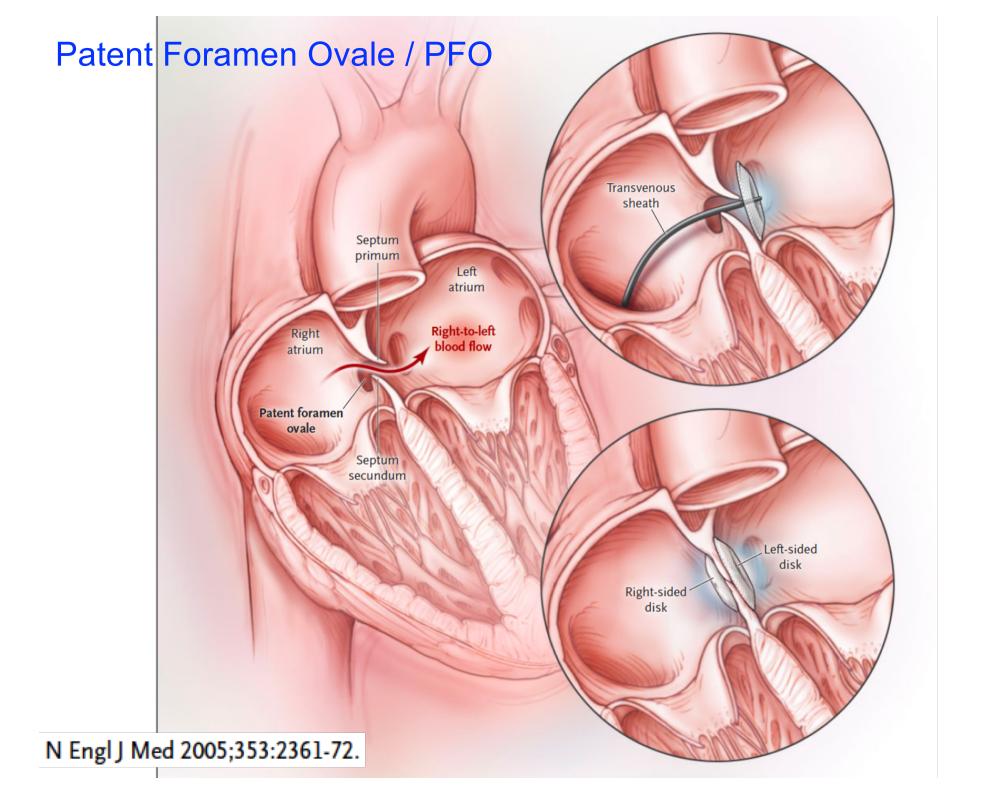
3. current indication ("when")





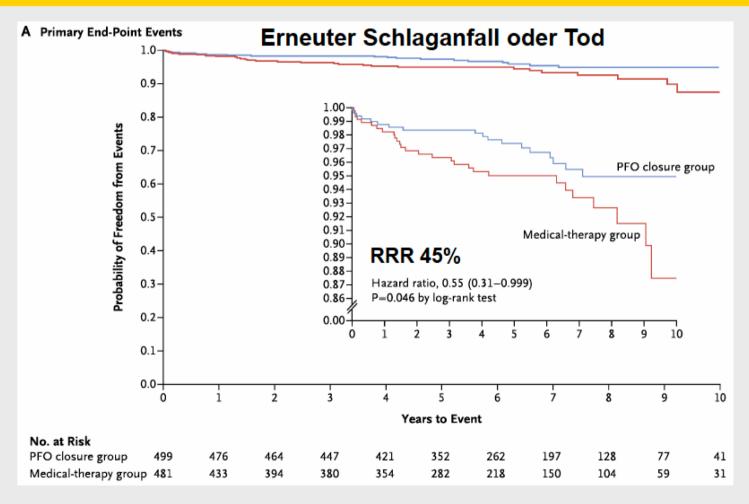






PFO Verschluss vs. medik. Therapie bei Z.n. kryptogenem Schlaganfall: RESPECT

Saver et al., N Engl J Med. 2017;377:1022-1032



Benefit ↑:

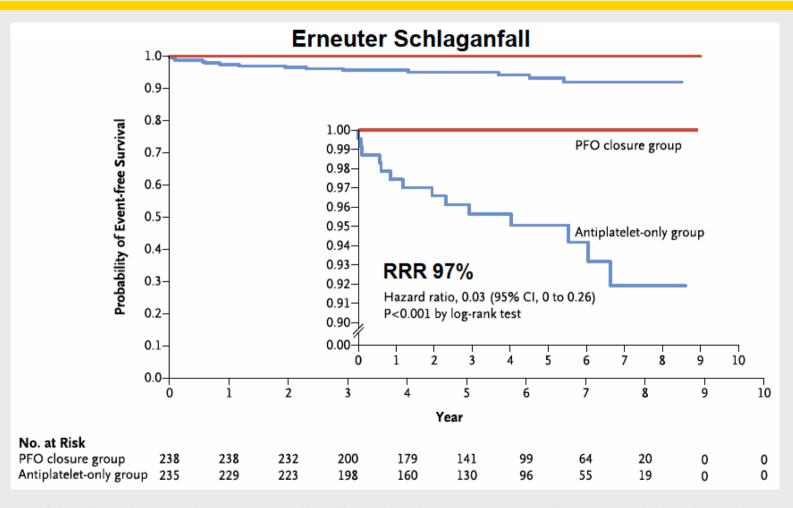
- Großer R-L-Shunt
- VH-Septum-Aneu.

VHF 0,2% vs. 0,2%

- N=980, Z.n. krypt. Schlaganfall, PFO im TEE, mittl. Alter 46 J., mittl. Follow-up 5,9 J., bis zu 10 J. FU
- Randomisiert Amplatzer PFO-Okkluder vs. medikamentöse Therapie (75% TAH, 25% OAK)

PFO Verschluss vs. medik. Therapie bei Z.n. kryptogenem Schlaganfall: CLOSE

Mas et al., N Engl J Med. 2017;377:1011-1021



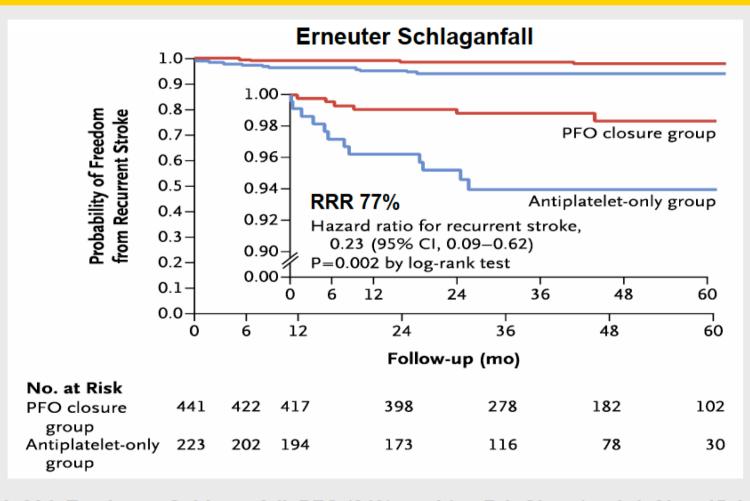
OAK vs. TAH: HR 0.44, n.s.

VHF 4,6% vs. 0,9%

- N=663, Z.n. krypt. Schlaganfall, PFO + ASA oder gr. R-L-Shunt, mittl. Alter 44 J., mittl. Follow-up 5,3 J.
- Randomisiert Okkluder-Device (50% Amplatzer) vs. antithrombozytäre Therapie vs. Antikoagulation

PFO Verschluss vs. medik. Therapie bei Z.n. kryptogenem Schlaganfall: REDUCE

Søndergaard et al., N Engl J Med. 2017;377:1033-1042



Neue Hirninfarkte in der Bildgebung nach 24 Monaten: HR 0.51

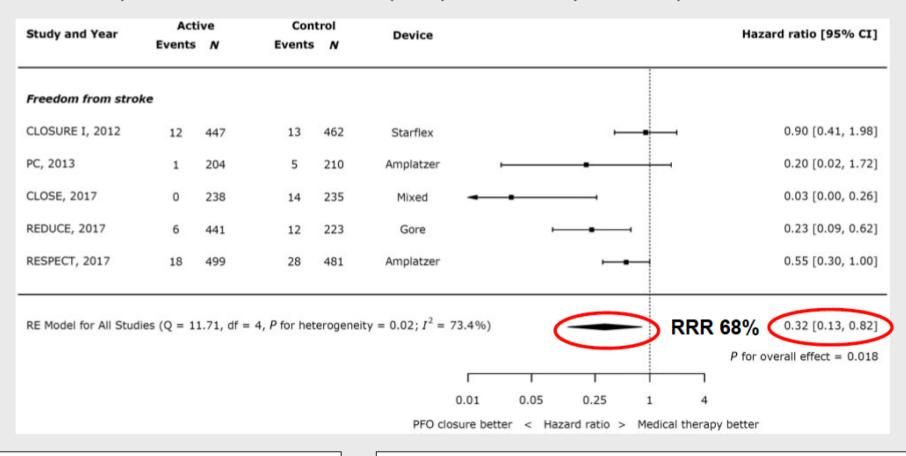
VHF 6,6% vs. 0,4%

- N=664, Z.n. krypt. Schlaganfall, PFO (81% mod./gr. R-L-Shunt), mittl. Alter 45 J., mittl. Follow-up 3,2 J.
- Randomisiert Okkluder-Device (Helex Septal / Cardioform Septal Okkluder) vs. antithrombozytäre Ther.

PFO Verschluss vs. medik. Therapie bei Z.n. kryptogenem Schlaganfall: Meta-Analyse

Ahmad et al., Eur Heart J. 2018;39:1638-1649

5 RCTs, N=3.440: CLOSURE-I, PC, RESPECT, CLOSE, Gore-REDUCE



Neu aufgetretenes VHF: HR 4,68

Benefit ↑: Großer R-L-Shunt (VH-Septum-Aneu. =)







Presseinformation

Ende des Patts: Kardiologen und Neurologen empfehlen Schirmchen zum Schutz vor Schlaganfall

13. August 2018 – Ein vergleichsweise einfacher Eingriff zum Verschluss des offenen Foramen ovale (PFO) kann das Risiko für einen Schlaganfall deutlich verringern, wenn zuvor eine sorgfältige Diagnostik keine Hinweise auf andere Schlaganfallursachen erbrachte. Das ist die wichtigste Aussage der heute veröffentlichten gemeinsamen S2e-Leitlinie "Kryptogener Schlaganfall und offenes Foramen ovale" der Deutschen Gesellschaft für Neurologie (DGN), der Deutschen Schlaganfall-Gesellschaft (DSG) und der Deutschen Gesellschaft für Kardiologie (DGK). "Wir

Indikation PFO Verschluss bei Z.n. kryptogenem Schlaganfall: S2-Leitlinie DGN / DSG / DGK

Diener et al., S2e-Leitlinie, 2018; in: Deutsche Gesellschaft für Neurologie (Hrsg.); online: www.dgn.org/leitlinien

Empfehlung 1

Bei Patienten zwischen 16 und 60 Jahren mit einem (nach neurologischer und kardiologischer Abklärung) kryptogenen ischämischen Schlaganfall und offenem Foramen ovale mit moderatem oder ausgeprägtem Rechts-Links-Shunt soll ein interventioneller PFO-Verschluss durchgeführt werden.

