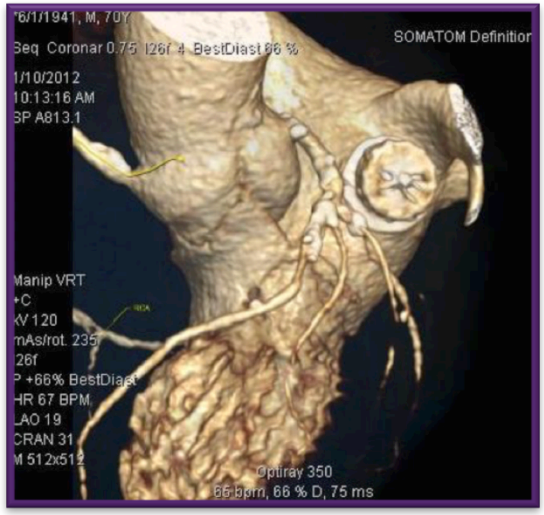
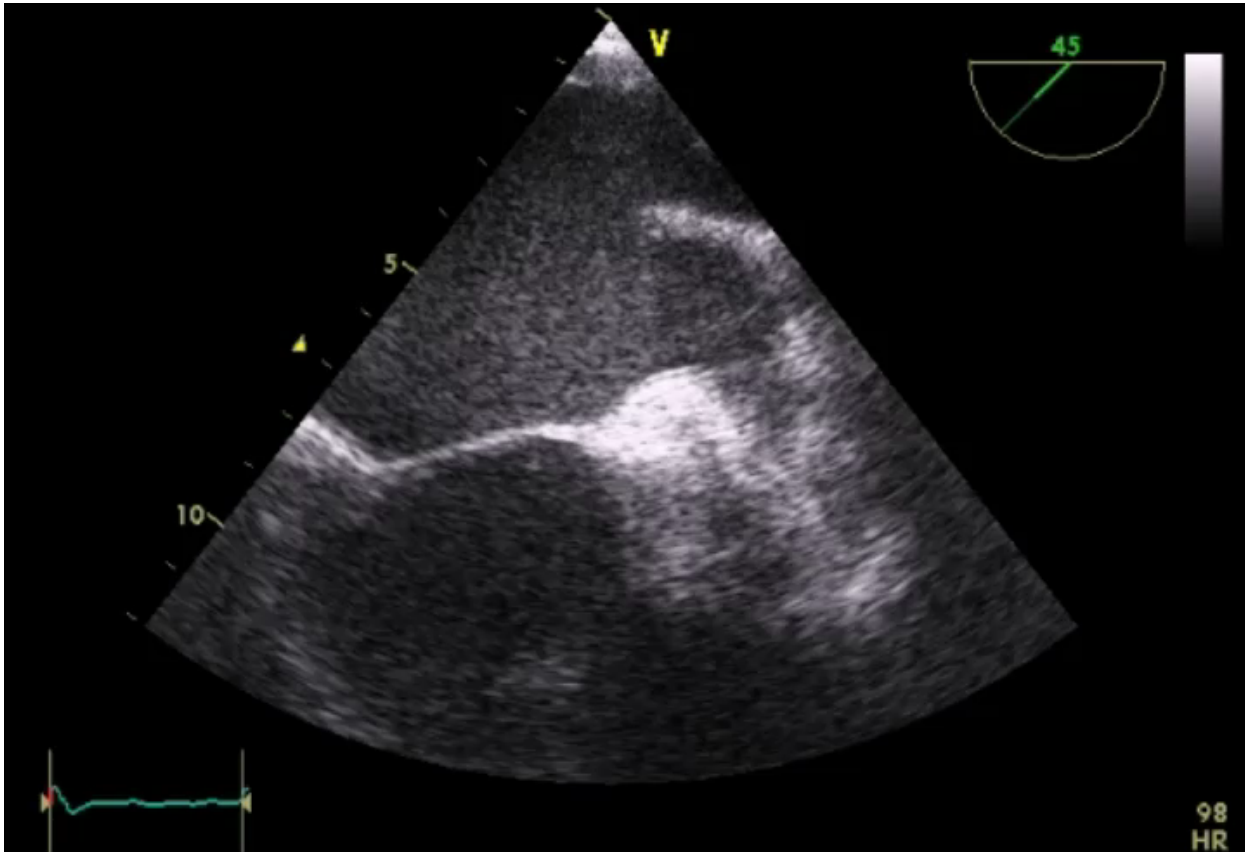
Aurikellukning ved atrieflimren og kontraindikation for AK-behandling

