

Aurikellukning ved atrieflimmer (AF)



Orale antikoagulantia og Atrieflimmer (AF)

CHADS₂DS₂-VASc score > 1

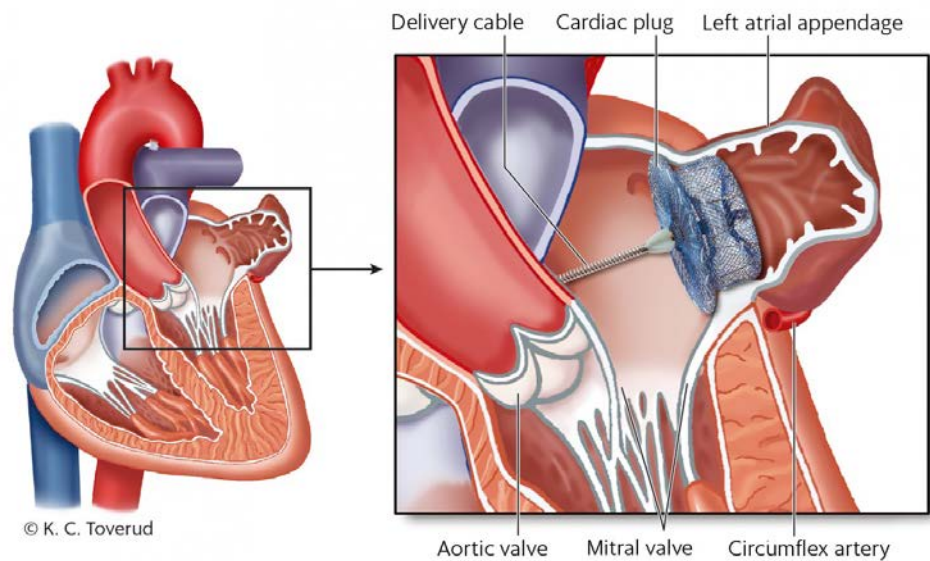
- Orale antikoagulantia; klasse 1A anbefaling
- VKA og NOAK er lige effektive
- NOAK vælges eller VKA hvis velkontrolleret (INR 2-3 > 70% af tiden)

Subpopulationer med tidligere stroke/TIA og AF

- Højere risiko for (recidiv) stroke end i primærprofylaksen (både AIS og ICH)
- Re-Stroke profylaksen: NOAK er lige så effektiv som VKA
- NOAK foretrækkes som 1. valg for at undgå blødninger; især ICH

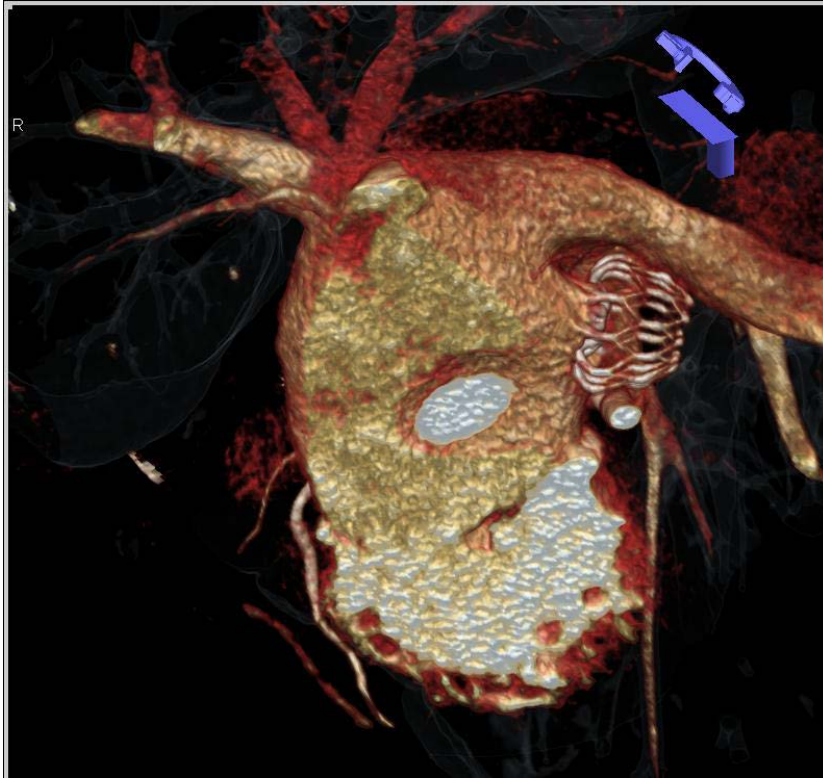
LAAO; non-pharmakologisk behandling ved AF