Empfehlungsgrad A, Evidenzebene I

Empfehlung 2

Bei Patienten mit einem kryptogenen ischämischen Insult und offenem Foramen ovale, die einen PFO-Verschluss ablehnen, gibt es keine Hinweise auf eine Überlegenheit einer oralen Antikoagulation gegenüber einer Behandlung mit einem Thrombozytenfunktionshemmer. Daher sollte die Sekundärprävention mit Aspirin oder Clopidogrel erfolgen.

Empfehlungsgrad B, Evidenzebene II

Empfehlung 4

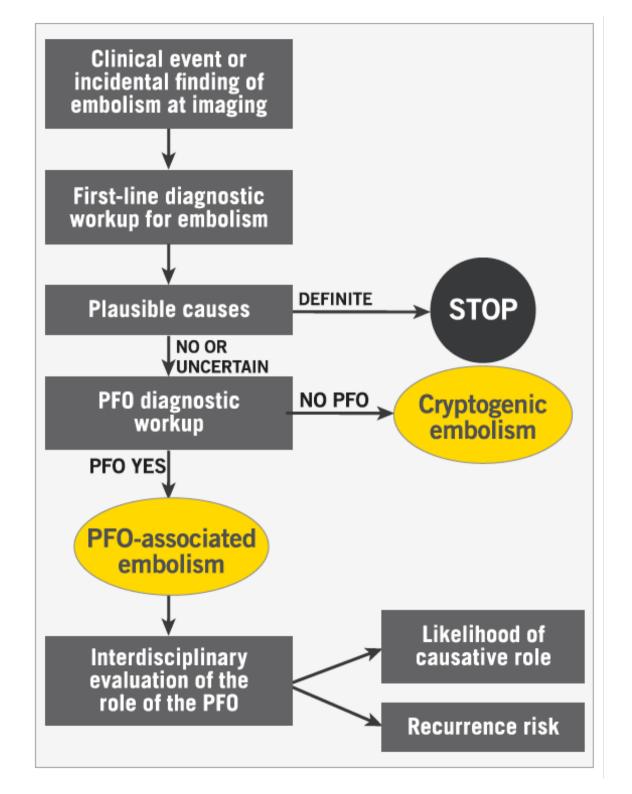
Vorhofflimmern, Perikardtamponaden sowie Lungenembolien sind beschriebene Komplikationen im Rahmen und nach Implantation eines Okkluders. Die Ereignisse sind aber so selten, dass sie den Empfehlungsgrad für die Implantation nicht beeinflussen sollten.

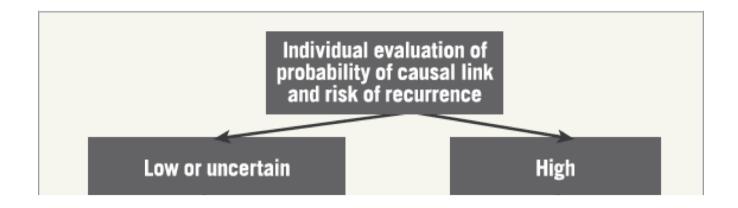
Empfehlungsgrad A, Evidenzebene Ia

European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism









LIKELIHOOD OF CAUSAL LINK

Atrial septal aneurysm

High

- Atrial septal hypermobility
- Moderate/severe shunt
- -Simultaneous PE or DVT

OTHER FEATURES TO BE CONSIDERED

- Imaging features of embolism (cortical vs. deep)
- PFO size and tunnel length
- Chiari network
- Prominent Eustachian valve
- Clinical clues (long travel, immobilisation, straining activity, recent major surgery, previous DVT or PE, OSAS)
- -Age <55 years old
- Risk factors for stroke
- RoPE score

RISK OF RECURRENCE

ligh

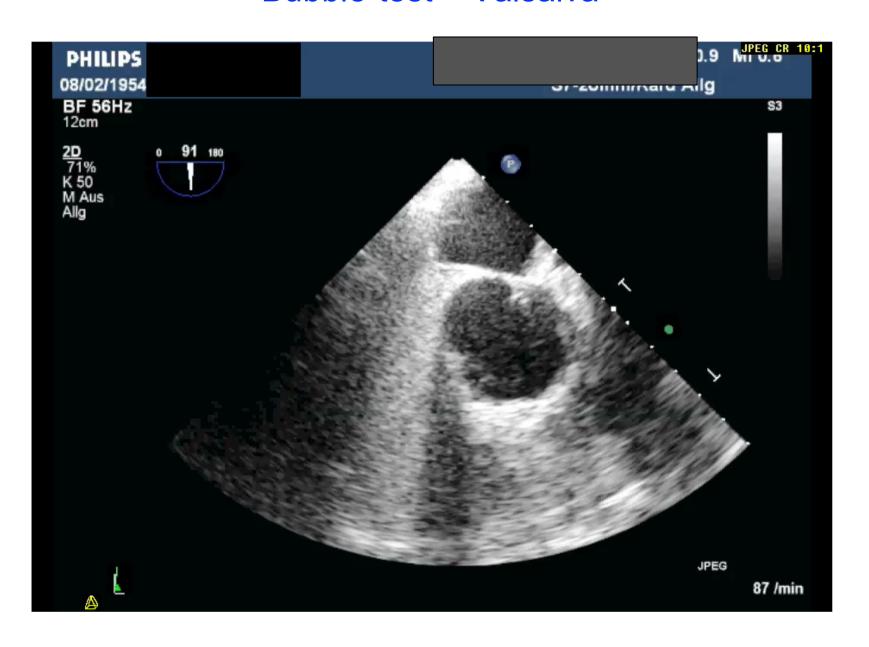
Atrial septal aneurysm

-Coagulation disorders

OTHER FEATURES TO BE CONSIDERED TO ASSESS RISK

- -Older age
- PFO size
- Need for antiplatelets vs. OAC
- Stroke vs. TIA as index event
- Stroke on Rx with antiplatelets or OAC

Bubble-test + Valsalva



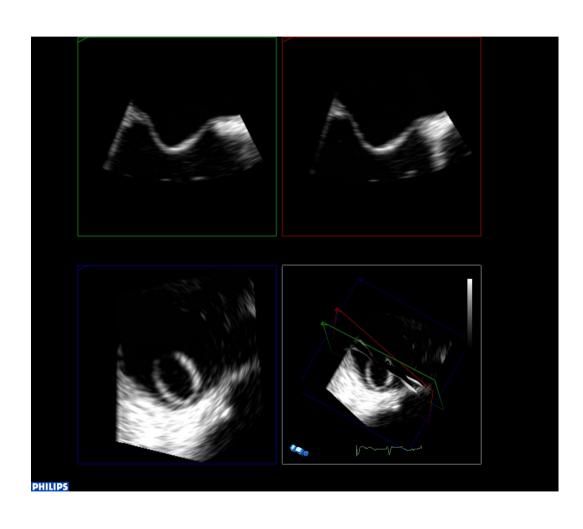
PFO-Grading: "bubble-crossing" RA to LA

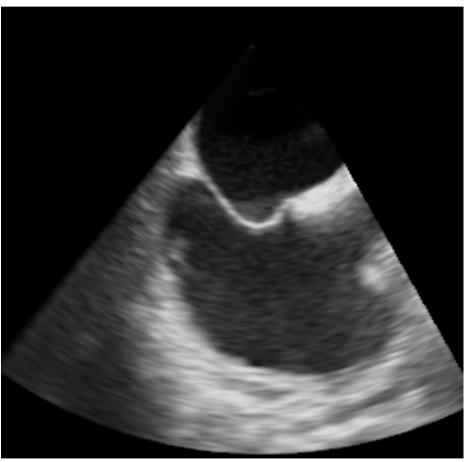
- grade 0: no bubble
- grade I: minimal (0-5 bubbles)
- grade II: moderate (6-20 bubbles)
- grade III: severe (>20 bubbles)

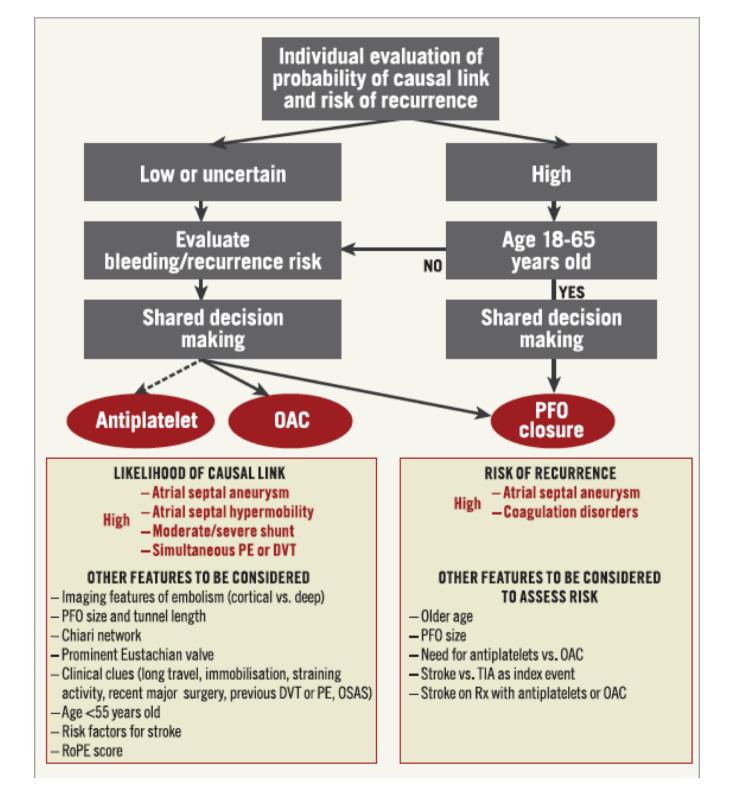




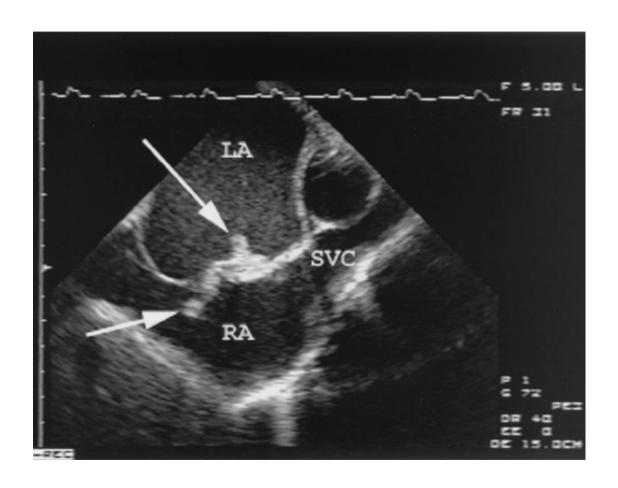
Atrial-Septal-Aneurysm (ASA)