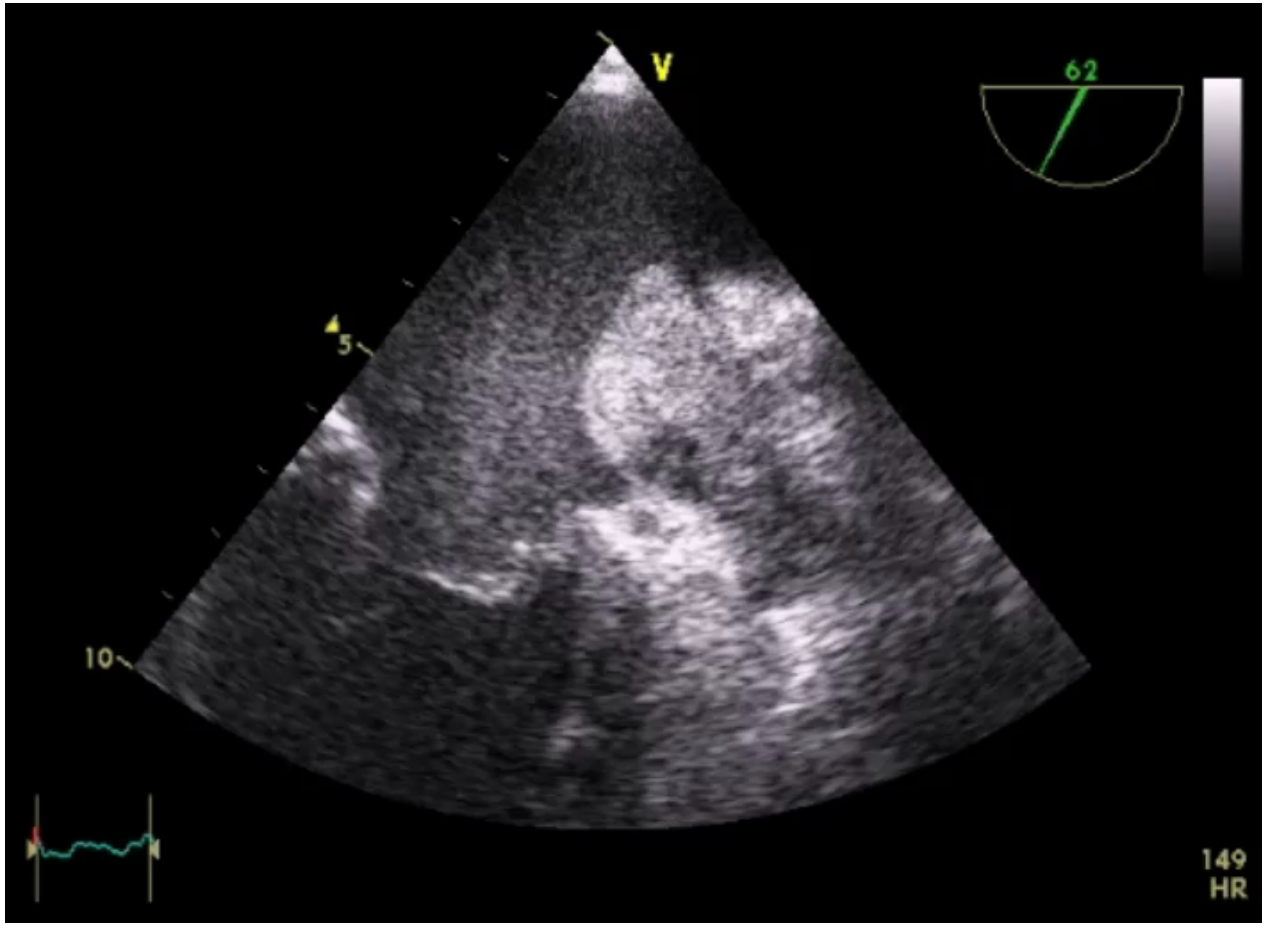


Jens Erik Nielsen-Kudsk
Ass. Professor, MD, DMSc
Department of Cardiology
Aarhus University Hospital, Skejby
Denmark

Stroke ved AF er et strukturelt problem



Stroke ved AF er et strukturelt problem



N(OAC) ved AF, en delikat balance

Forebygge Stroke
CHA_2DS_2-VASc

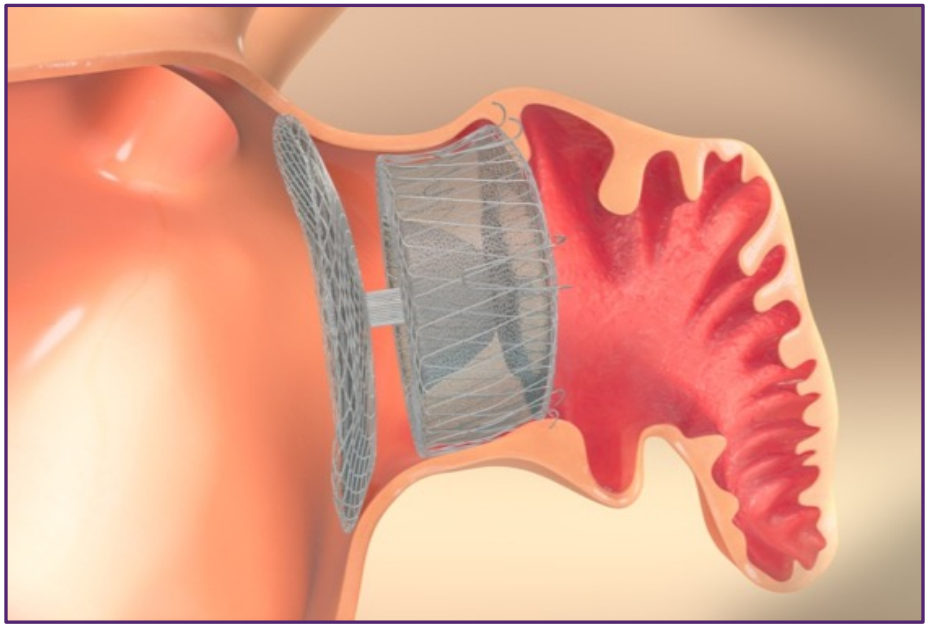
Undgå Blødning
HAS-BLED

Phillippe Petit; Twin Towers Walk; 1974

N(OAC) ved AF; problemer

- Alvorlig blødning (5% per year)
- Samtidig behandling med thrombocyt hæmmere
  - Warfarin+ASA: 7-8%
  - Warfarin+ASA+clopidogrel: 15%
- Interaktioner
- Fluktuerende nyrefunktion
- Afbrydelser (kirurgi, tandlæge etc.)
- Compliance
  - INR, 35% af tiden udenfor therapeutisk interval
  - NOACS 20-25% er stoppet efter 2 år
- Underanvendelse

