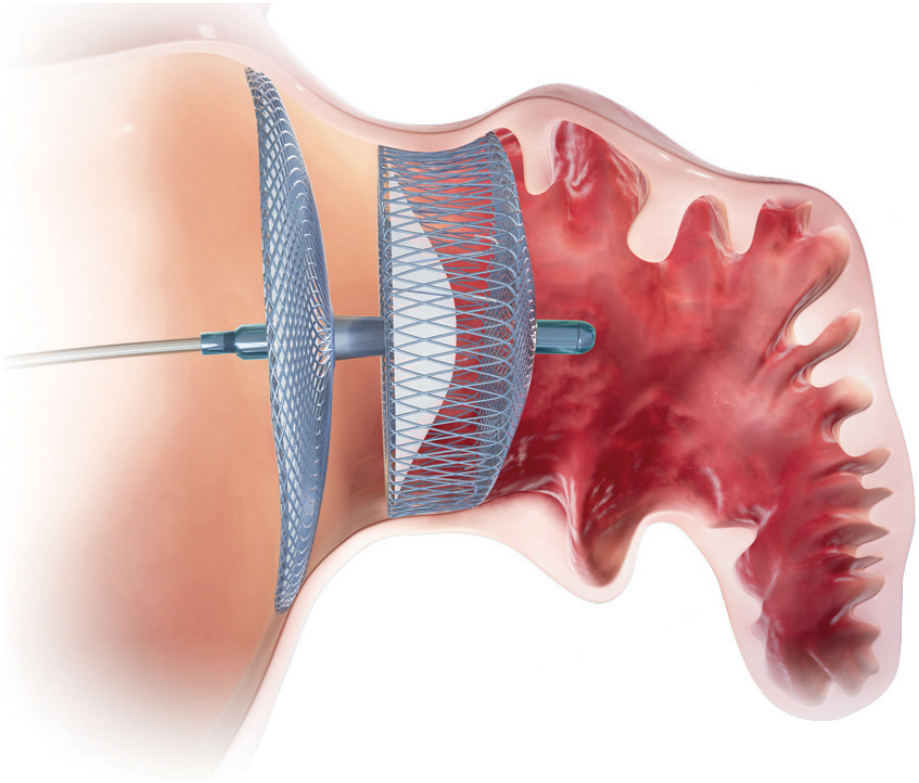
Vorhofflimmern und nie wieder Antikoagulation- der Verschluss des linken Vorhofohres als wirksame Alternative



Der interventionelle Verschluss des linken Vorhofohres

Der kardioembolische Insult bei Vorhofflimmern macht etwa 15% der etwa 2 Millionen Schlaganfälle/Jahr (US, EU) aus.

Altersabhängige Morbidität: 1.5% in der Gruppe 50 – 60 Jahre, 24% in der Gruppe > 80 Jahre

Über alle Altersgruppen verteilt 5-fach erhöhtes Risiko

Bestimmte Merkmale erhöhen das Risiko

Der interventionelle Verschluss des linken Vorhofohres

CHADS-score

C (1) - Congenital Heart Failure
H (1) - Hypertension
A (1) - Age > 75 years
D (1) - Diabetes
S (1) - Stroke

CHA_2DS_2-VASc – score

C (1) - Congenital Heart Failure
H (1) - Hypertension
A (2) - Age > 75 years
D (1) - Diabetes
S (2) - Stroke
V (1) - Vascular disease
A (1) - Age 65 – 74 years
Sc (1) - Sex category (female > 65)

Jährliches Schlaganfallrisiko:

CHA_2DS_2-VASc = 1	0.6%
CHA_2DS_2-VASc = 4	4%
CHA_2DS_2-VASc = 9	12%

Therapieempfehlung *

OAK bei allen Patienten mit CHA_2DS_2-VASc ≥ 1

*Camm et al.
2012 focused update of the ESC Guidelines für the managment of atrial fibrillation. Eur Heart J, 33, 2719-2747

OAK und Blutungen

0.5 - 1.2% jährliches Risiko einer ICB

3 - 5% Risiko einer GI-Blutung, weiter erhöht durch ASS

HAS – BLED score

H – Hypertension
A – Age > 65 years
S – previous stroke
B – previous bleeding
L – Labile INR
E – Elevated liver or kidney parameters
D – Drug or Alcohol abuse

HAS-BLED = 1 0.7% major bleeding
HAS-BLED = 4 4% major bleeding

→ HAS-BLED ≥ 3 per definitionem „Hohes Blutungsrisiko“

3 verschiedene Therapieformen:

1. VKA (Phenprocuomon / Warfarin)
   + nachgewiesene Reduktion des Risikos um 65%
   + effektiver als antithrombozytäre Therapie

   - Blutungsrisiko
   - Monitoring
   - Adjustierung bei Interaktionen mit Nahrungsmitteln und Medikamenten
   - Noncompliance, zu niedrige TTR

➡ Marcumar wird erheblich zu wenig verschrieben !

3 verschiedene Therapieformen:

2. NOAK
   + non-inferior im Vergleich zu VKA
   + geringeres Risiko einer ICB
   + kein Monitoring

   - Akkumulation bei cNI
   - Weglassen über wenige Dosen ist problematisch
   - Weiterhin signifikant erhöhtes Blutungsrisiko
   - Partiell höhere Rate an GI-Blutungen im Vergleich zu VKA
   - Antagonisierung nur partiell

   (Dabigatran – Idarucizumab (Praxbind) 01/2016, Andexanat alfa gegen Api, -Edo, -Rivaroxaban, a.e. 2018)

   → NOAKs ersetzen VKA anstatt mehr Patienten zu behandeln !