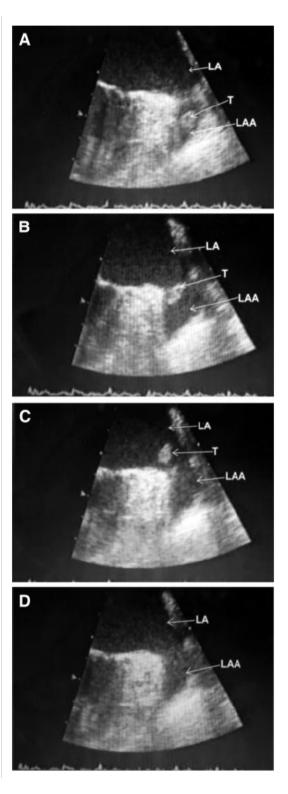


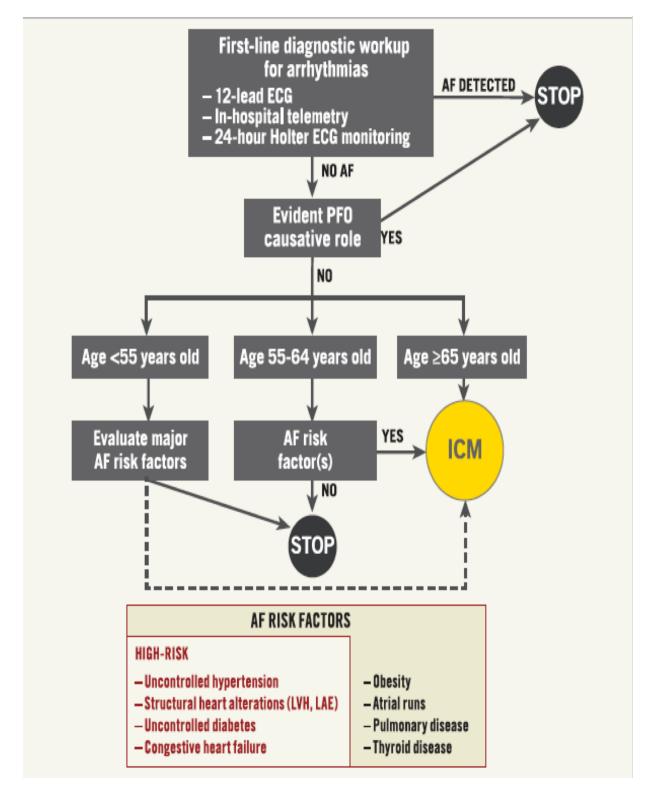




Embolic Stroke: PFO and paradoxical embolism vs int. silent AF and LAA embolism





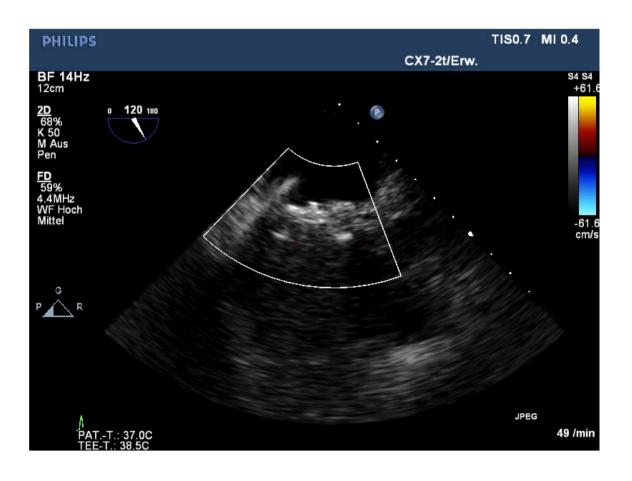


Unexplained embolic stroke

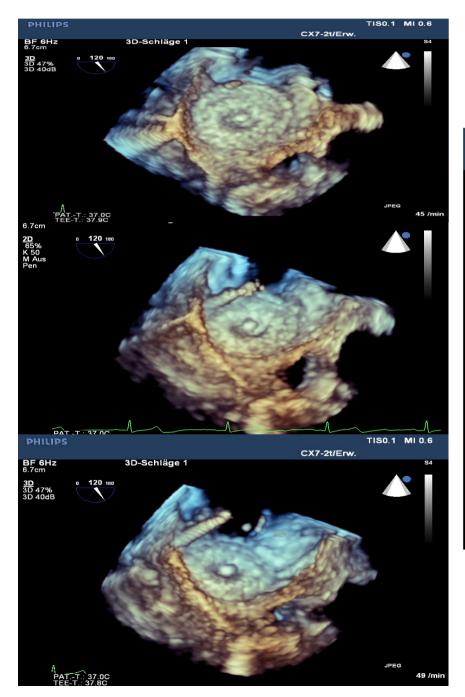


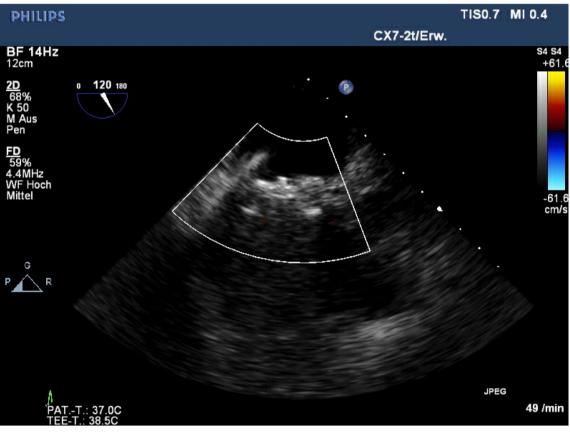
AF Detection vs PFO

Transseptal Puncture for AF-Ablation Post Septal Occluder Implantation



Transseptal Puncture for AF-Ablation Post Septal Occluder Implantation





PFO-Summary

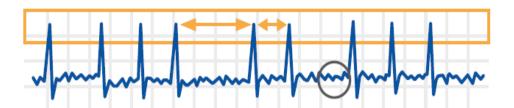
 Significant recurrence risk reduction in cryptogenic stroke patients post PFO closure vs drugs (at low event rates) in three RCT's

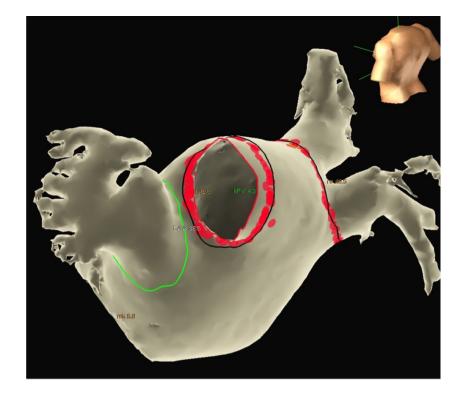
S2-guideline (DGN/DGK/DSG)

PFO-closure in young (16-60 yrs.) crpytogenic stroke pts. with moderate to severe R-L-Shunt

Search for AF in elderly patients!

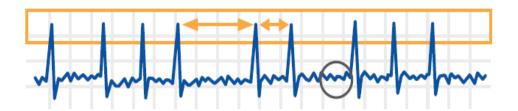
OAC not superior to antiplatelet therapy!

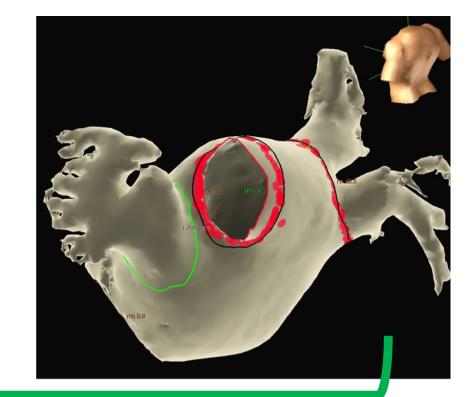




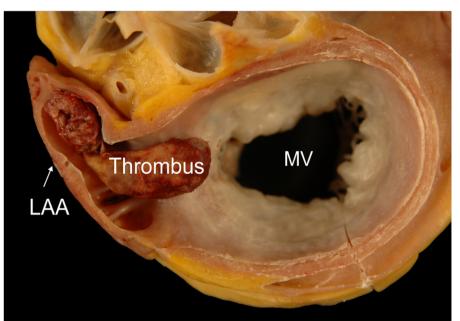






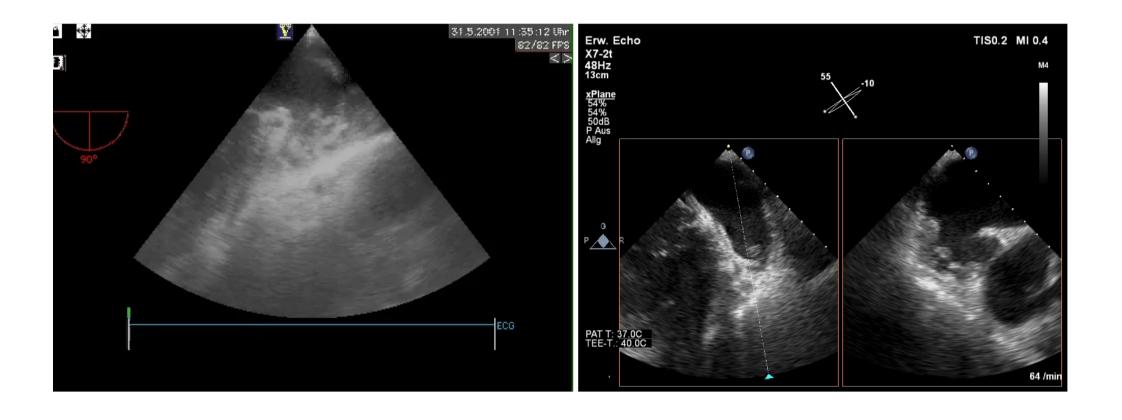








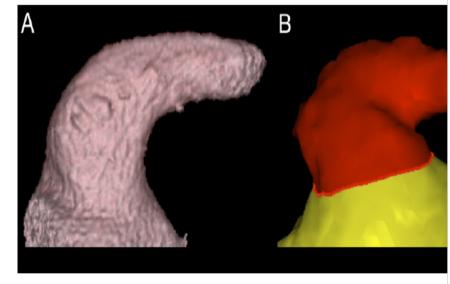
TEE findings in Stroke Patients "LAA is the smoking gun"