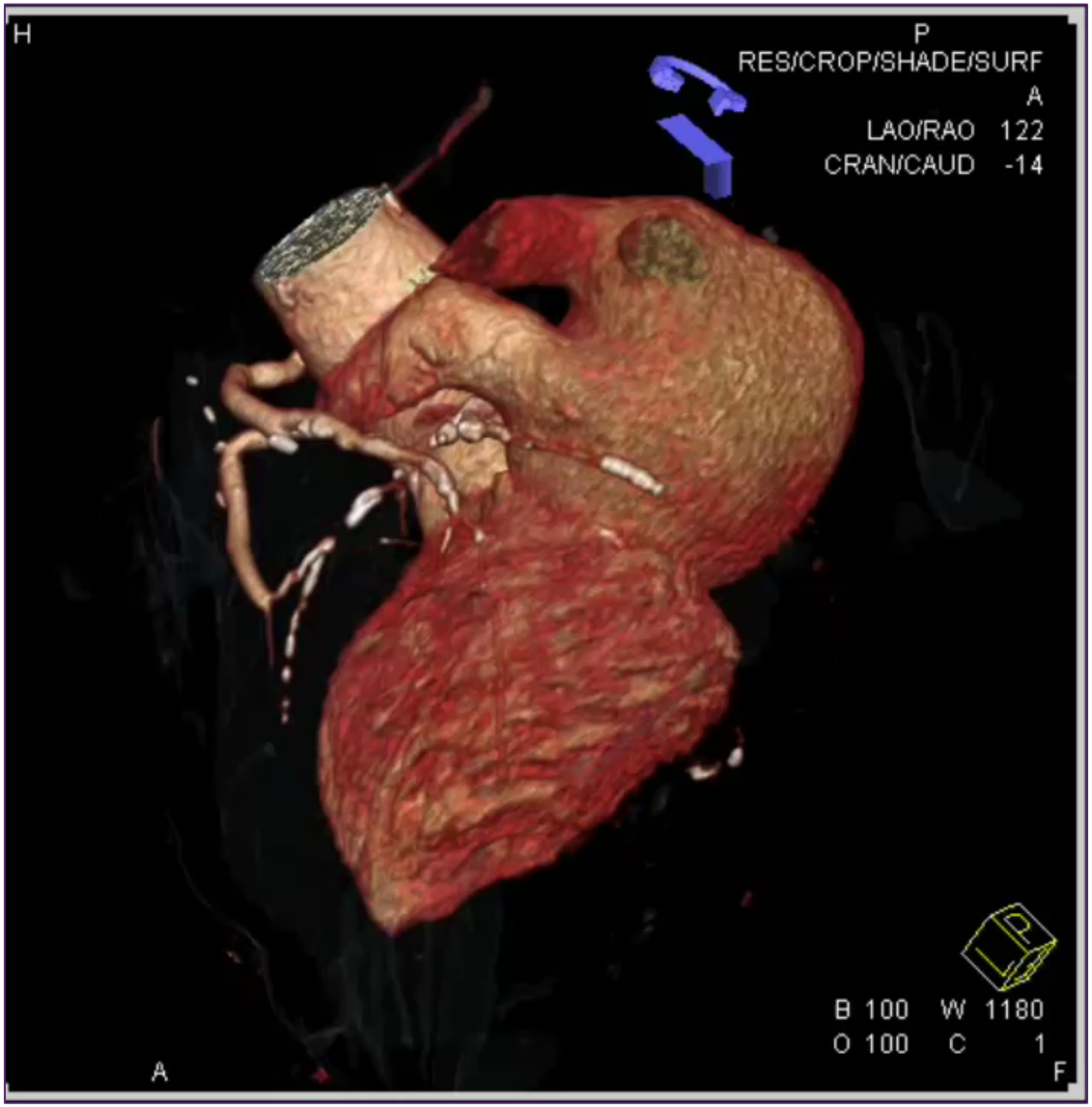
LAAO, løsningen på et strukturelt problem