Der interventionelle Verschluss des linken Vorhofohres

Drug/Study	Baseline Characteristics/ Endpoints	Randomization Arms	Event Rates [%/yr]		Overall Outcome
			Effectiveness	Safety	
Dabigatran RE-LY[26]	Baseline characteristics: 18,113 pts, 71 yrs, $CHADS_2$: 2.1 Effectiveness: Stroke and systemic embolism Safety: Major hemorrhage	110 mg dabigatran twice daily	1.53	2.71	Compared to warfarin: 110 mg dabigatran: non-inferior stroke prevention and significantly less bleeding. 150 mg dabigatran: superior stroke prevention and similar bleeding risk. 110 mg dose: similar risk for GI bleeding. 150 mg dose: significantly higher risk for GI bleeding
		150 mg dabigatran twice daily	1.11	3.11	
		Adjusted dose warfarin	1.69	3.36	
Rivaroxaban ROCKET-AF[27]	Baseline characteristics: 14,264 pts, 73 yrs, $CHADS_2$: 3.47 Effectiveness: All-case stroke and non-CNS systemic embolism Safety: Major and clinically relevant non-major bleeding	20 mg rivaroxaban daily	2.12 (ITT)	3.60	Rivaroxaban is non-inferior to warfarin in prevention of stroke and non-CNS systemic embolism. Major bleeding rates of rivaroxaban and warfarin are similar.
		Adjusted dose warfarin	2.42 (ITT)	3.45	

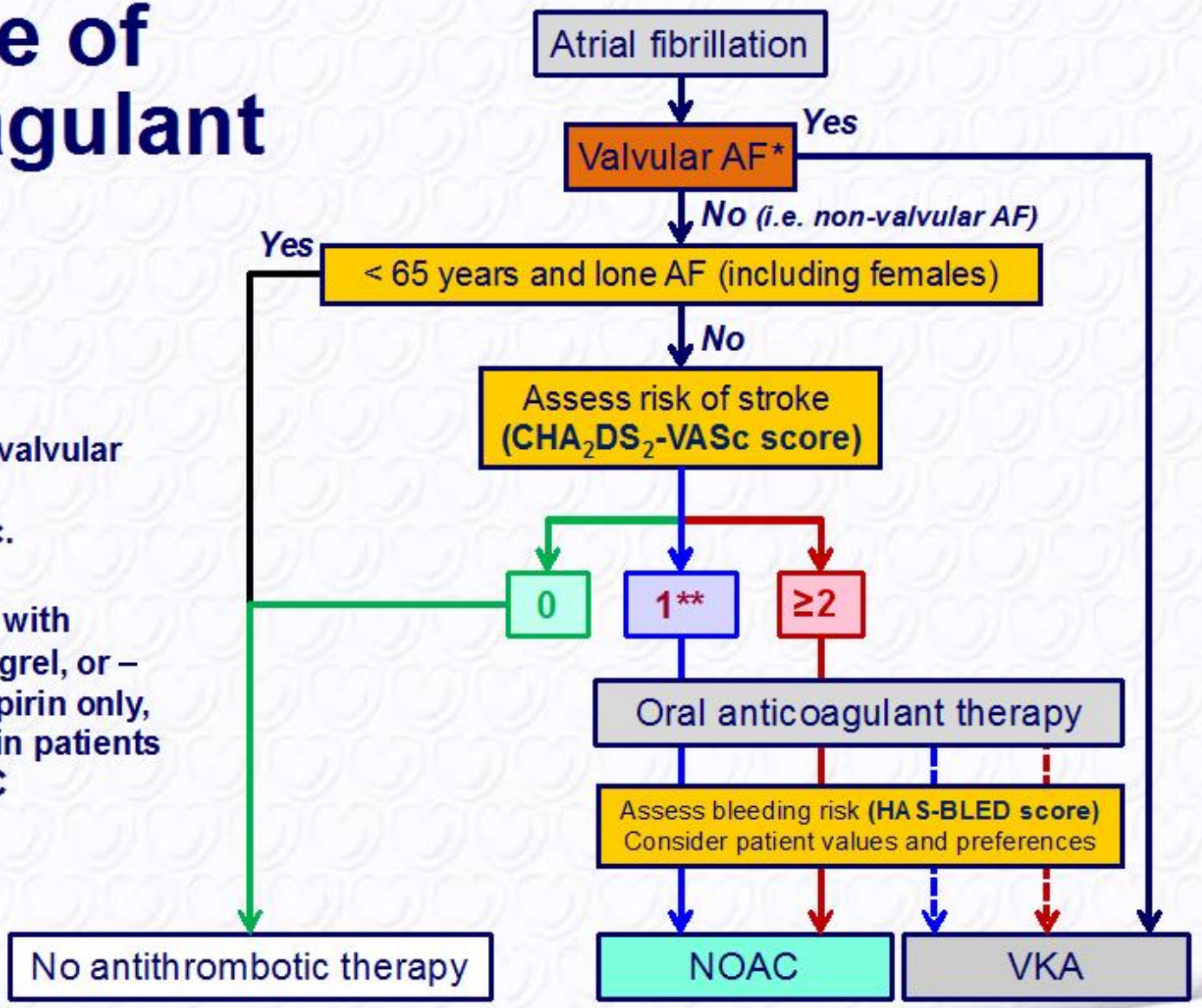
TTR 64%

Nur 55% TTR !