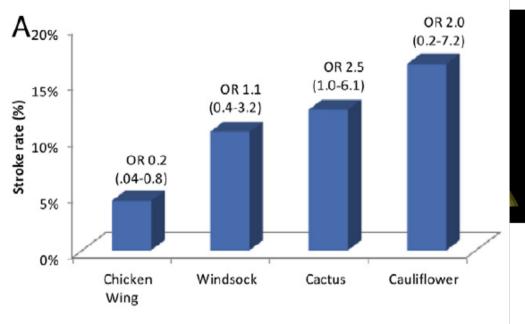
Kaktus

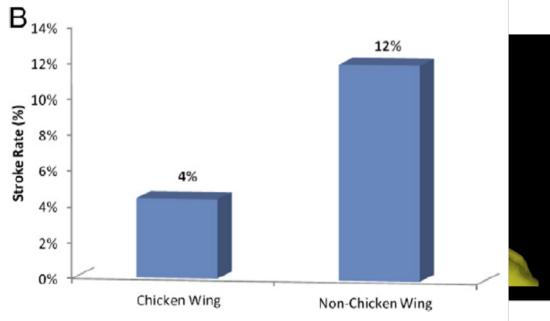
A B

"chicken wing"

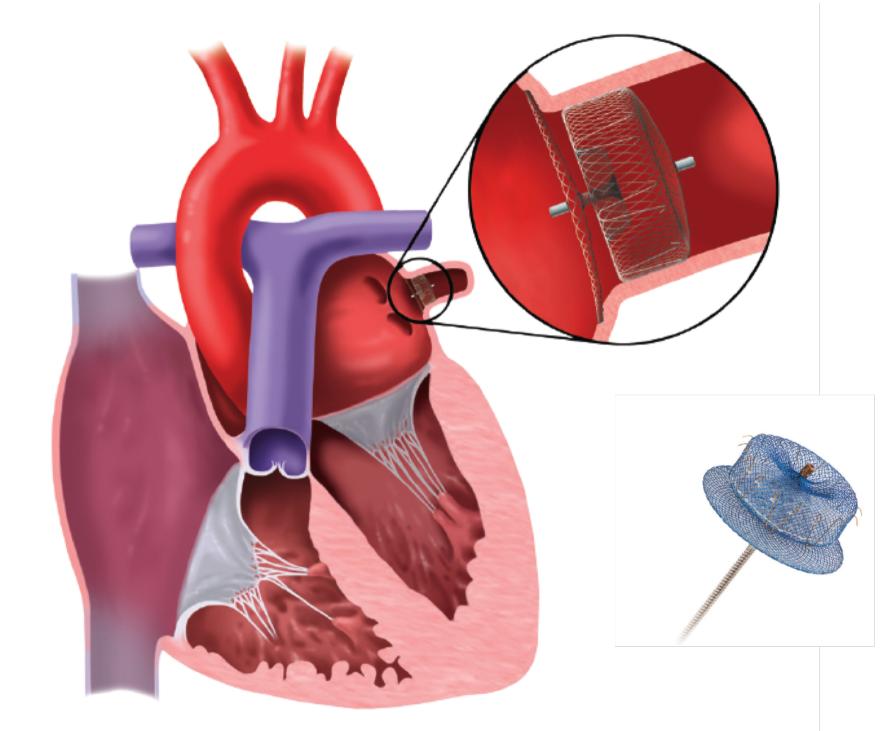


Blumenkohl



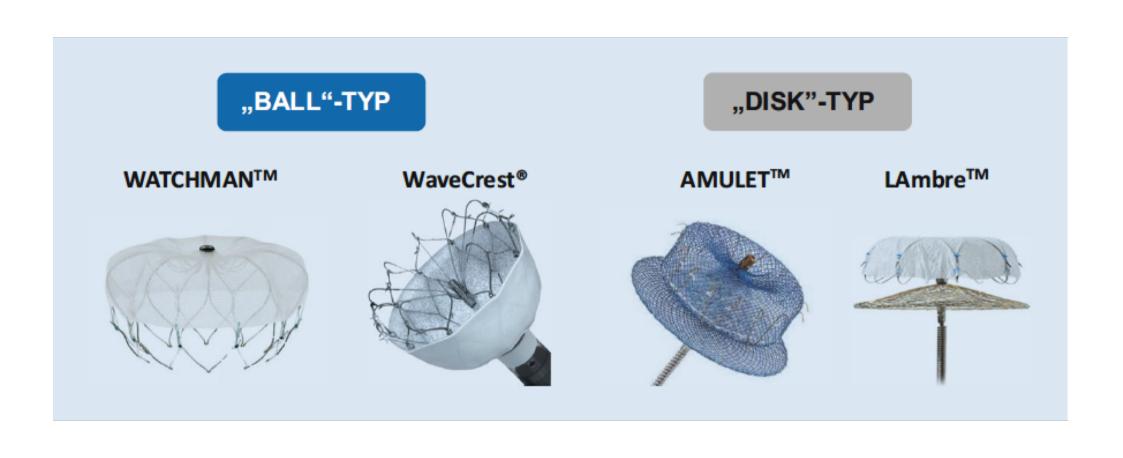


(J Am Coll Cardiol 2012;60:531-8)









Endothelial coverage – in vivo animal study



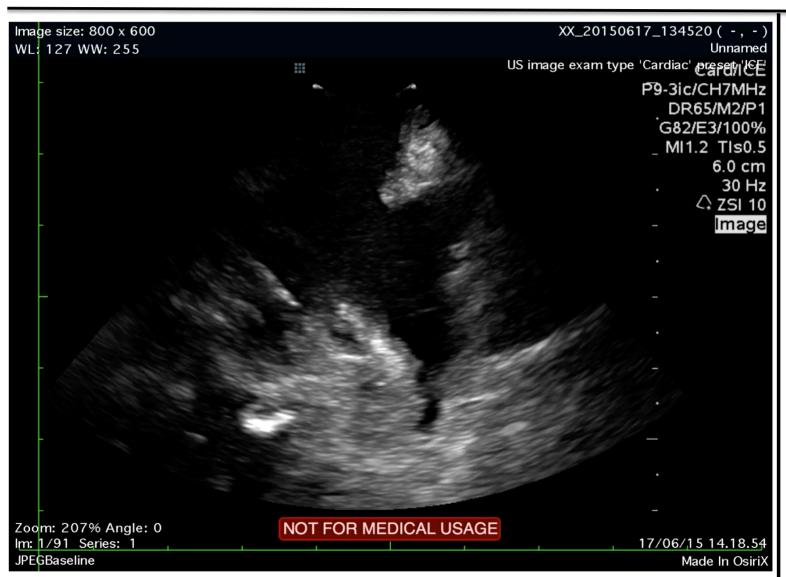








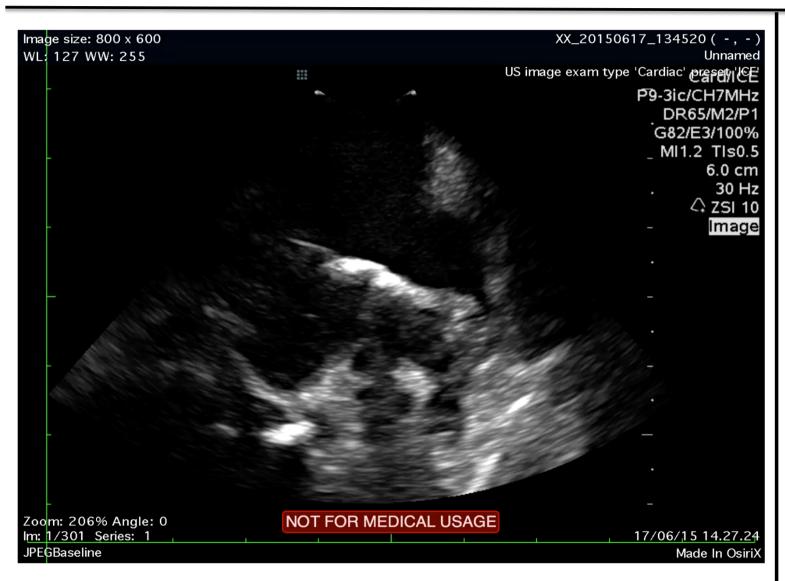
LAAO guided by ICE; patient case



ICE catheter
near the
LUPV ridge
and sligthly
posterior flexed

A lobe is coming off in the superior part of the LAA neck

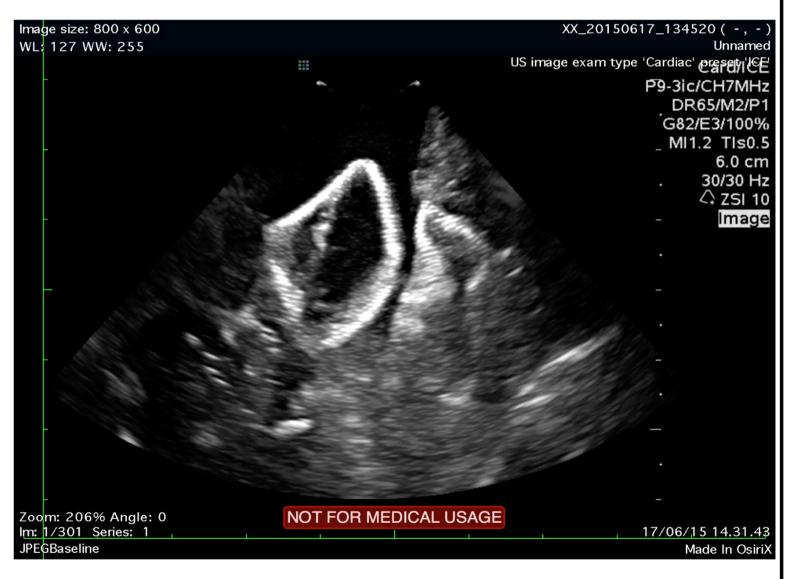
LAAO guided by ICE; patient case



The lobe of a 28 mm
Amplatzer
Amulet
fully expanded in the "landing zone" (neck of LAA)