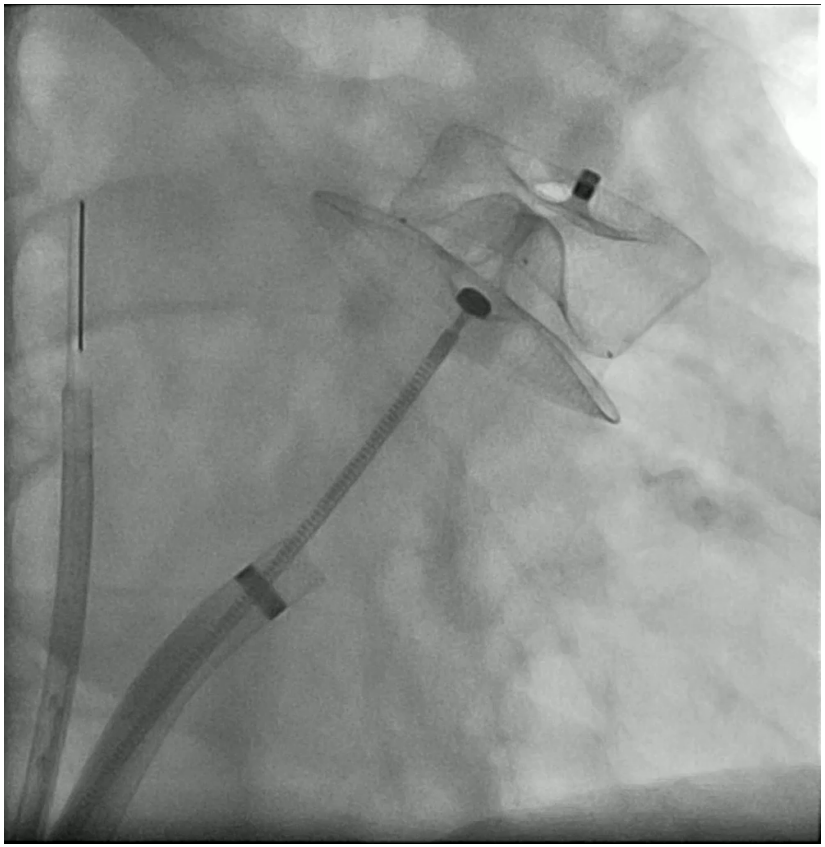
WATCHMAN®

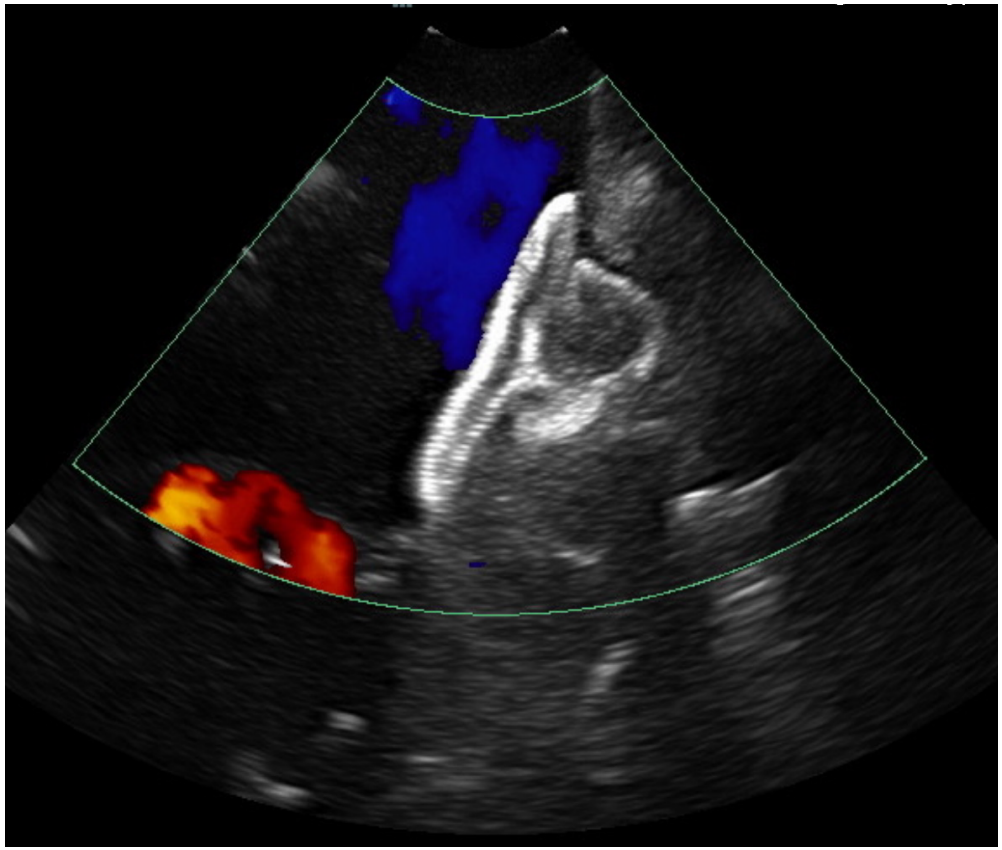
AMPLATZER®
Amulet

Præ-procedure CT



LAAO; udføres i LA vejledt af ICE





Protect-AF, proof-of-concept

AF, CHADS2 2.2/2.3, tolererer OAC

	Intervention group		Control group		Rate ratio (intervention/control [95% CrI])	Posterior probabilities	
	Events/patient-years	Observed rate (events per 100 patient-years [95% CrI])	Events/patient-years	Observed rate (events per 100 patient-years [95% CrI])		Non-inferiority	Superiority
ITT population*							
Primary efficacy†	21/694·1	3·0 (1·9–4·5)	18/370·8	4·9 (2·8–7·1)	0·62 (0·35–1·25)	>99·9%	90·0%
Ischaemic stroke	15/694·6	2·2 (1·2–3·5)	6/372·3	1·6 (0·6–3·6)	1·34 (0·60–4·29)	71·8%	20·1%
Cardiovascular/unexplained death	5/708·4	0·7 (0·2–1·5)	10/374·9	2·7 (1·2–4·4)	0·26 (0·08–0·77)	>99·9%	99·3%
Haemorrhagic stroke	1/708·4	0·1 (0·0–0·5)	6/373·4	1·6 (0·6–3·1)	0·09 (0·00–0·45)	>99·9%	99·8%
Systemic embolism	2/707·8	0·3 (0·0–0·8)	0/374·9	0	..	..	..
All stroke	16/694·6	2·3 (1·3–3·6)	12/370·8	3·2 (1·6–5·2)	0·71 (0·35–1·64)	99·3%	76·9%
All-cause mortality	21/708·4	3·0 (1·9–4·5)	18/374·9	4·8 (2·8–7·1)	0·62 (0·34–1·24)	>99·9%	90·7%
Primary safety‡	49/658·8	7·4 (5·5–9·7)	16/364·2	4·4 (2·5–6·7)	1·69 (1·01–3·19)	..	..