Der interventionelle Verschluss des linken Vorhofohres

Apixaban AVERROES[28]	Baseline characteristics: 5,600 pts, 73 yrs, $CHADS_2$: 2.1 Effectiveness: Stroke and systemic embolism Safety: Major bleeding	5 mg apixaban twice daily	1.6	1.4	Compared to aspirin, apixaban provides superior prevention for stroke and systemic embolism and has similar bleeding risks.
		81 – 324 mg aspirin daily	3.7	1.2	
TTR 66% **Apixaban ARISTOTLE[29]**	Baseline characteristics: 18,201 pts, 70 yrs, $CHADS_2$: 2.1 Effectiveness: Ischemic or hemorrhagic stroke or systemic embolism Safety: Major bleeding	5 mg apixaban twice daily	1.27	2.13	Prevention for stroke and systemic embolism by apixaban is non-inferior/ superior to warfarin. Apixaban is associated with significantly lower major bleeding rate compared to warfarin.
		Adjusted dose warfarin	1.60	3.09	
TTR 68% **Edoxaban ENGAGE AF-TIMI[30]**	Baseline characteristics: 21,105 pts, 72 yrs, $CHADS_2$: 2.8 Effectiveness: Stroke (ischemic or hemorrhagic) Safety: Major bleeding	60 mg edoxaban daily	1.18	2.75	Compared to warfarin: Stroke prevention: 30 mg and 60 mg doses are non-inferior. Favorable trend for 60 mg and unfavorable trend for 30 mg. Bleeding: significantly less for both doses.
		30 mg edoxaban daily	1.61	1.61	
		Dose adjusted warfarin	1.50	3.43	

Choice of Anti-coagulant



- Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC

www.escardio.org/guidelines

European Heart Journal 2012;33:2719-2747 - doi:10.1093/eurheartj/ehs253

EUROPEAN SOCIETY OF CARDIOLOGY®

Recommendations	Class	Level
Where dabigatran is prescribed, a dose of 150 mg b.i.d. should be considered for most patients in preference to 110 mg b.i.d., with the latter dose recommended in: • elderly patients, age ≥ 80 • concomitant use of interacting drugs (e.g. verapamil) • high bleeding risk (HAS-BLED score ≥3) • moderate renal impairment (CrCl 30–49 mL/min).	IIa	B
Where rivaroxaban is being considered, a dose of 20 mg o.d. should be considered for most patients in preference to 15 mg o.d., with the latter dose recommended in: • high bleeding risk (HAS-BLED score ≥3) • moderate renal impairment (CrCl 30–49 mL/min).	IIa	C
Baseline and subsequent regular assessment of renal function (by CrCl) is recommended in patients following initiation of any NOAC, which should be done annually but more frequently in those with moderate renal impairment where CrCl should be assessed 2–3 times per year.	IIa	B
NOACs (dabigatran, rivaroxaban, and apixaban) are not recommended in patients with severe renal impairment (CrCl <30 mL/min).	III	A

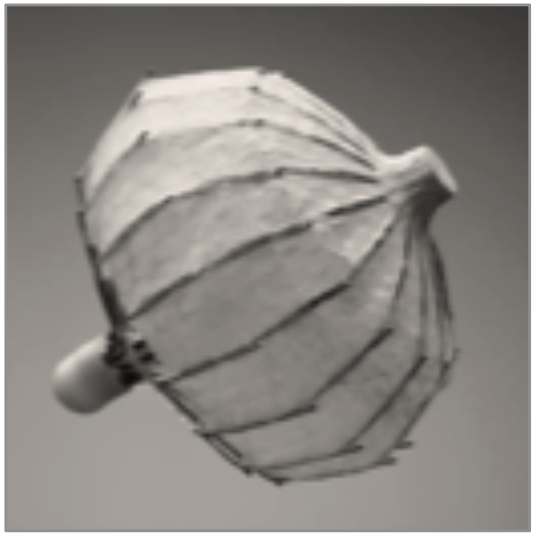
European Heart Journal 2012;33:2719-2747 - doi:10.1093/eurheartj/ehs253

3. Option: Verschluß des linken Vorhofohres

Review of Published Reports Detailing the Frequency and Site of Thrombus Location in Patients With Nonrheumatic Atrial Fibrillation

Setting	No. of Patients	Thrombus Location (n, %)		
		LA Appendage	LA Cavity	Total
Total	2208	249 (11.3)	29 (1.3)	278 (12.6)

Der interventionelle Verschluss des linken Vorhofohres

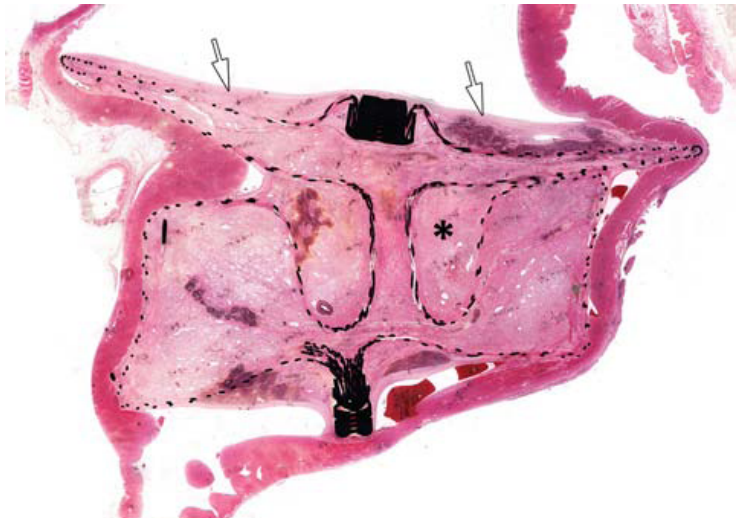


PLAATO™ Device

WATCHMAN™
LAA Closure Device

AMPLATZER™
Left Atrial Appendage Occluders

Studien und Datenlage zum LAA - Verschluss



PROTECT AF Study (2009, WATCHMAN Device)

First randomized trial comparing LAA occlusion to warfarin

707 subjects with nonvalvular AF and $CHADS_2$ score > 1

- 59 centers in the US
- Follow-up with TEE at 45 days, six months and one year
- 87% were able to stop warfarin therapy at 45-day follow-up

Primary Efficacy Endpoint

- All stroke (ischemic and hemorrhagic), CV or unexplained death, systemic embolism

Primary Safety Endpoint

- Device embolization requiring retrieval
- Pericardial effusion requiring drainage
- Cranial, GI or other significant bleed

Holmes et al. Percutaneous Closure of the left atrial appendage vs. warfarin therapy for prevention of stroke in pts with AF. Lancet 374(9689), 534 – 542, 2009.