- Tidl. studier har vist at embolier opstår i auriklet i 91%
- LAAO udføres via en transkutan katetermetode
- Lukkeren dækkes af endothelet i løbet af 3 måneder

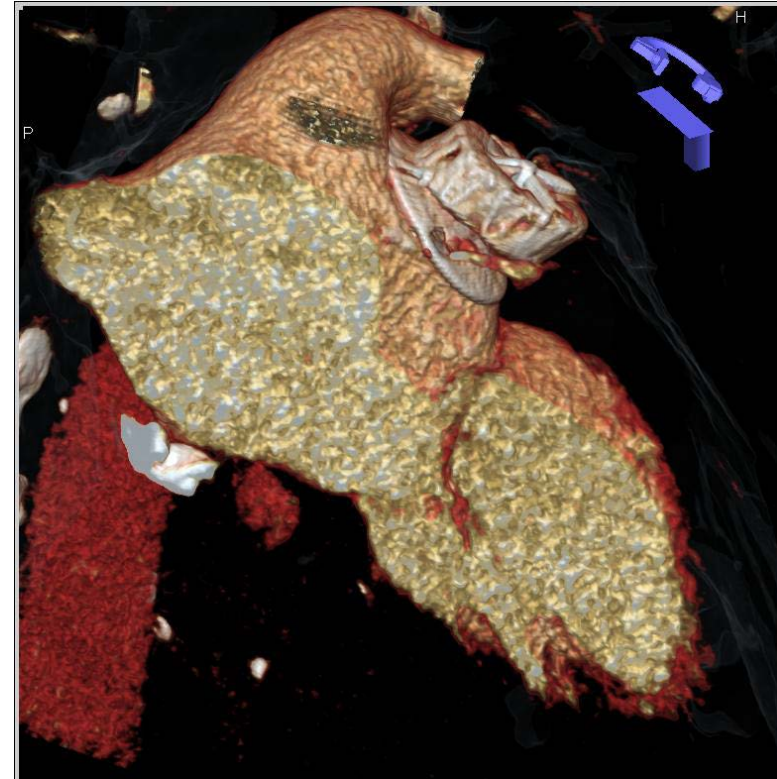


Lunde et al Tidsskr Nor Lægeforen 2018

LAAO; stroke profylakse ved AF



Watchman device



Amulet device

Guidelines for LAAO

European Guidelines (2016):

- AF patients with contraindications for long-term OAC (IIb, level B)

FDA approved LAAO (2014 and 2016):

- Pt's at high risk of Stroke or SE...
- Suitable for VKA
- Have an appropriate rationale for LAAO as an alternative to VKA taking into account safety and effectiveness of device vs. VKA

ECS 2016 AF guideline endorsed by ESO

Recommendations for occlusion or exclusion of the left atrial appendage

| Recommendations | Class ^a | Level ^b | Ref ^c |
|--|--------------------|--------------------|------------------|
| After surgical occlusion or exclusion of the LAA, it is recommended to continue anticoagulation in at-risk patients with AF for stroke prevention. | I | B | 461, 462 |
| LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause). | IIb | B | 449, 453, 454 |
| Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery. | IIb | B | 463 |
| Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients undergoing thoracoscopic AF surgery. | IIb | B | 468 |

AF = atrial fibrillation; LAA = left atrial appendage.

^aClass of recommendation.

^bLevel of evidence.

^cReference(s) supporting recommendations.