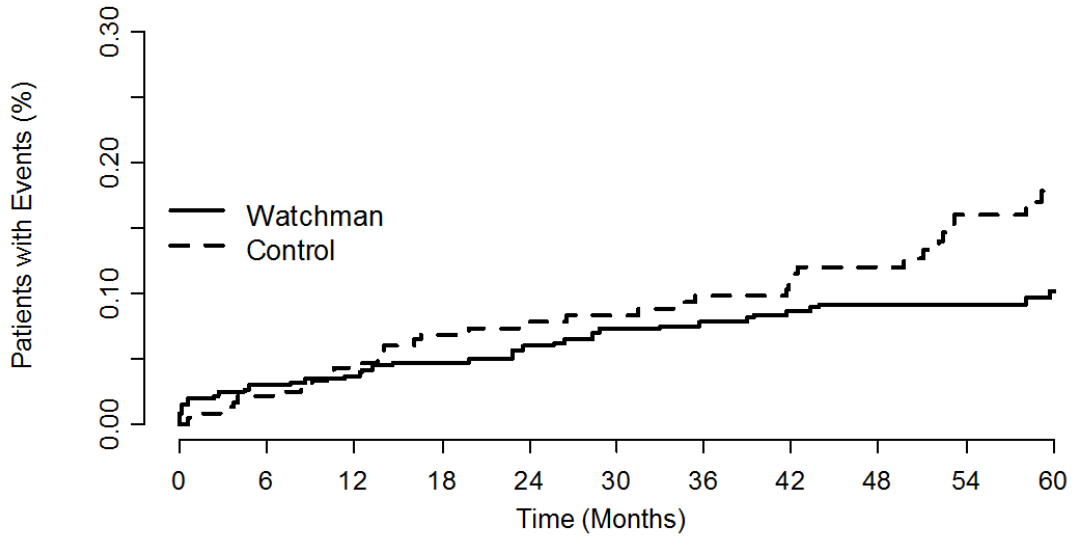
Serious pericardial effusion
Major bleeding
Device embolization
Procedure-related stroke

Major bleeding
Intracranial bleeding

Holmes-DR et al.
Lancet 2009;374:534-42

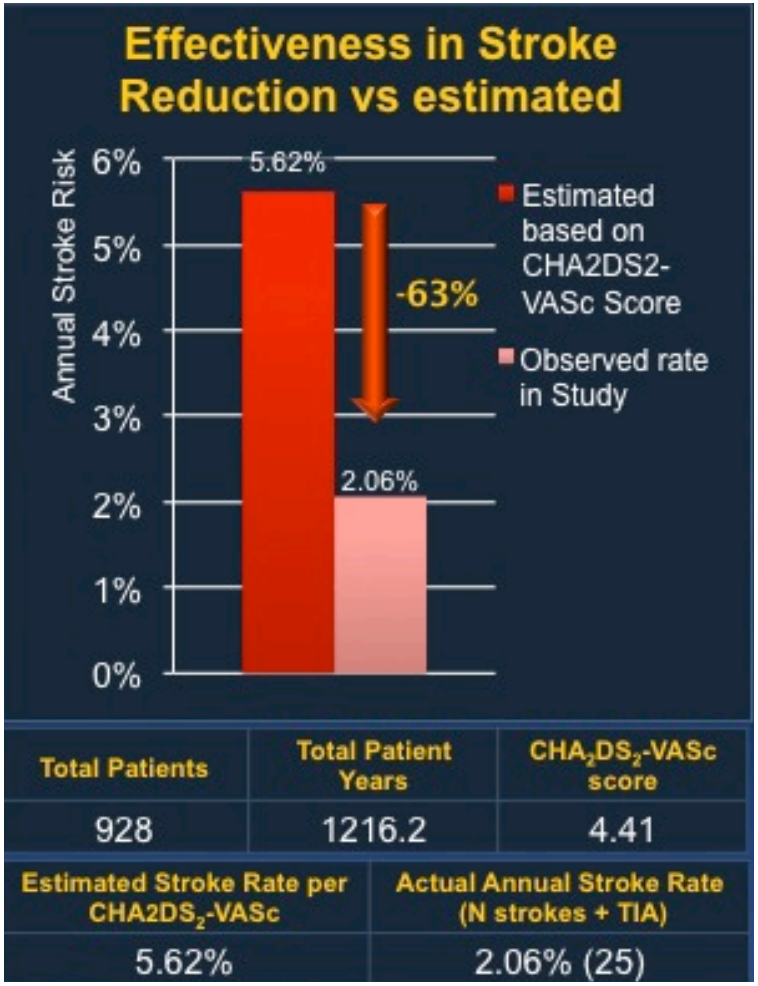
Protect-AF, 4-års data, primary endpoint