PROTECT AF Four-year Study Results

Mean 45-month follow-up = 2,621 patient years

Primary Efficacy Endpoint:

- Overall event rate:
  - 2.3% for the WATCHMAN™ device
  - 3.8% for control, which showed superiority for device at four years
- Driven by an increase in rates of hemorrhagic stroke (0.2% vs. 1.1%) and cardiovascular or unexplained death (1.0% vs. 2.4%) in the control group

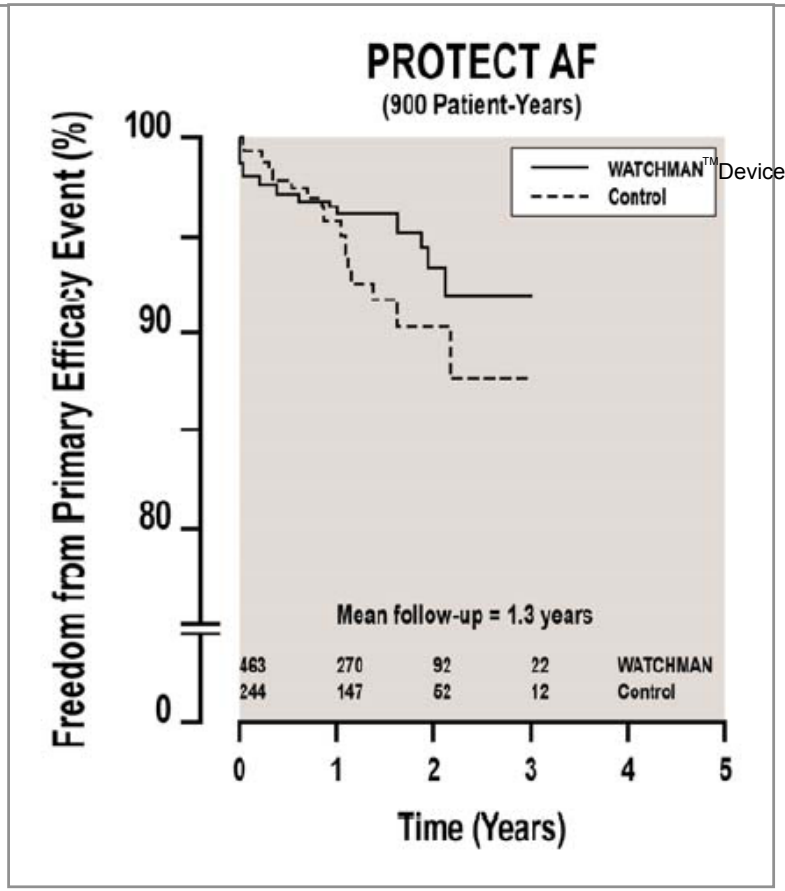
Primary Safety Endpoint:

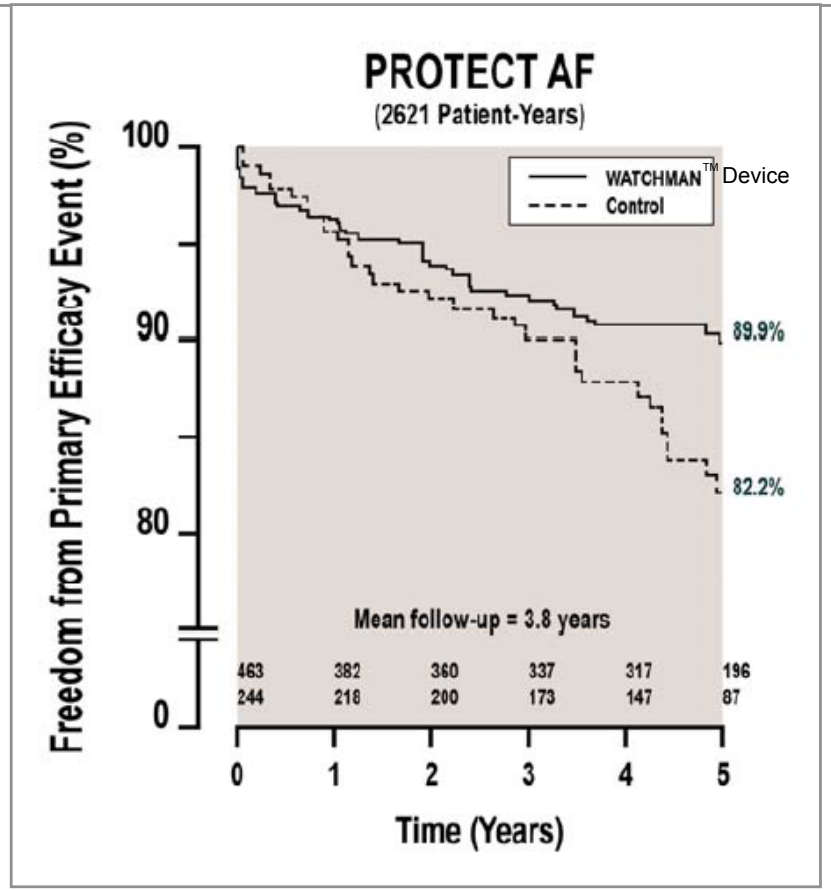
- 3.6% WATCHMAN device vs. 3.1% Control (per 100 patient years), which is noninferior at four years