Evidens for LAAO

TABLE 3 Efficacy Rates at 5 Years (2:1 Randomization)

| | PROTECT AF Subjects | | | | | PREVAIL-Only Subjects | | | | |
|--------------------------------------|---------------------------|-------|----------------------------|-------|---------|---------------------------|-------|----------------------------|-------|---------|
| | Device Group (n = 463) | | Control Group (n = 244) | | p Value | Device Group (n = 269) | | Control Group (n = 138) | | p Value |
| | No. of Events | Rate* | No. of Events | Rate* | | No. of Events | Rate* | No. of Events | Rate* | |
| Primary efficacy: stroke/SE/CV death | 40/1,787.7 | 2.24 | 34/929.4 | 3.66 | 0.04 | 37/1,038.3 | 3.65% | 15/530.4 | 2.94% | 0.47 |
| All stroke | 26/1,781.7 | 1.46 | 20/929.4 | 2.15 | 0.23 | 19/1,042.4 | 1.97% | 7/530.4 | 1.29% | 0.32 |
| Ischemic stroke | 24/1,781.7 | 1.35 | 10/932.8 | 1.07 | 0.49 | 17/1,043.1 | 1.68% | 4/533.3 | 0.73% | 0.13 |
| Hemorrhagic stroke | 3/1,837.7 | 0.16 | 10/945.6 | 1.06 | 0.005 | 2/1,084.6 | 0.18% | 3/538.0 | 0.54% | 0.23 |
| Systemic embolism | 3/1,837.1 | 0.16 | 0 | N/A | N/A | 1/1,080.6 | 0.09% | 0/540.9 | N/A | N/A |
| CV/unexplained death | 19/1,843.2 | 1.03 | 22/948.9 | 2.32 | 0.009 | 18/1,084.7 | 1.79% | 10/540.9 | 1.98% | 0.76 |

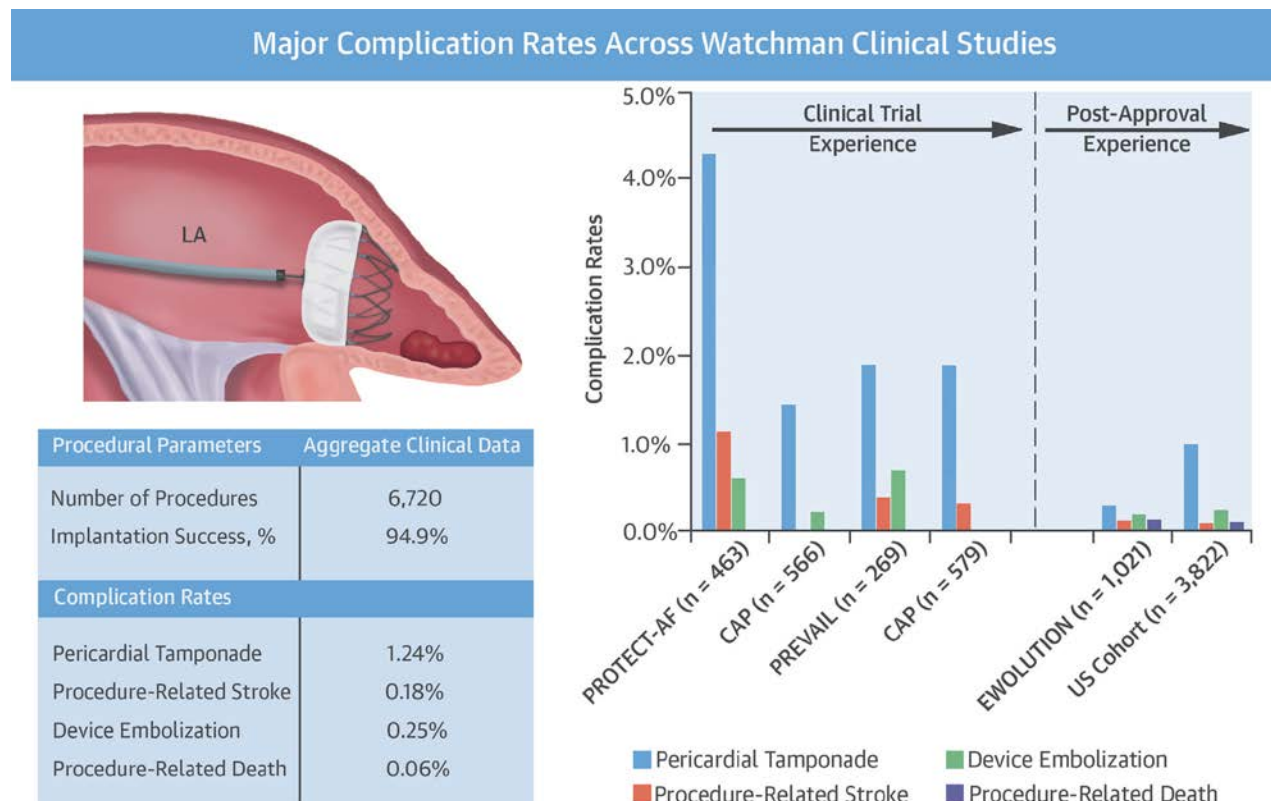
*Events are per 100 patient-yrs.
CV = cardiovascular; SE = systemic embolism; other abbreviations as in Table 1.