Analysis	Watchman Group (n = 463) Events/ Patient-Years	Watchman Group (n = 463) Observed Rate (Events per 100 Patient-Years) (95% CI)	Warfarin Group (n = 244) Events/ Patient-Years	Warfarin Group (n = 244) Observed Rate (Events per 100 Patient-Years) (95% CI)	Hazard Ratio (Watchman/Warfarin) (95% CI)	P Value
Primary Efficacy Outcomes						
Intention-to-treat	39/1720.2	2.3 (1.7,3.1)	34/900.8	3.8 (2.7,5.3)	0.61 (0.38, 0.97)	0.0348
Post-procedure	33/1710.1	1.9 (1.4,2.7)	34/900.8	3.8 (2.7,5.3)	0.52 (0.32,0.84)	0.0072



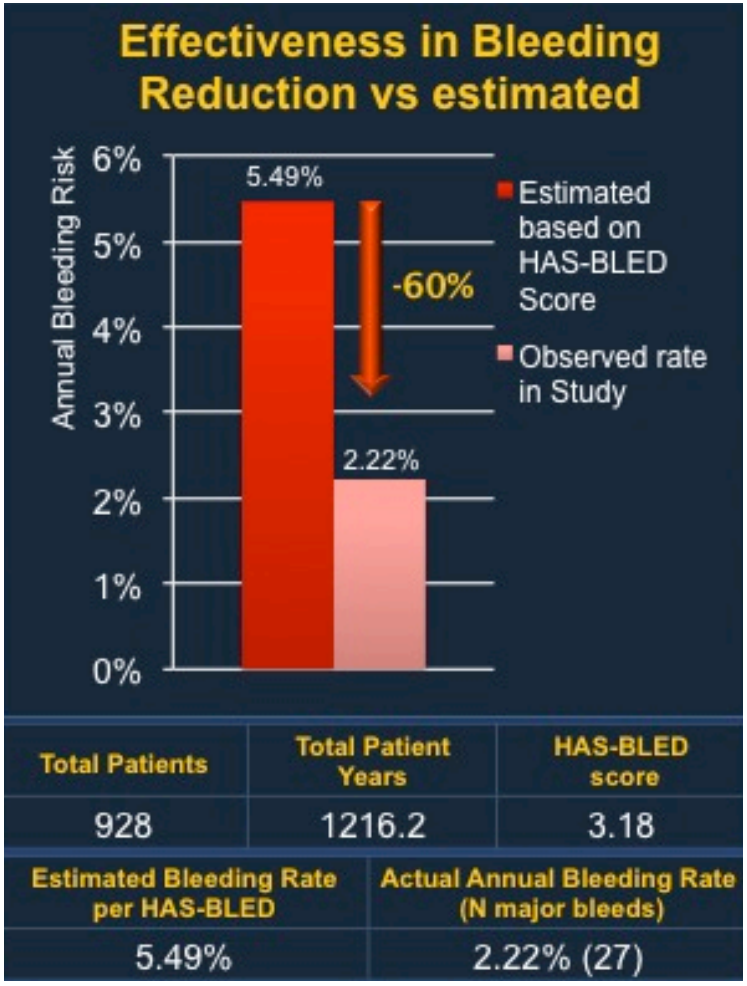
Reddy-V
HRS, May 2013

Multicenter ACP erfaring



Total Patients	Total Patient Years	CHA_2DS_2-VASc score
928	1216.2	4.41

Estimated Stroke Rate per $CHA2DS_2$-VASc	Actual Annual Stroke Rate (N strokes + TIA)
5.62%	2.06% (25)



Total Patients	Total Patient Years	HAS-BLED score
928	1216.2	3.18

Estimated Bleeding Rate per HAS-BLED	Actual Annual Bleeding Rate (N major bleeds)
5.49%	2.22% (27)

Tzikas-A, .., Nielsen-Kudsk-JE et al.
Eurointervention 2016, 11, 1170-9

LAA occlusion vs. standard care in patients with atrial fibrillation and intracerebral hemorrhage

A propensity score matched follow-up study

Jens Erik Nielsen-Kudsk, Ass. Prof., MD, DMSc
Dept. Cardiology, Aarhus University Hospital, Skejby
Denmark

Investigators; Nordic LAAO centers

- **Jens Erik Nielsen-Kudsk**, Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark
- **Søren Paaske Johnsen**, Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark
- **Per Wester**, Stroke Center, Umea University Hospital, Umea, Sweden
- **Dorte Damgaard**, Department of Neurology, Aarhus University Hospital, Aarhus, Denmark
- **Juha Lund**, Department of Cardiology, Turku University Hospital, Turku, Finland
- **Ole De Backer**, Department of Cardiology, Rigshospitalet, Copenhagen, Denmark
- **Sami Pakarinen**, Department of Cardiology, Helsinki University Hospital, Helsinki, Finland
- **Jacob Odenstedt**, Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden
- **Saila Vikman**, Department of Cardiology, Tampere University Hospital, Tampere, Finland
- **Bo Sahlgren**, Department of Cardiology, Karolinska Institute, Solna, Stockholm, Sweden
- **Ole Kongstad**, Department of Cardiology, Skåne University Hospital, Lund, Sweden
- **Derk Krieger**, Comprehensive Stroke Center, Dept. Neurology, University of Zurich, Zurich, Suisse
- **Mårten Rosenqvist**, Department of Cardiology, Karolinska Institute, Danderyd, Stockholm, Sweden

Background

- Patients with **atrial fibrillation** (AF) and **an intracerebral hemorrhage** (ICH) have a high risk of both ischemic stroke and recurrent ICH.
- There is **no consensus** on **how to treat** AF post-ICH and such patients are **often** left **without anticoagulation** due to the fear of recurrent serious bleedings.
- Transcatheter left atrial appendage occlusion (**LAAO**) **might** be of potential clinical **benefit** in this patient group.
- The **aim** of this study was to **compare** the clinical outcome of **LAAO** versus **standard medical care** in patients with AF and a prior ICH.
- This was done in a **propensity score matched** follow-up trial with the LAAO and standard care groups matched according to stroke and bleeding risks (CHA_2DS_2-VASc and HAS-BLED scores).