Intention-to-treat analyses showed LAA occlusion relative risk reduction:

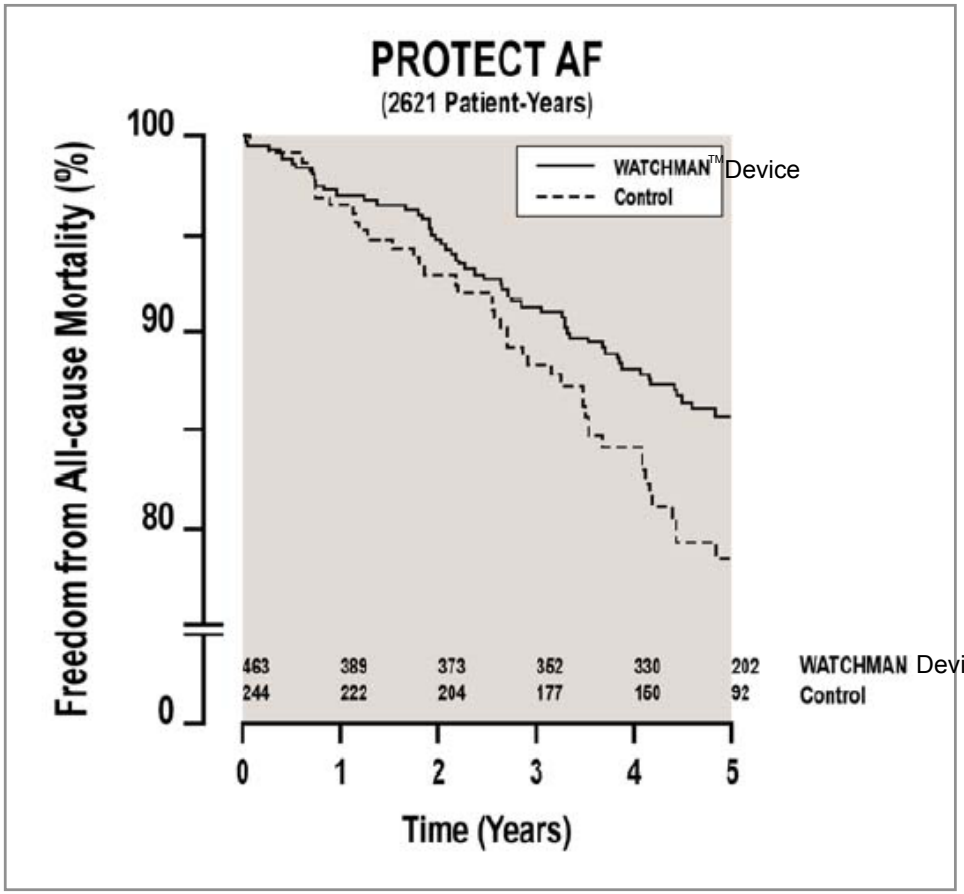
- 34% for all-cause mortality
- 40% for stroke/embolic event/cardiovascular death
- 60% for cardiovascular mortality

PROTECT AF Primary Efficacy Endpoint





PROTECT AF All-Cause Mortality



PREVAIL Study (2014, WATCHMAN Device)

Second randomized trial comparing LAA closure to warfarin

- 407 randomized patients from 41 US centers
- Intended to confirm results of PROTECT AF and demonstrate improved acute safety profile
- Inclusion of new centers and new operators to document that enhancements to the training program are effective

Three co-primary endpoints:

- Rate of death, ischemic stroke, systemic embolism and complications, requiring major cardiovascular or endovascular intervention at seven days post implant or discharge
- Comparison of the composite of stroke, systemic embolism and cardiovascular/unexplained death at 18 months
- Comparison of ischemic stroke and systemic embolism occurring greater than seven days post randomization (followed to 18 months)

Holmes D et al. Prospective randomized evaluation of the Watchman left atrial appendage…. JACC 64, 1 – 12, 2014

PREVAIL Primary Endpoints

Endpoint 1: Primary Efficacy (composite of all stroke, systemic embolism, and cardiovascular/unexplained death at 18 months)

- The WATCHMAN™ device is not non-inferior to warfarin.

Endpoint 2: Late Ischemic Primary Efficacy (Stroke, Systemic embolism, CV/ Unexplained death occurring more than seven days post-implant)

- The WATCHMAN device is not non-inferior to warfarin.

Endpoint 3: Early Safety

- The WATCHMAN device is non-inferior to warfarin.