Reddy-VV et al.; JACC 2017;24:2964-75

Protect AF "proof of concept studie" - RCT. Kun 18% af ptt havde haft stroke/TIA. Alle skulle kunne tåle VKA
Prevail et efterfølgende studie mhp belysning af sikkerheden/bivirkninger

Komplikationer og succesrate ved LAAO

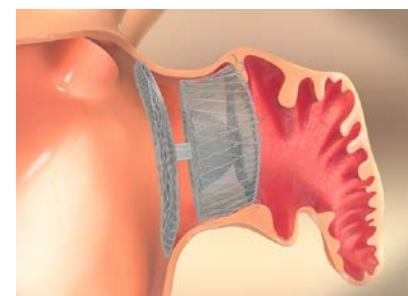
Watchman (n=6720)



Reddy-VV et al.; JACC 2017;3:253-61

Amulet Observational Study (n=1088)

| Results | |
|----------------------------------|-------------|
| Successful implantation | 99% |
| Closure < 3mm (follow up) | 98.2% |
| Major AE | 3.2% |
| Major bleeding: | 2.4% |
| Pericardial effusion/tamponade | (1.2%) |
| Pericardiocentesis | (0.9%) |
| Surgery | (0.3%) |
| Vascular complications | 0.9% |
| Death – | 0.2% |
| 1 cardiac perforation | |
| 1 cardiorespiratory arrest/shock | |
| Device embolization | 0.1% |



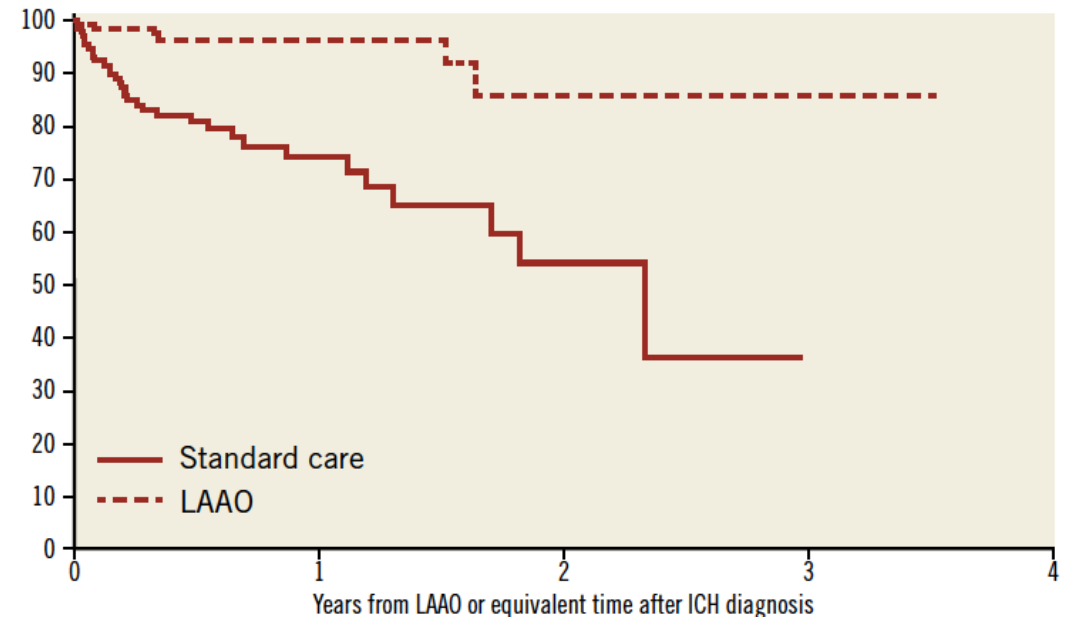
Landmesser-U et al.; Eurointervention 2017;13:867-76