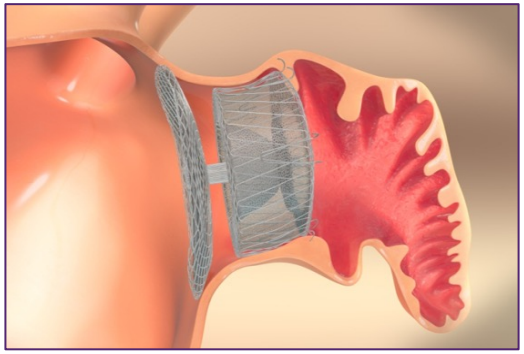
Methods

- **Study population:**
  - **LAAO:** Nordic LAAO patients, treated between 2009-2015. n=172 (*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 2005-2014. n=787
- **Design:** Propensity-score matched follow-up study
  - Used to balance stroke and bleeding risks in the two patient groups
  - Matched CHA_2DS_2-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

LAAO procedure

- Amplatzer Cardiac Plug (ACP) or Amplatzer Amulet (n=176)
- Procedural success 97.7% (172/176)
- Periprocedural complications 4.0% (7/176)
  - 1 ICH (full spontaneous recovery), 1 hematemesis, 3 vascular access site bleedings
  - 1 device migration, 1 pericardial effusion
  - No mortality
- Includes learning-curve of new implanters