PREVAIL Endpoint Event Rates

Ischemic stroke and systemic embolism rates favored warfarin

Hemorrhagic stroke rates favored the WATCHMAN™ device group

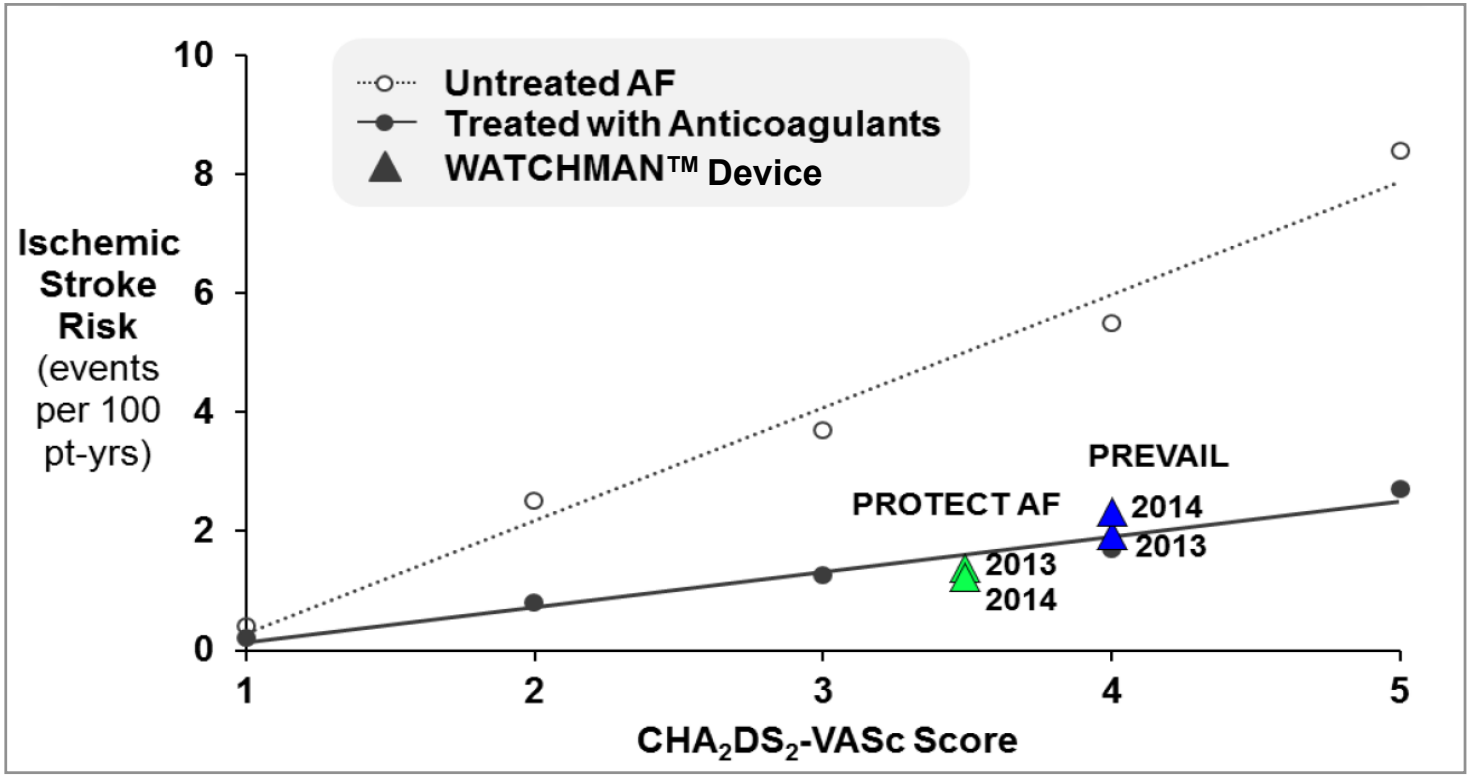
Death (CV or unexplained) rates favored the WATCHMAN device group

PREVAIL-only Endpoint Events and Event Rates (Sponsor and FDA analyses)

Dataset Date	Endpoint Event	WATCHMAN™ Device		Control	
		N Events / Total Pt-yrs	Rate (95% CI)	N Events / Total Pt-yrs	Rate (95% CI)
June 2014	Stroke-Ischemic	13/564.9	2.30 (1.23, 3.94)	1/298.1	0.34 (0.01, 1.87)
	Stroke-Hemorrhagic	2/577.3	0.35 (0.04, 1.25)	2/300.1	0.67 (0.08, 2.41)
	Systemic Embolism	1/576.9	0.17 (0.004, 0.97)	0/300.2	0.00 (0.00, 1.23)
	Death (Cardiovascular or Unexplained)	8/578.1	1.38 (0.60, 2.73)	6/300.2	2.00 (0.73, 4.35)

Summary of WATCHMAN™ Device Trials

Patients treated with the WATCHMAN™ device have had lower stroke rates than an untreated AF population in both randomized trials.