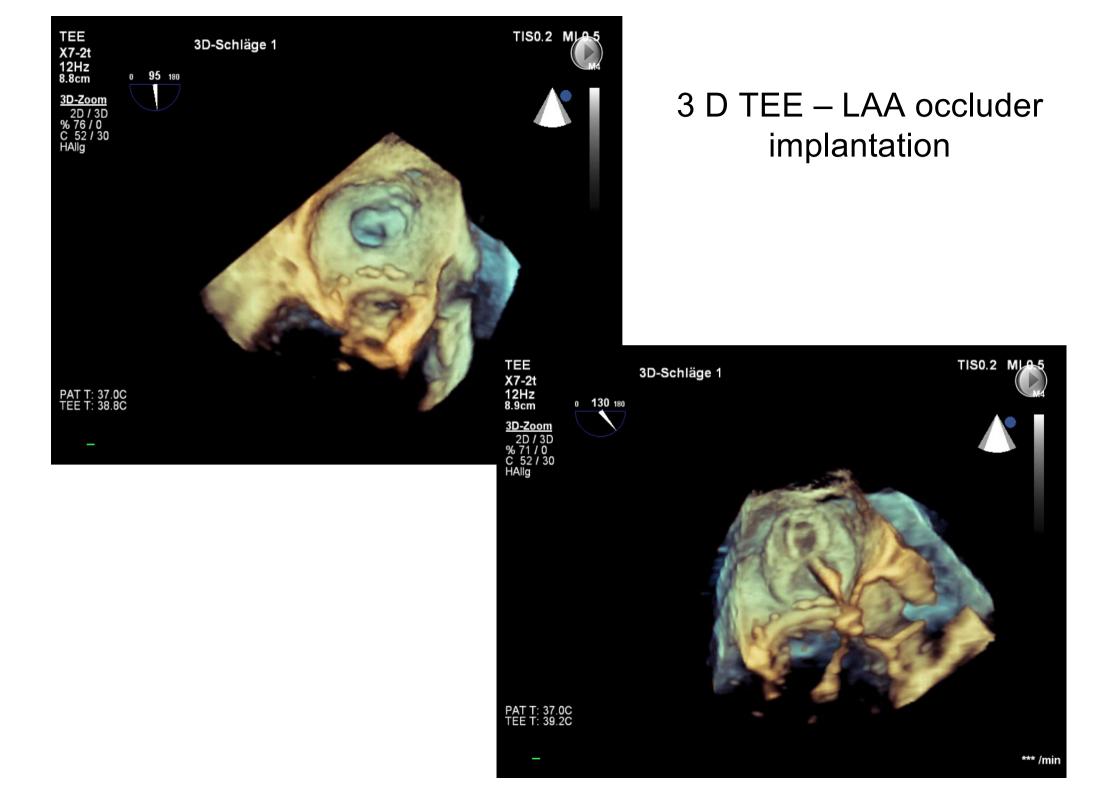
Note the relation to the Circumflex

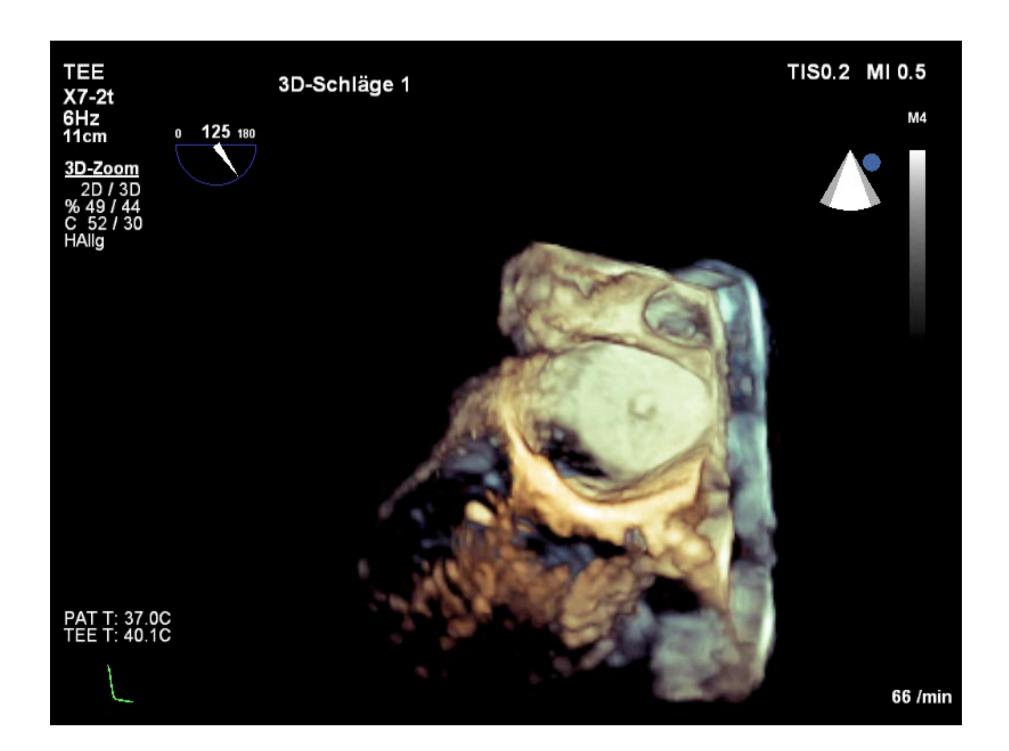
LAAO guided by ICE; patient case



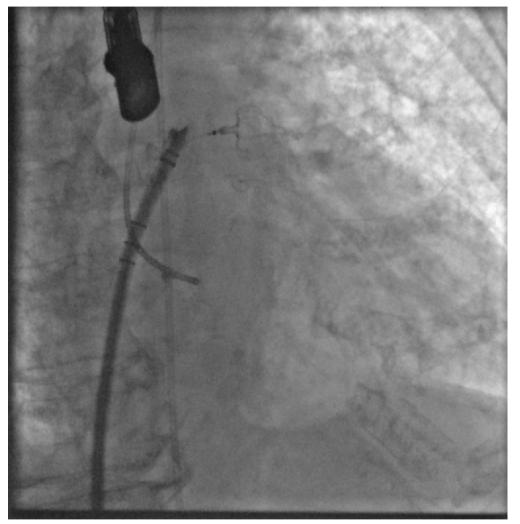
The disc of a 28 mm
Amplatzer
Amulet is formed to cover the LAA orifice







LAA-Perforation



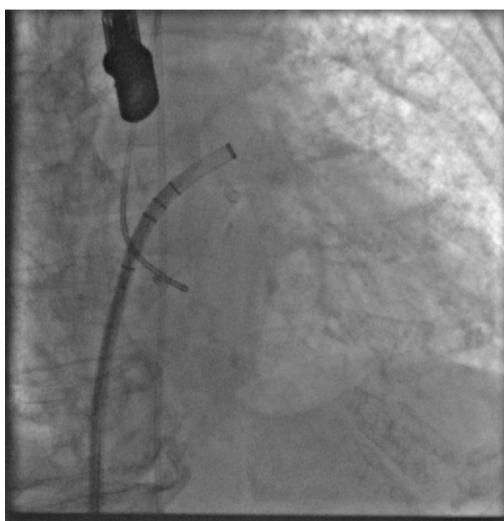


Table 4: Complications during index hospital stay

N	641		
MACCE (death, stroke, MI)	4 events in 3 pts. (0.5%)		
Death	2 (0.3%)		
Stroke	I (0.2%)		
Myocardial infarction	I (0.2%)		
Other severe complications	30 events in 26 pts. (4.1%)		
Severe bleeding	7 (1.1%)		
Pericardial effusion, surgical treatment	2 (0.3%)		
Pericardial effusion, interventional	13 (2.0%)		
AV fistula	6 (0.9%)		
Dislocation, separate revision	2 / 637 (0.3%)		
MACCE and other severe complications	34 events		
	in 29 pts. (4.5%) 🖒		
Moderate Complications	72 events in 63 pts. (9.8%)		
Moderate bleeding	12 (1.9%)		
Pericardial effusion, conservative	11 (1.7%)		
Hemato / Pneumothorax, non-surgical	2 (0.3%)		
Non-fatal resuscitation (without organ dysfunction)	3 (0.5%)		
Groin hematoma	18 (2.8%)		
Site infection	I (0.2%)		
Dislocation, catheter-based retraction	7 / 637 (1.1%)		
Other, non-surgical treatment	18 (2.8%)		
Total complications	106 events in 81 pts (12.6%)		

Number of events and patients and percentage among documented patients are shown. No transient ischemic attack was reported. Other complications comprise infections, epileptic seizures, and cardiac or renal failure.

LAARGE Registry

Evidence and Clinical Data in AF patients at High Risk for Bleeding

- I. Prospective registries with ",calculated" efficacy and safety (n>500)
 - ACP, EWOLUTION, AMULET
 - LAARGE
- 2. Prospective registries with "propensity score matching"
 - Nordic ICH
 - Bern experience (n=1000 Pts.)
- 3. Ongoing RCT's:
 - ASAP TOO
 - CLOSURE AF
 - STROKECLOSE

LAARGE-Registry

55 German Cardiology Dept.

All-comers for LAA occlusion (N=641 pts.)

Prospective Data collection

- proc. data

- 1 year follow-up

PI: J. Brachmann

T. Lewalter

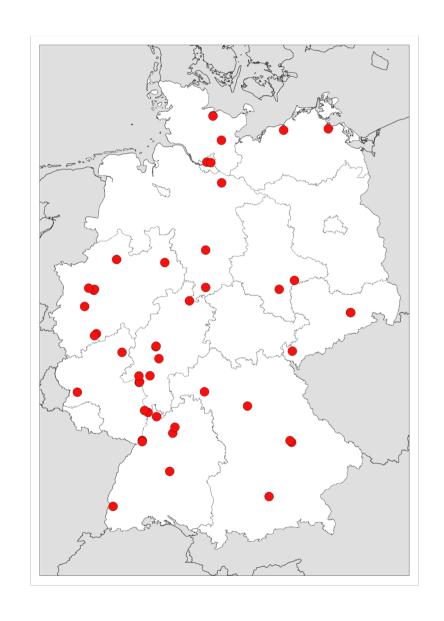


Table 1: Patient characteristics and risk profile

N	641			
Age [years], median (IQR)	77 (72, 81)			
Female	38.8% (249/641)			
Hypertension	93.0% (596/641)			
Congestive heart failure	27.3% (175/641)			
Vascular disease	51.0% (327/641)			
Diabetes	34.0% (218/641)			
Chronic kidney disease	37.8% (242/640)			
Anemia	22.2% (142/641)	(Hb<8g/dl)		
Labile INR	15.3% (98/641)			
Chronic hepatic disease	9.7% (62/641)			
Alcohol abuse	4.1% (26/641)			
CHA ₂ DS ₂ -Vasc Score, mean	4.5 ± 1.6			
HAS-BLED Score, mean	3.9 ± 1.1			



1 year FU Data – LAARGE Registry - Stroke rate -

Observed Stroke rate - 8 pts. with strokes: 1.3% (1 periprocedural)