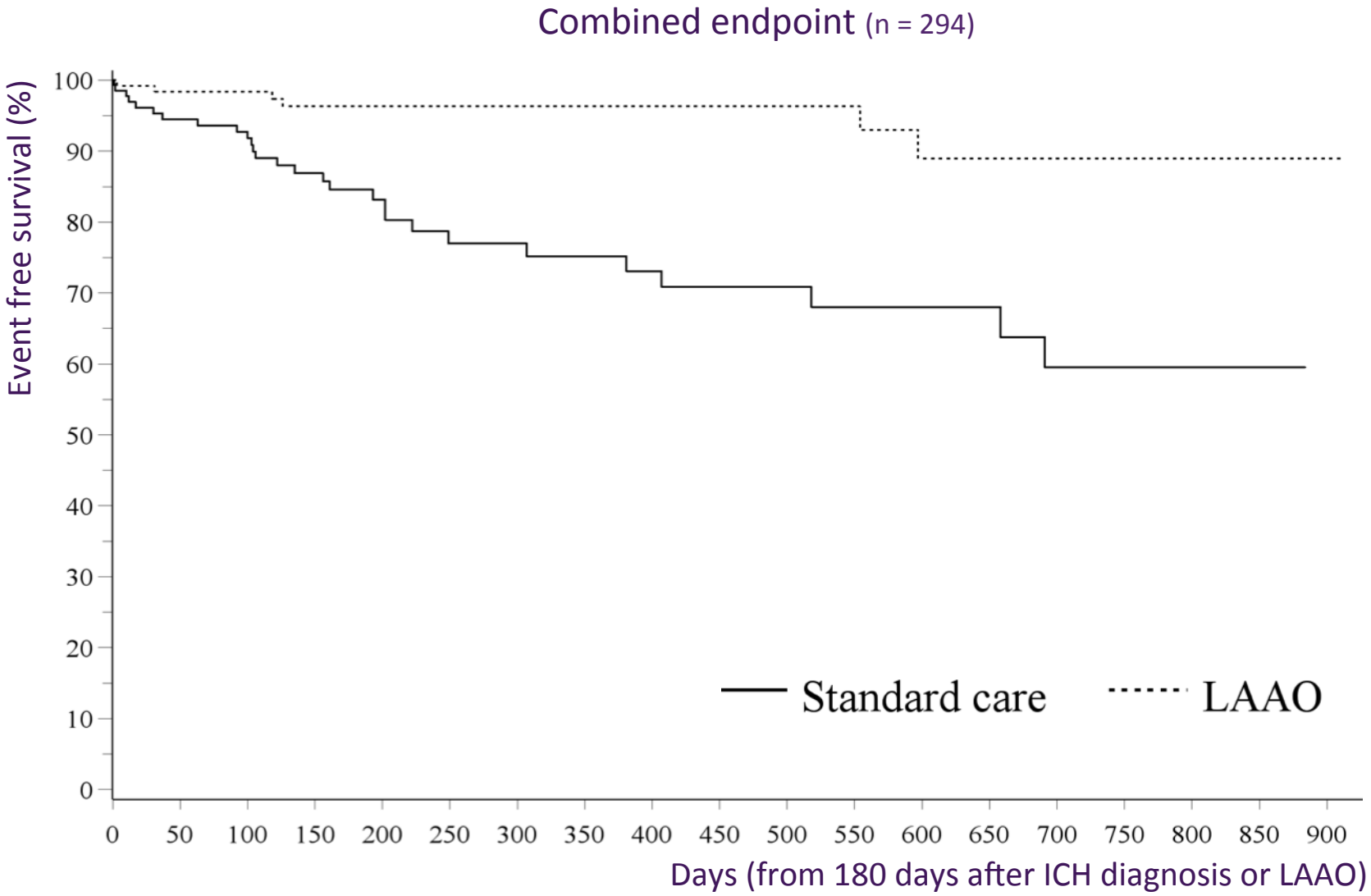
Amplatzer LAA Occluder

Patient characteristics

Characteristics (propensity score matched patients)	Standard care (n=147)	LAAO (n=147)
Age, mean (SD)	**73.3** (9.1)	**71.9** (8.7)
Gender (male) n (%)	**97** (66.0)	**96** (65.0)
CHA_2DS_2-VASc mean (SD)	**4.0** (1.5)	**3.9** (1.5)
HAS-BLED mean (SD)	**4.2** (0.8)	**4.2** (0.8)
Antithrombotic treatment	(during follow-up)	(at latest follow-up)
Warfarin	**20%**	**0%**
NOAC	**23%**	**0%**
Platelet inhibitors	**37%**	**71%**
No treatment	**44%**	**29%**

Median follow-up time: 166 days (25%/75% quartile: 70/458 days)
Median time from ICH to LAAO: 189 days (25-4533 days)

Ischemic stroke/major bleeding/mortality



Events

Clinical outcome	Standard care (n=147)	LAAO (n=147)
Ischemic stroke/major bleeding/mortality		
Events	**28**	**6**
Event rate (events/1000 patient years) (95% CI)	**278.9** (229.3 - 339.2)	**47.9** (40.2-57.1)
Ischemic stroke		
Events	**5**	**2**
Event rate (events/1000 patient years) (95%)	**48.6** (40.1-59.0)	**15.5** (13.0-18.4)
Major bleeding		
Events	**9**	**4**
Event rate (events/1000 patient years) (95%)	**88.3** (72.7-107.2)	**31.7** (26.6-37.7)
ICH	**3**	**1**
Mortality		
Events	**23**	**2**
Event rate (events/1000 patient years) (95%)	**216.9** (179.3-262.4)	**15.4** (13.0-18.3)

Hazard ratios

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	**0.19** (0.08-0.46)*	**81%**
Ischemic stroke	**0.35** (0.07-1.79)	**65%**
Major bleeding	**0.39** (0.12-1.28)	**61%**
ICH	**0.29** (0.03-2.82)	**71%**
Mortality	**0.08** (0.02-0.32)*	**92%**

*$p<0.05$

Additional PS-match analysis:

OAC-treated standard care patients

ICH patients with AF treated either by standard medical care or LAAO.
All standard care patients **started oral anticoagulant** within 180 days after ICH

Characteristics (propensity score matched patients)	Standard care, OAC (n=103)	LAAO (n=103)
Age, mean (SD)	**74.8** (9.0)	**72.9** (9.6)
Gender (male) n (%)	**64** (62.1)	**64** (62.1)
CHA_2DS_2-VASc mean (SD)	**4.0** (1.5)	**3.8** (1.5)
HAS-BLED mean (SD)	**4.2** (0.7)	**4.1** (0.7)
Antithrombotic treatment	(during follow-up)	(at latest follow-up)
Warfarin	**72%**	**0%**
NOAC	**100%**	**0%**
Platelet inhibitors	**18%**	**65%**
No treatment	**0%**	**35%**

Additional PS-match analysis:

OAC-treated standard care patients

ICH patients with AF treated either by standard medical care or LAAO.
All standard care patients **started oral anticoagulant** within 180 days after ICH

Clinical outcome HR by Cox-regression analysis n = 103 in each PS-matched patient group	**LAAO vs. Standard care Hazard ratio (95%CI)**	**Relative risk reduction (%)**
Ischemic stroke/major bleeding/mortality	**0.26** (0.09-0.80)*	**74%**
Ischemic stroke	**0.32** (0.06-1.56)	**68%**
Major bleeding	**0.66** (0.11-3.94)	**34%**
ICH	**0.51** (0.05-5.65)	**49%**
Mortality	**0.28** (0.06-1.36)	**72%**

Conclusion

- These study data suggests transcatheter LAAO to be a beneficial stroke prevention strategy in patients with atrial fibrillation and prior intracerebral hemorrhage
- The results should be confirmed in a randomized clinical trial
- A Nordic randomized clinical LAAO trial (STROKECLOSE) will start recruiting in 2016

STROKECLOSE

- Prevention of Stroke by Left Atrial Appendage Closure in AF Patients after Intracerebral Hemorrhage.
  A Multicenter Randomized Clinical Trial.
- Nordic trial; LAAO tested against medical therapy 2:1
  N=750; FU 2 years
- Medical therapy: OAC; NOAC; anti-platelets or none
- Investigator driven; Karolinska Trial Alliance
- Recruiting will start SEP 2016

Hvornår skal LAAO overvejes?

Transkateter LAA lukning:
AF med betydende stroke risiko (CHA_2DS_2-VASc score ≥2) og
Kontraindikation for OAC (typisk tidligere alvorlig blødning) eller
Høj risiko for blødning (HAS-BLED score ≥3/4/5) eller
Manglende compliance overfor OAC eller
Stroke til trods for OAC (hvis vaskular årsag usandsynlig)
Langtids indikation for triple antithrombotisk terapi

STROKECLOSE

Thank you for your attention!