Der interventionelle Verschluss des linken Vorhofohres

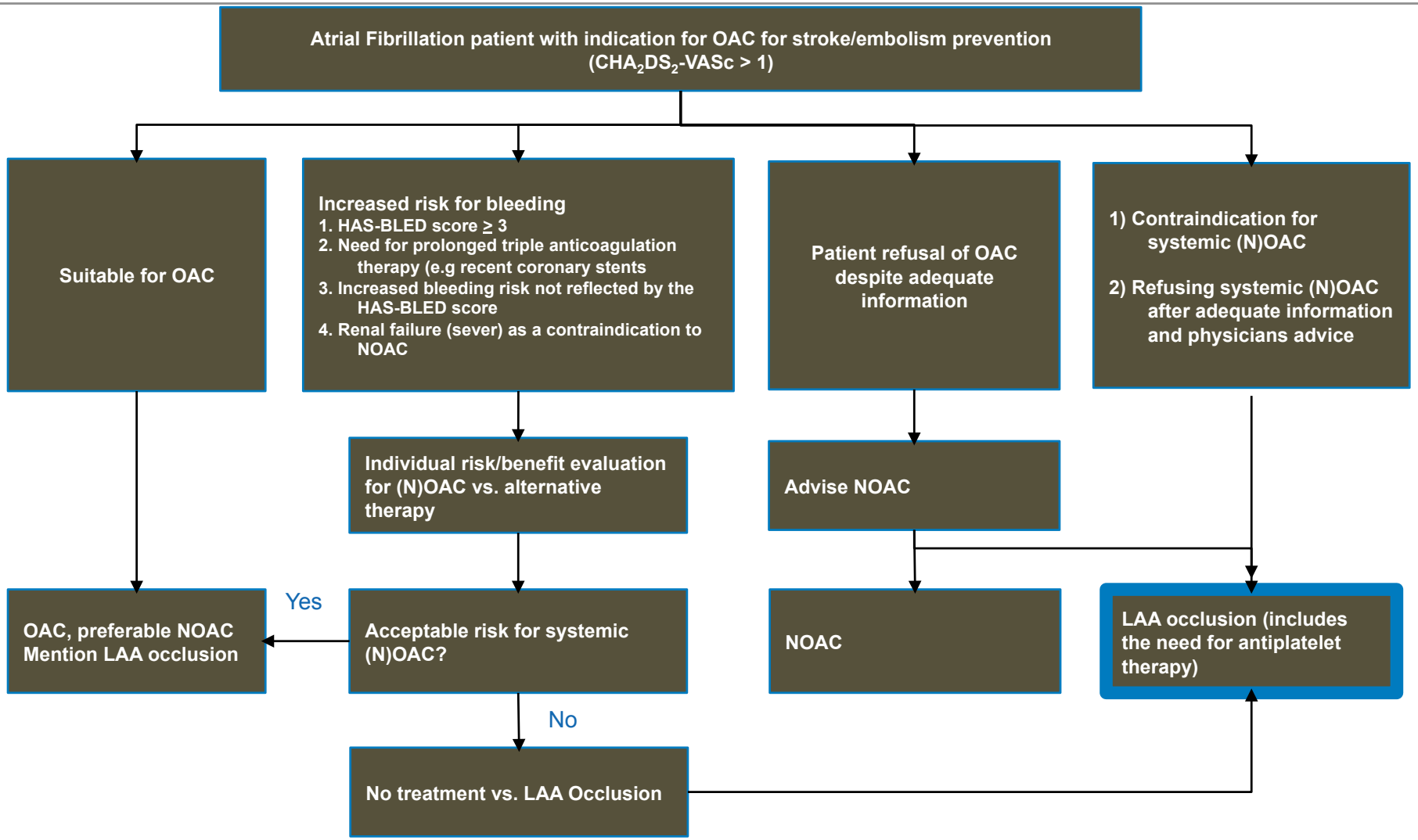
Recommendations for LAA closure/occlusion/excision

Recommendations	Class	Level
Interventional percutaneous LAA closure may be considered in patients with very high stroke risk and contraindications for long-term anticoagulation	IIb	B

Classes of recommendation		
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion*	*May be considered*

Levels of evidence	
Level of evidence B	*Data derived from a single randomized clinical trial or large non-randomized studies*

Der interventionelle Verschluss des linken Vorhofohres



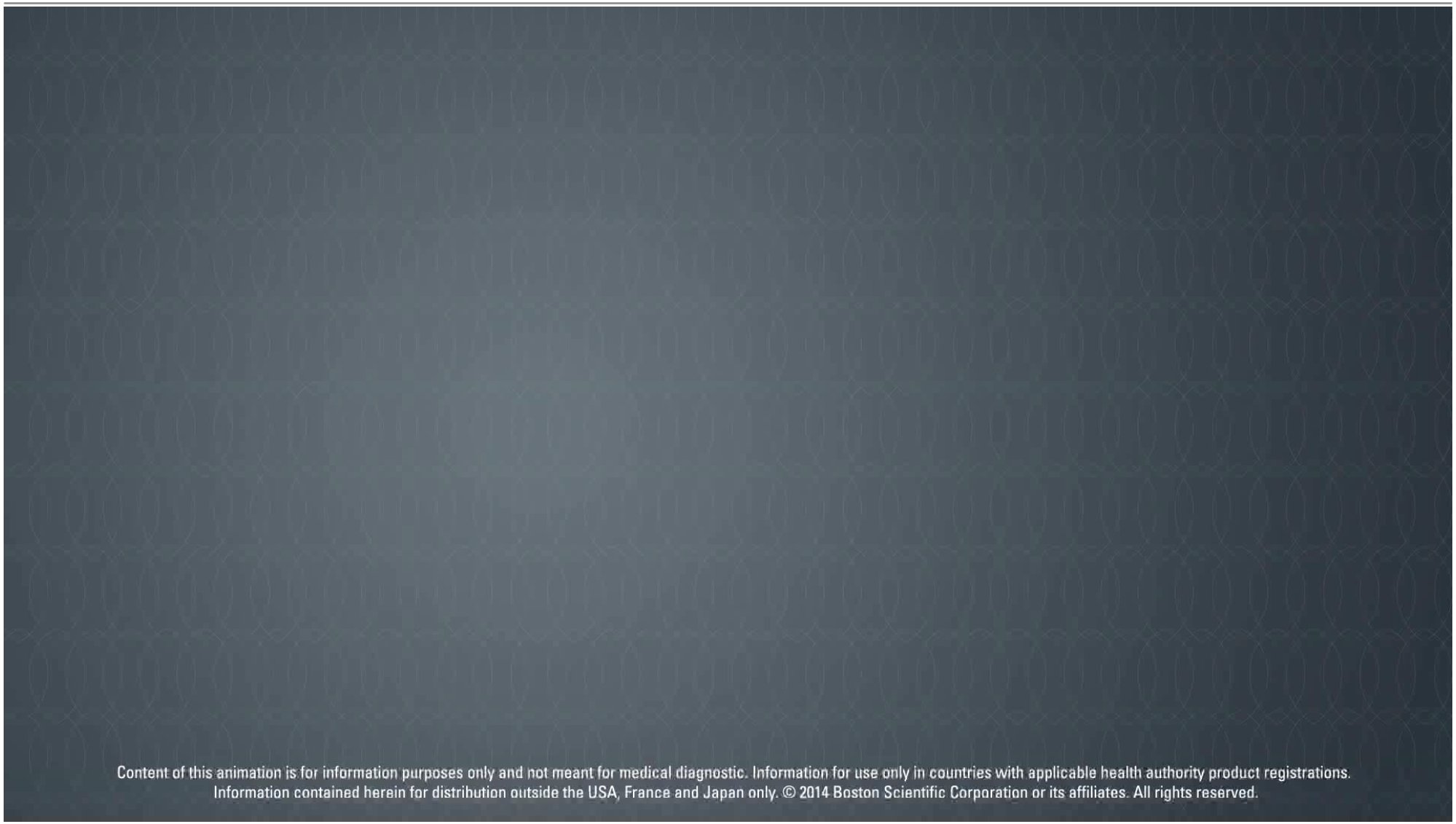
Meier et al.. (2014). EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion. *Europace*, 16, 1397-1416

Zusammenfassung: Wann ggf. LAA-Okkluder?