LAAO; Nordisk propensity score matched ptt; AF/ICH

AF/ICH patients treated by LAAO (ACP/Amulet 2009-2015) or standard medical care (n=302)
PS-matched according to CHA₂DS₂VASc and HASBLED score

| Outcome | Hazard ratio (95% CI) |
|---|-----------------------|
| Ischaemic stroke/major bleeding/ all-cause mortality | 0.16 (0.07-0.37) |
| Ischaemic stroke | 0.21 (0.05-1.00) |
| Major bleeding | 0.28 (0.09-0.85) |
| recurrent ICH | 0.10 (0.01-0.81) |
| All-cause mortality | 0.11 (0.03-0.51) |

ICH: intracerebral haemorrhage; LAAO: left atrial appendage occlusion



Meta-analyse af 3 observationelle ICH studier

TABLE 1. Characteristics of Participating Subjects

Biffi et al; Annals of Neurol 2017

| Variable | RETRACE | | MGH | | ERICH | |
|----------------------|--------------|------------|--------------|-------------|--------------|-------------|
| | Nonlobar ICH | Lobar ICH | Nonlobar ICH | Lobar ICH | Nonlobar ICH | Lobar ICH |
| No. of subjects | 340 | 202 | 159 | 102 | 134 | 75 |
| Demographics | | | | | | |
| Age, yr ^a | 74.6 (7.8) | 74.7 (7.9) | 70.5 (9.8) | 73.4 (10.5) | 71.7 (11.8) | 73.8 (11.1) |
| Sex, male | 211 (62) | 119 (59) | 98 (62) | 51 (50) | 75 (56) | 45 (60) |

- Alle ptt. på AK behandling ved ICH
- Ingen med tidligere ICH
- AK genoptaget efter 1-2 mdr.

TABLE 3. Oral Anticoagulation Resumption and Outcomes following Intracerebral Hemorrhage

| Outcome ^a | All ICH | | | Nonlobar ICH | | | Lobar ICH | | |
|------------------------------|---------|-----------|----------------------|--------------|-----------|----------------------|-----------|-----------|----------------------|
| | HR | 95% CI | <i>p</i> | HR | 95% CI | <i>p</i> | HR | 95% CI | <i>p</i> |
| Mortality | 0.27 | 0.19–0.40 | <0.0001 ^b | 0.25 | 0.14–0.44 | <0.0001 ^b | 0.29 | 0.17–0.45 | <0.0001 ^b |
| Favorable outcome, mRS = 0–3 | 4.15 | 2.92–5.90 | <0.0001 ^b | 4.22 | 2.57–6.94 | <0.0001 ^b | 4.08 | 2.48–6.72 | <0.0001 ^b |
| All-cause stroke | 0.47 | 0.36–0.64 | <0.0001 ^b | 0.41 | 0.25–0.67 | 0.0004 ^b | 0.51 | 0.37–0.76 | 0.0006 ^b |
| Recurrent ICH | 1.20 | 0.95–1.58 | 0.21 | 1.17 | 0.89–1.54 | 0.27 | 1.26 | 0.88–1.71 | 0.22 |
| Ischemic stroke | 0.44 | 0.29–0.66 | <0.0001 ^b | 0.39 | 0.21–0.74 | 0.004 ^b | 0.48 | 0.25–0.75 | 0.003 ^b |