Expected Stroke rate: 4.6%



Relative Stroke Risk Reduction: 72%



1 year FU Data – LAARGE Registry- Major bleeding rate -

Observed major Bleeding rate: 10/639 pts. = 1,6%

Expected major bleeding rate: 8,8%

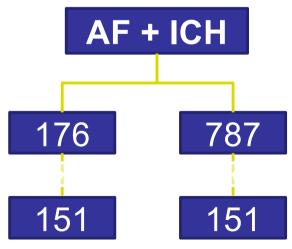


Relative major bleeding Risk Reduction: 82%

LAA occlusion vs. standard care in patients with atrial fibrillation and intracerebral hemorrhage¹ A propensity score matched follow-up study

Study population:

- LAAO: Nordic LAAO patients, treated between 2009 and 2015. n = 176
 (Sweden: Gothenburg, Stockholm and Lund; Finland: Tampere, Turku and Helsinki, Denmark: Copenhagen and Aarhus)
- ACP and AMPLATZER™ Amulet™ devices (St. Jude Medical) used for LAAO
- Standard care: Danish ICH patients with atrial fibrillation who survived at least 180 days after admission with ICH between 2005 and 2014. n = 787
- Design: Propensity-score matched follow-up study
 - Used to balance stroke and bleeding risks
 - Matched CHA₂DS₂-VASc, HAS-BLED scores and each separate risk factor for stroke and bleeding
- Primary endpoint: Composite clinical outcome
 - All cause mortality
 - Acute ischemic stroke
 - Major bleeding*



^{*} Intracranial hemorrhage, hospitalization needed, Hb-decrease > 2 g/dL or requiring blood transfusion

^{1.} Nielsen-Kudsk, J., Paaske Johnsen, S., Wester, P., Damgaard, D., Airaksinen, J., Lund, J., . . . Krieger, D. W. (2017). Left atrial appendage occlusion versus standard medical care in patients with atrial fibrillation and intracerebral hemorrhage: A propensity score matched follow-up study. EuroIntervention. doi:10.4244/EIJ-D-17-00201.

Hazard ratios¹

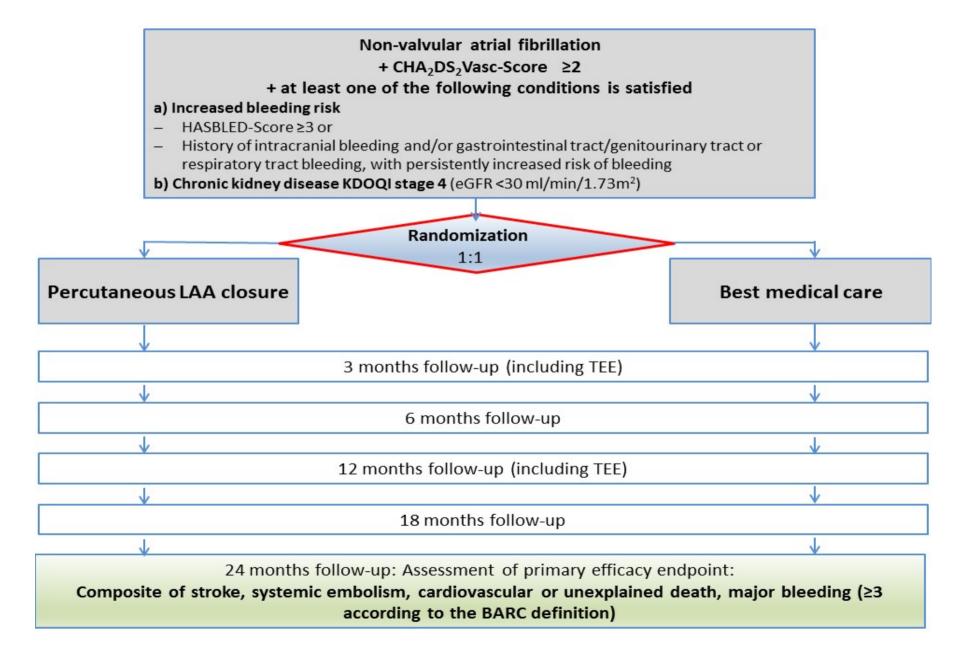
Clinical outcome HR by Cox-regression analysis n = 147 in each PS-matched patient group	LAAO vs. Standard care Hazard ratio (95% CI)	Relative risk reduction (%)
Ischemic stroke/major bleeding/mortality	0.16 (0.07-0.37)*	81%
Ischemic stroke	0.21 (0.05-1.00)	65%
Major bleeding	0.28 (0.09-0.85)*	61%
 Recurrent ICH 	0.10 (0.01-0.81)*	71%
All-cause mortality	0.11 (0.03-0.51)*	92%

STROKECLOSE Randomized Trial initiated

^{1.} Nielsen-Kudsk, J., Paaske Johnsen, S., Wester, P., Damgaard, D., Airaksinen, J., Lund, J., . . . Krieger, D. W. (2017). Left atrial appendage occlusion versus standard medical care in patients with atrial fibrillation and intracerebral hemorrhage: A propensity score matched follow-up study. EuroIntervention. doi:10.4244/EIJ-D-17-00201.

^{*} p<0.05

CLOSURE - AF



EHRA/EAPCI CONSENSUS STATEMENT

EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion

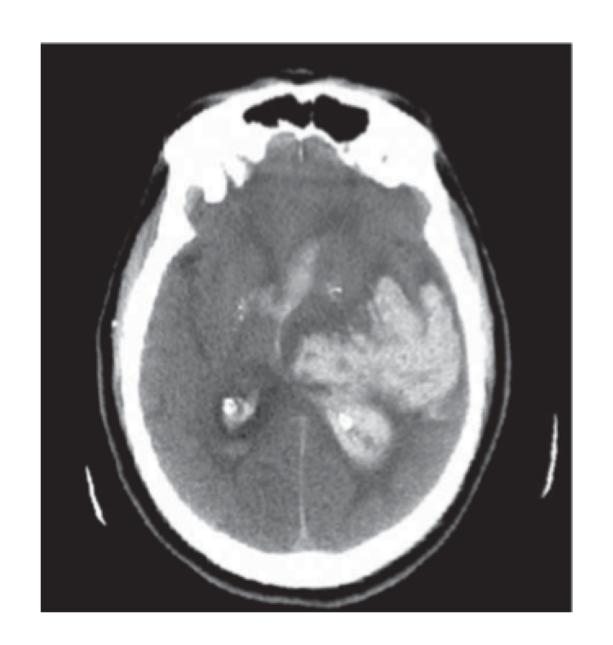
Bernhard Meier (EAPCI Chairperson) (Switzerland)¹, Yuri Blaauw (The Netherlands)², Ahmed A. Khattab (Switzerland)¹, Torsten Lewalter (Germany)³, Horst Sievert (Germany)⁴, Claudio Tondo (Italy)⁵, Michael Glikson (EHRA Chairperson) (Israel)⁶*

Document Reviewers: Gregory Y. H. Lip (UK), Jose Lopez-Minguez (Spain), Marco Roffi (Switzerland), Carsten Israel (Germany), Dariusz Dudek (Poland), Irene Savelieva (on behalf of EP-Europace, UK)

Update expected spring 2019



*Note: In case of strict contraindication to antiplatelet therapy, patient is not eligible for LAAO implantation, but for epicardial LAA occlusion or thoracoscopic LAA clipping

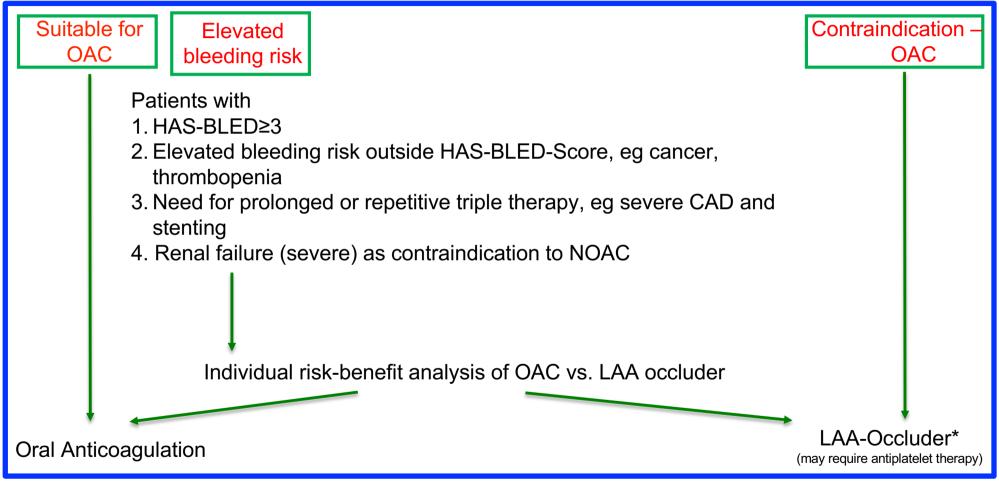


"Absolute" Contraindication for Long-Term OAC

- ,,Untreatable" source of
 - Intracranial/intraspinal bleeding (eg diffuse amyloid angiopathy)
 - severe gastroint. (diffuse angiodysplasia) or urogen. bleeding
- Severe side effects under vit-k-antagonists + contraindication for NOAC (severe renal insufficiency)