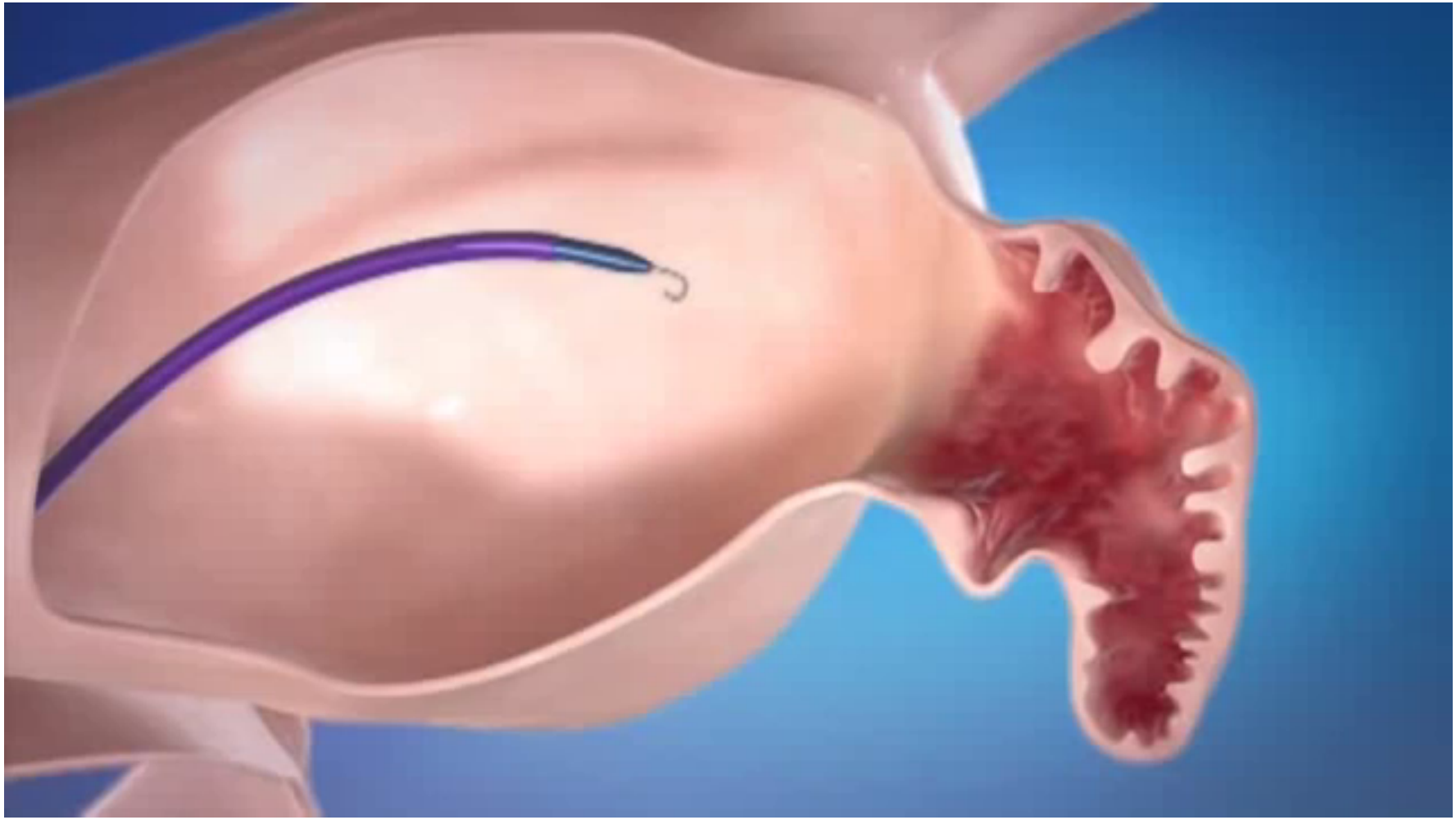
1. Wiederkehrende Insulte unter OAK
2. Z.n. ICB
3. Z.n. anderer schwerer Blutung (v.a. GI, pulmonal)
4. Erschwerende Komorbiditäten
5. Unverträglichkeiten gegenüber VKA/NOAK
6. Kontraindikationen (NI, Leberinsuffizienz)
7. Patientenwunsch
8. Triple-Therapie

Die Implantation

Der interventionelle Verschluss des linken Vorhofohres



Der interventionelle Verschluss des linken Vorhofohres



Der interventionelle Verschluss des linken Vorhofohres

Diskutieren Sie Ihren Fall !

Hürth (02233) – 594 547

Ausblick auf die nächste Veranstaltung:

DI, 12.4., 19:30

Thema:

„ Interdisziplinäre Therapie von Lungenerkrankungen“

Vortrag 1:

Leitliniengerechte Therapie der COPD

Vortrag 2:

Chirurgie bei Lungenerkrankungen mit Schwerpunkt auf dem Therapieangebot im Sana Krankenhaus Hürth

3 FB-Punkte beantragt