STROKECLOSE; Nordic RCT; AF/ICH

Prevention of **Stroke** by Left Atrial Appendage Closure in Atrial Fibrillation Patients After Intracerebral Hemorrhage



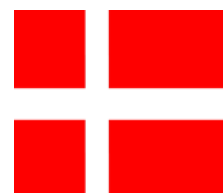
Hypothesis: LAAO is superior to standard medical care in AF patients with a prior ICH

Design: 2:1 randomization LAAO (Amulet) vs. standard medical care

Study design:

- Multicenter prospective randomized open-label controlled trial with blinded outcome evaluation (PROBE) design
- 750 patients 2:1 randomized to LAAO vs best medical treatment enrolled
- 1-12 months after the ICH and followed for a minimum of two years
- Follow-up 2 years

Investigator-initieret; økonomisk grant fra Abbott
Sponsor: Karolinska Trial Alliance





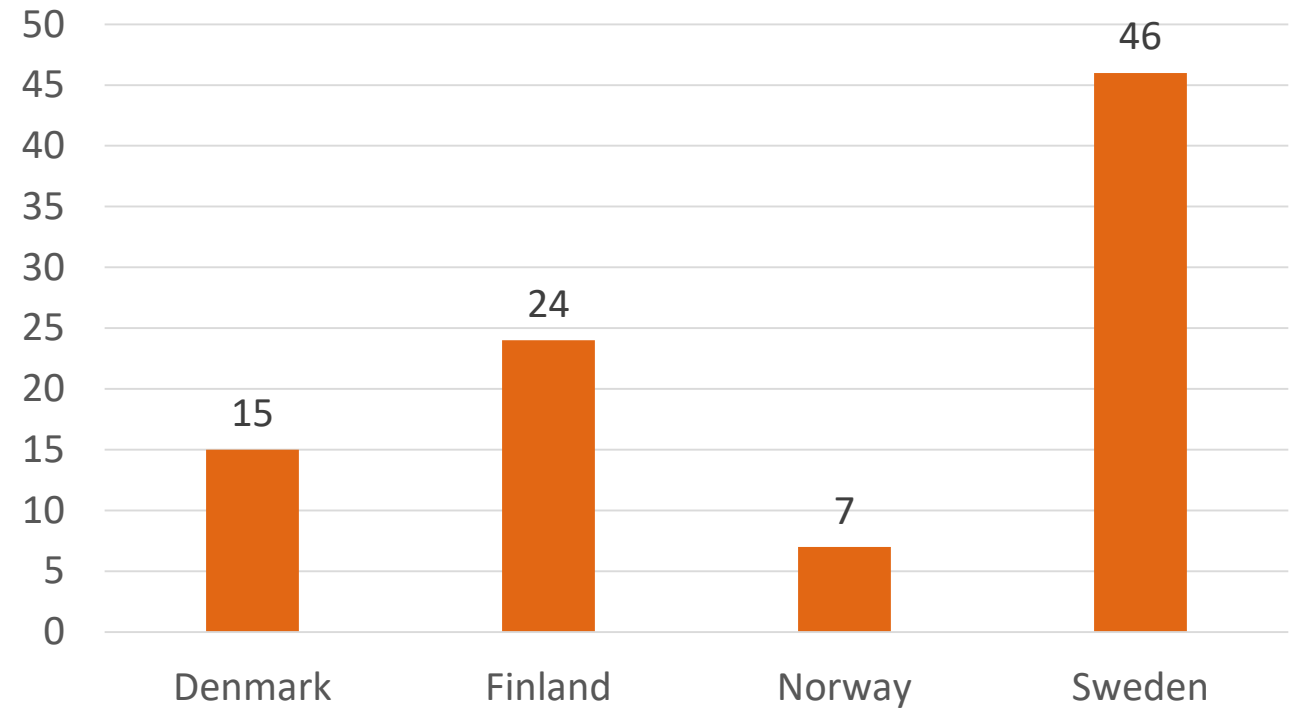
STROKECLOSE status

- 4 countries, 19 sites
- 95 randomized patients

Kontaktpersoner neurologi DK:

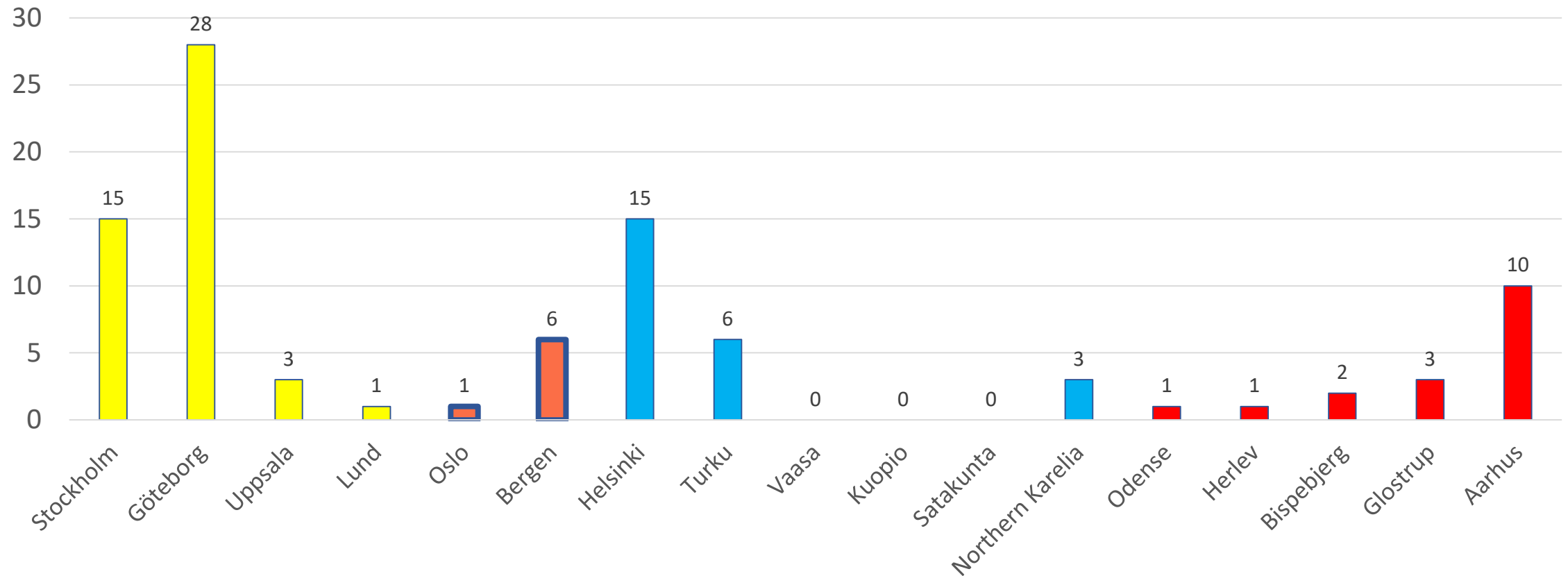
- Dorte Damgaard (AUH)
- Helle Iversen (Glostrup/RH)
- Christina Kruuse (Herlev)
- Karen Aegedius (Bispebjerg)
- Marie Folke (Bispebjerg)
- Anne Mette Homburg (OUH)
- Alex Christensen (OUH)