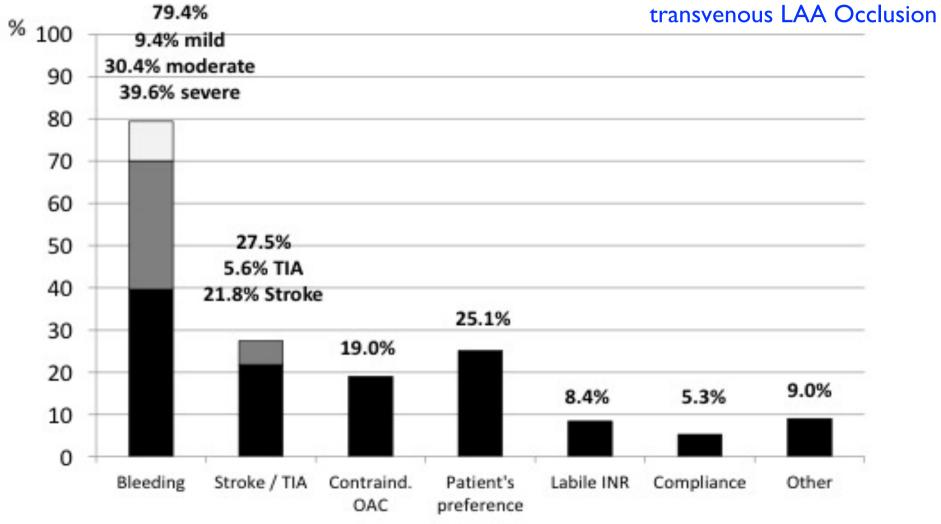


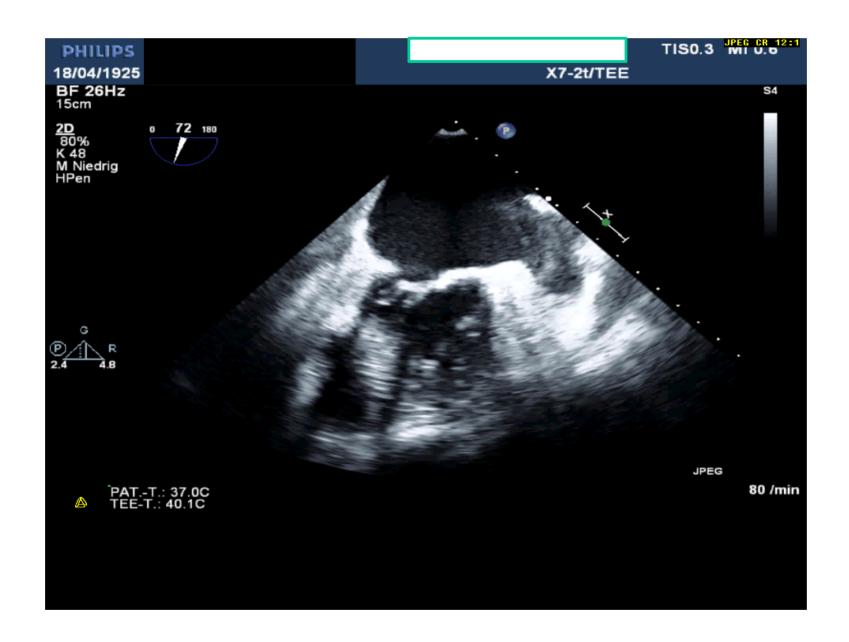
*Note: In case of strict contraindication to antiplatelet therapy, patient is not eligible for LAAO implantation, but for epicardial LAA occlusion or thoracoscopic LAA clipping



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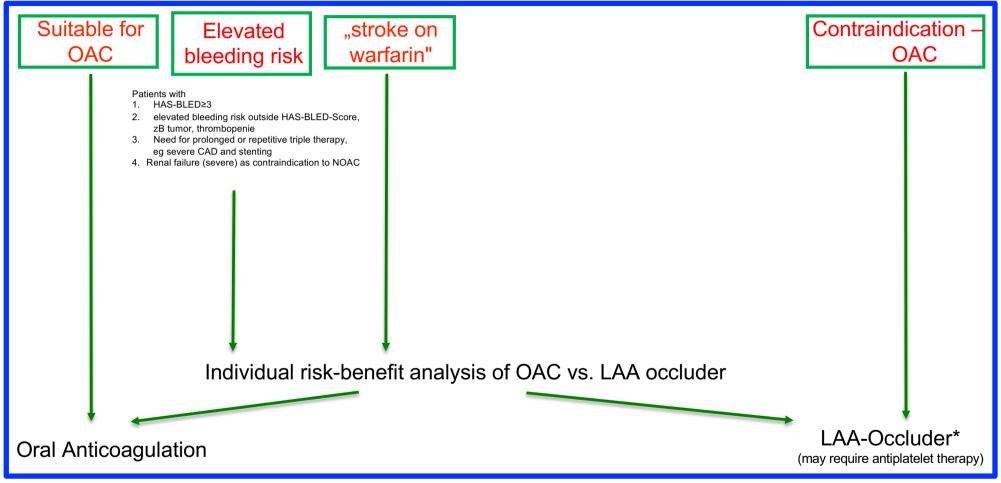




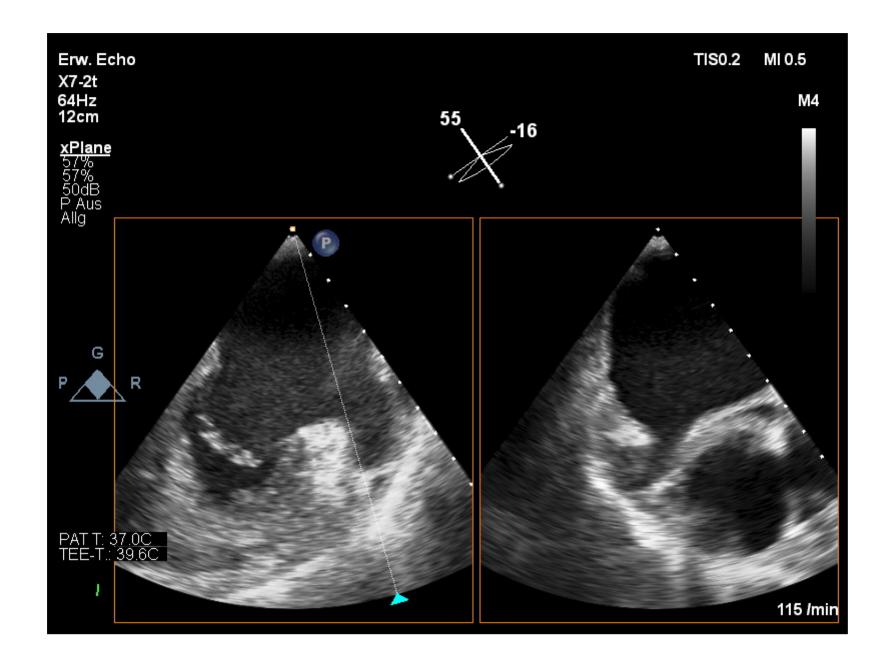


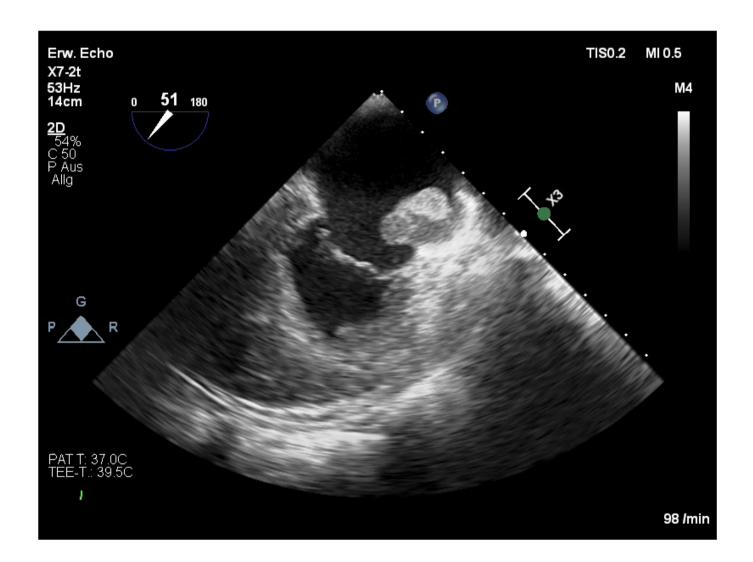
Thrombus formation under standard OAC ("malignant LAA")

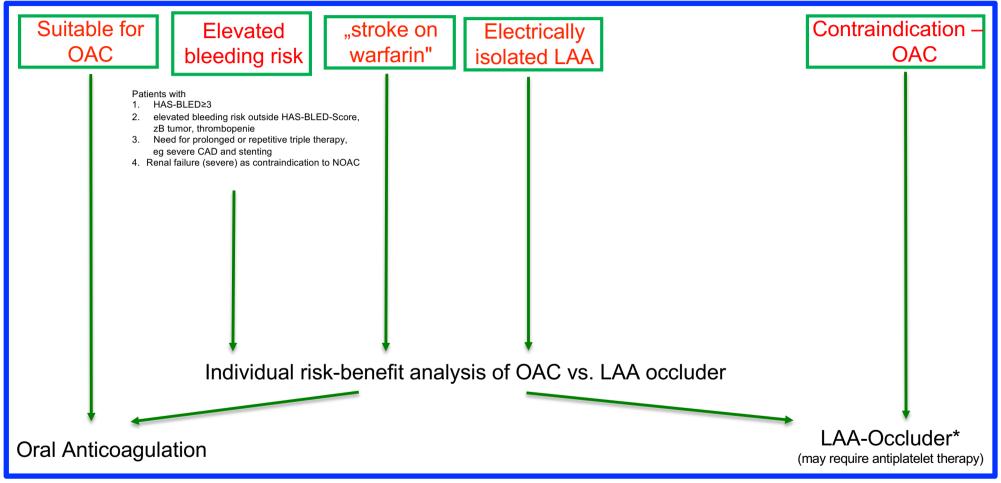
Patient/CHA2DS2- Vasc	Afib/ Pretreatment	EF Disease	V LAA (m/s)	NOAK	6 weeks Thr. +/-	12 weeks Thr. +/-
M.M.,f, 59y Score: 5 Acute isch. stroke	Pers ASS+Clopi	35%, GFR 38, CAD, DM, HTN	<0.2	Apix 2x5mg + Clopidogrel	+ (regr.) -> Apix+Clopi	No Thrombus -> Apix mono
U.N., m, 76y Score: 6	Long pers Mar.+ASS	65% CAD, HTN, TIA	<0.2	Dabi 2x150mg ASS 100/Clop.	No Thrombus -> Dabi mono	No Thrombus LAA implant
H.S., f, 72y Score: 5	Pers. Mar. + ASS	60% CAD, DM, HTN	<0.2	Dabi 2x150mg ASS 100mg/Clopidogrel	No Thrombus -> Dabi mono, ASS 100	No Thrombus LAA implant
G.L., m, 72y Score: 4 Acute TIA	Pers Riva 1x20mg	20% KHK	<0.2	Dabi 2x150mg Clopi 75	+ (regr.) -> Dabi+Clopi	No Thrombus -> Dabi mono
W.V., m, 78y Score: 5 Acute isch. stroke	Long pers Marcumar	65%, AorticVR CAD, DM, HTN	0.3 Ostium!	Mar.+ASS + Clopi 75	+ (regr.)4Mo.! -> Dabi+Clopi	No Thrombus -> Bypass surgery + LAA excision



^{*}Note: In case of strict contraindication to antiplatelet therapy, patient is not eligible for LAAO implantation, but for epicardial LAA occlusion or thoracoscopic LAA clipping