Number of randomized patients per country



Alle centre

Number of randomized patients per site

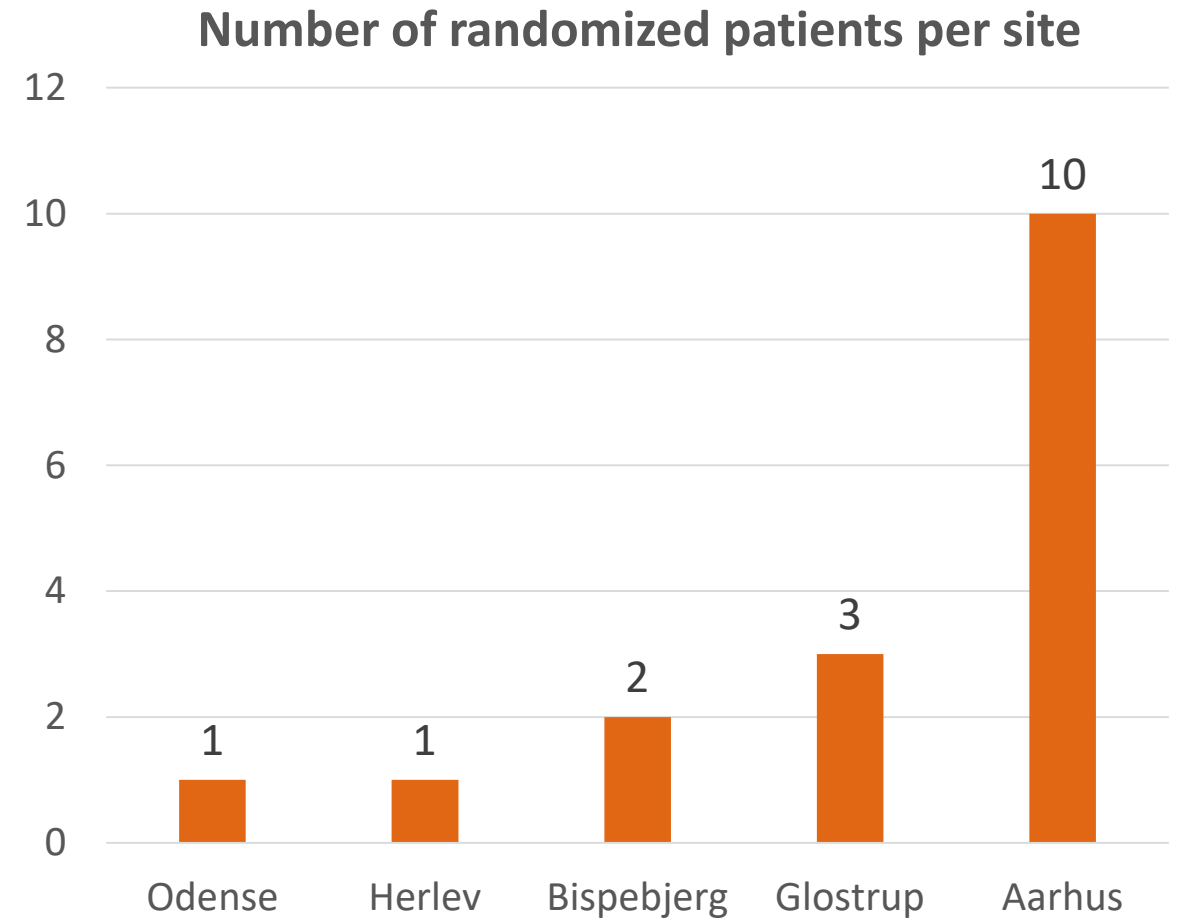


Danmark



Studie status

- 17 patient randomized in total



OCCLUSION-AF; Nordic RCT; LAAO vs. NOAC after AIS

Left Atrial Appendage **Occlusion** versus Novel Oral Anticoagulation for Stroke Prevention in Atrial Fibrillation (Occlusion-AF)

Hypothesis: LAAO is non-inferior to NOAC in AF patients with a prior ischemic stroke

Design: 1:1 randomization LAAO (Amulet or Watchman) vs. NOAC (all)

Study population: AF CHA₂DS₂VASc score ≥ 2 ; ischemic stroke or TIA (MRI positive) within 6 months; mRS ≤ 3 ; (n=750)

Primary combined endpoint: Stroke (ischemic and hemorrhagic), systemic embolism, major bleeding and all-cause mortality

Study sites: Stroke and LAAO centers in the Nordic countries (DK: AAUH, AUH, OUH)

Enrollement: 2 years

Follow-up: 2 years, long-term FU 5 yrs and 10 yrs

TAK for opmærksomheden