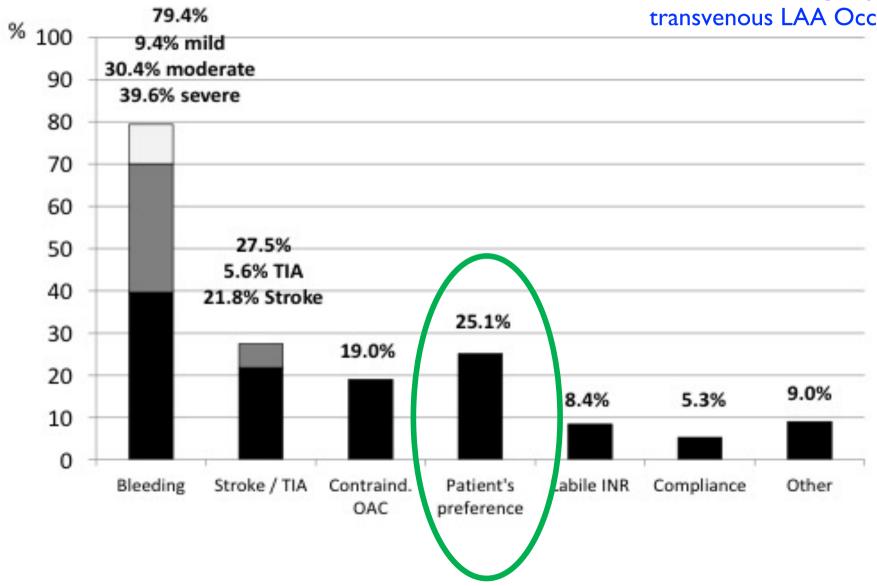


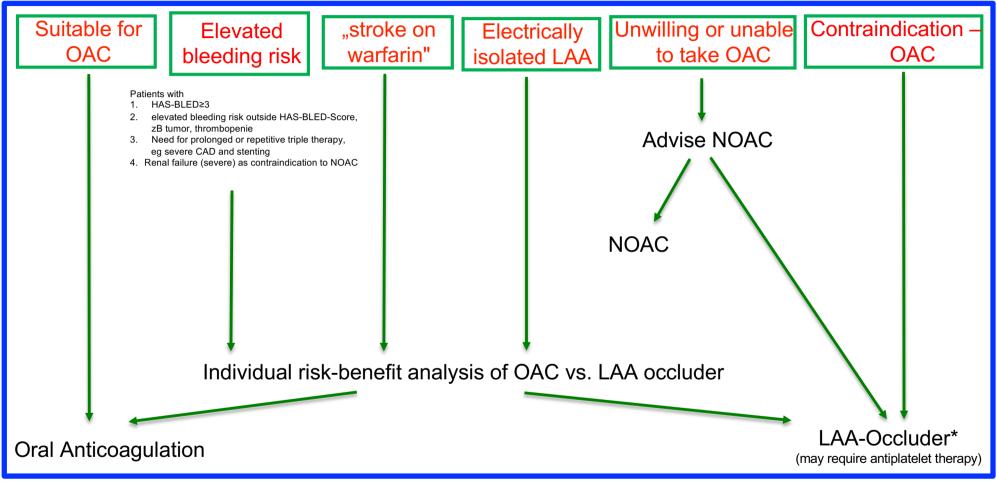
^{*}Note: In case of strict contraindication to antiplatelet therapy, patient is not eligible for LAAO implantation, but for epicardial LAA occlusion or thoracoscopic LAA clipping

"Drugs don't work in patients who don't take them."

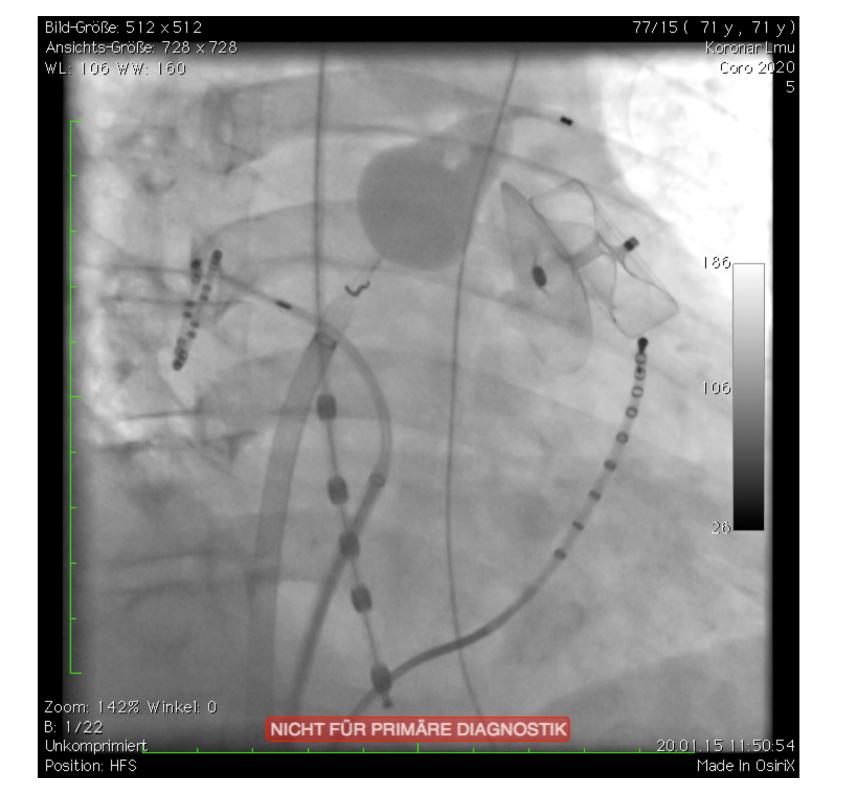
C. Everett Koop, MD

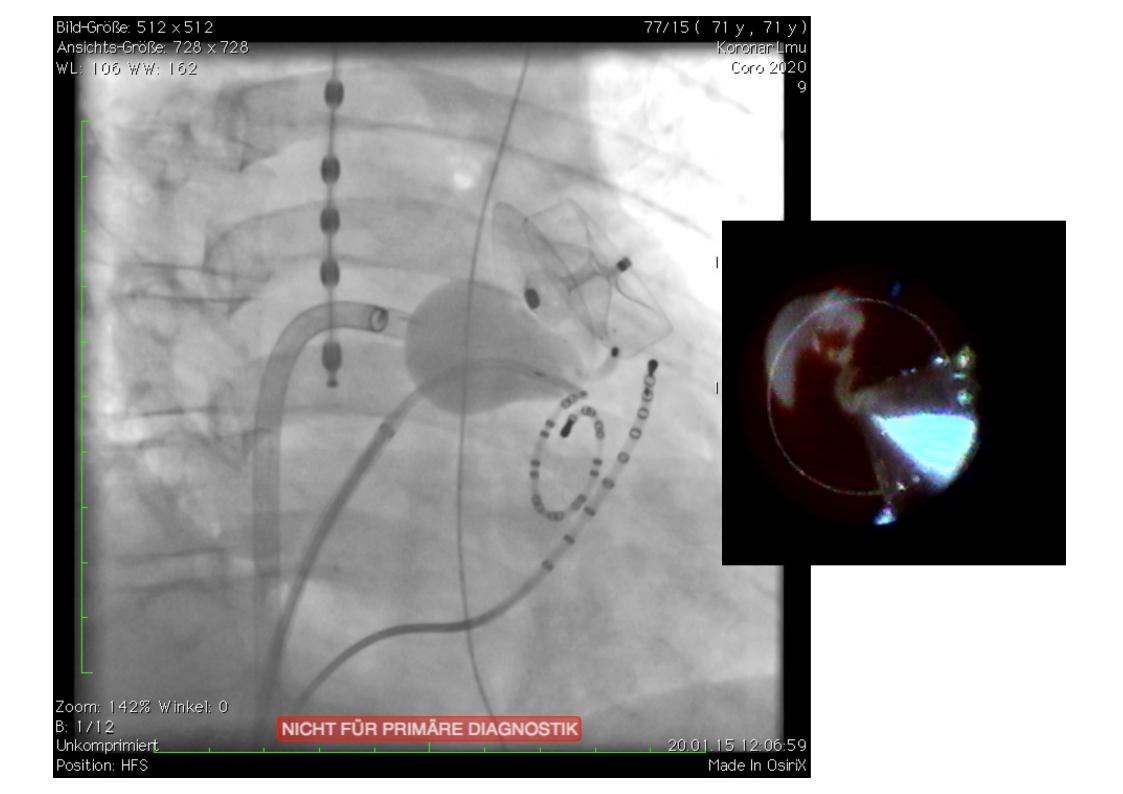






^{*}Note: In case of strict contraindication to antiplatelet therapy, patient is not eligible for LAAO implantation, but for epicardial LAA occlusion or thoracoscopic LAA clipping





Left atrial catheter ablation in patients with previously implanted left atrial appendage closure devices

Lisette I.S. Wintgens¹*, Martijn N. Klaver¹, Martin J. Swaans¹, Arash Alipour^{1,2}, Jippe C. Balt¹, Vincent F. van Dijk¹, Benno J.W.M. Rensing¹, Maurits C.E.F. Wijffels¹, and Lucas V.A. Boersma^{1,3}

¹Department of Cardiology, St Antonius Hospital, Koekoekslaan 1, 3435 CM Nieuwegein, the Netherlands; ²Department of Cardiology, Rivierenland Hospital, President Kennedylaan 1, 4002 WP Tiel, the Netherlands; and ³Department of Cardiology, Amsterdam UMC, Location AMC, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands

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Aims

Left atrial appendage closure (LAAC) is increasingly used as an alternative to oral anticoagulation (OAC) for stroke prevention in atrial fibrillation (AF) patients. Feasibility and safety of left atrial (LA) catheter ablation (CA) in patients with previously implanted LAAC devices have not been well studied. We report on the feasibility, safety, and efficacy of LA CA in the presence of a previously implanted LAAC device.

Methods and results

In this prospective cohort study consecutive patients that underwent LA CA with a previously implanted Watchman device were included. Periprocedural characteristics and long-term clinical follow-up were evaluated. Twenty-three LA CA procedures were performed in 19/162 AF patients with previously implanted Watchman devices [47% male, age 63.9 ± 6.2 years, CHA₂DS₂-VASc 4.0 (3.0–5.0); HASBLED 3.0 (2.0–4.0); 63% paroxysmal]. Left atrial CA was performed with irrigated radiofrequency (RF; n = 20, 87%) or phased RF (n = 3, 13%) in a mean of 18 months after LAAC implantation (range 4–80 months). Targets of CA consisted of pulmonary vein isolation (n = 19, 83%), superior vena cava isolation (n = 13, 57%), and additional linear lesions (n = 8, 35%). Procedures were carried out under vitamin K antagonist (VKA; n = 6, 26%), non-VKA OAC (NOAC; n = 8, 35%), or single antiplate-let therapy alone (n = 9, 39%). Left atrial CA was successful without any signs of interference from the device. Procedure-related complications were not observed. During a mean follow-up of 28 months, 11 patients (58%) had AF recurrence.

Conclusion

Left atrial CA after LAAC appears to be feasible, effective, and safe in this single centre cohort. Previously implanted Watchman device should not be a reason to relinquish CA in symptomatic AF patients, even in patients on single antiplatelet therapy alone.



Thank You For Your Attention!