STROKECLOSE

A Nordic randomized clinical trial of Left Atrial Appendage Occlusion (LAAO) in AF patients with a prior ICH

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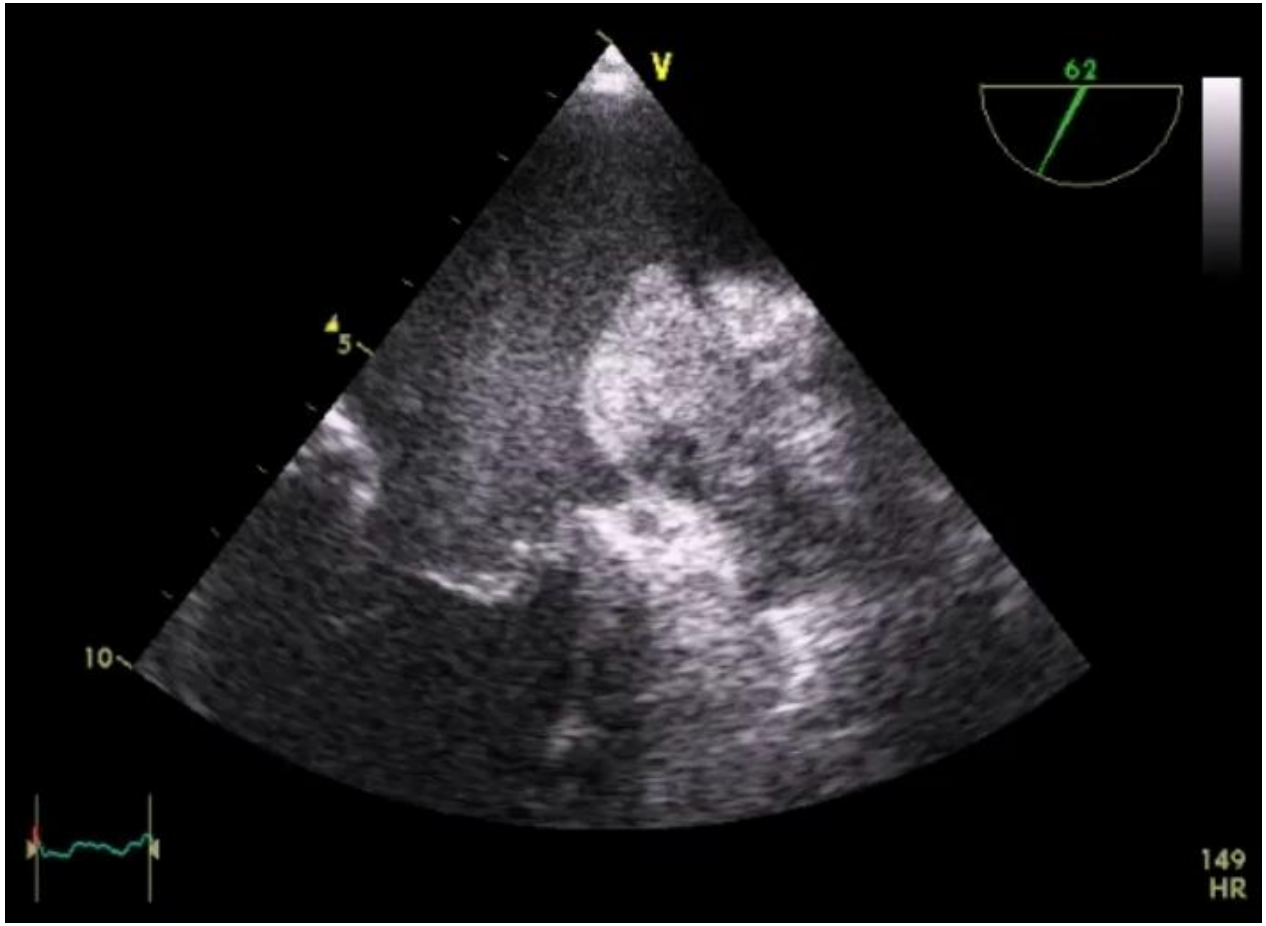
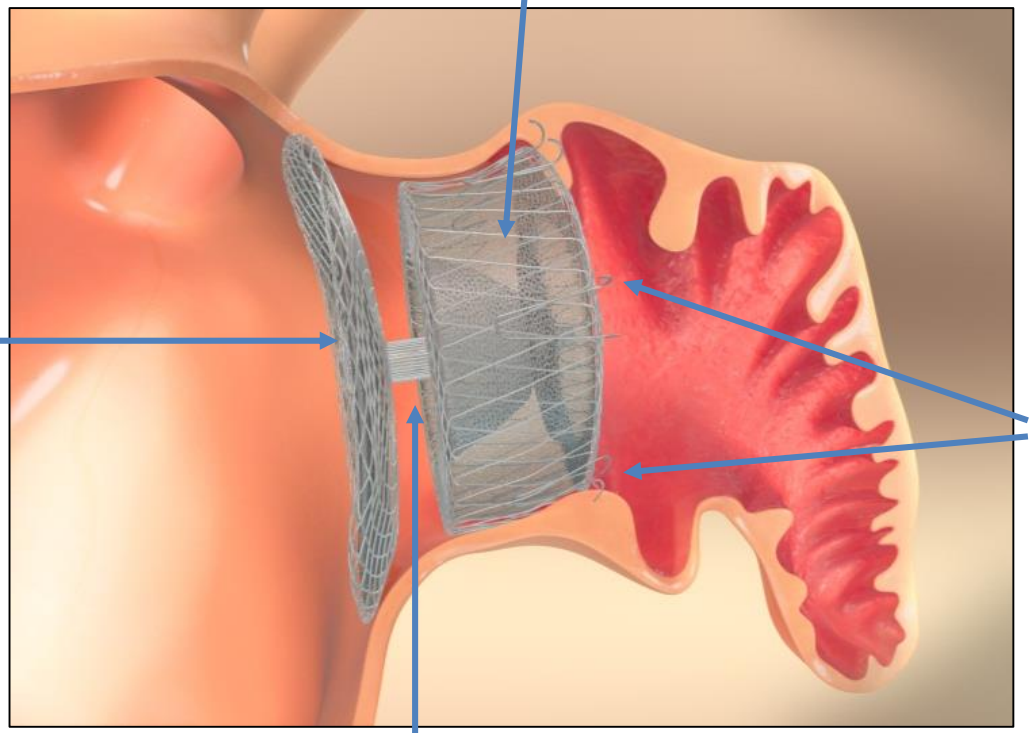
Thromboembolism in AF; a structural problem



LAAO; non-pharmacological stroke prevention

Amulet LAA occluder

Lobe
- Inside the LAA neck
- Designed to conform to LAA anatomy



Disc
- Completely seal at the orifice

Waist
- Maintains tension between lobe and disc
- Allows device to self-orient

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.

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Prevention of **STROKE** by Left Atrial Appendage **CLOS**ur**E** in Atrial Fibrillation Patients after Intracerebral Hemorrhage - A Multicenter Randomized Clinical Trial

– a Nordic randomized clinical trial

Investigator-initiated and investigator-run study
Sponsored by Karolinska Trial Alliance (KTA)
Supported by a grant from Abbott

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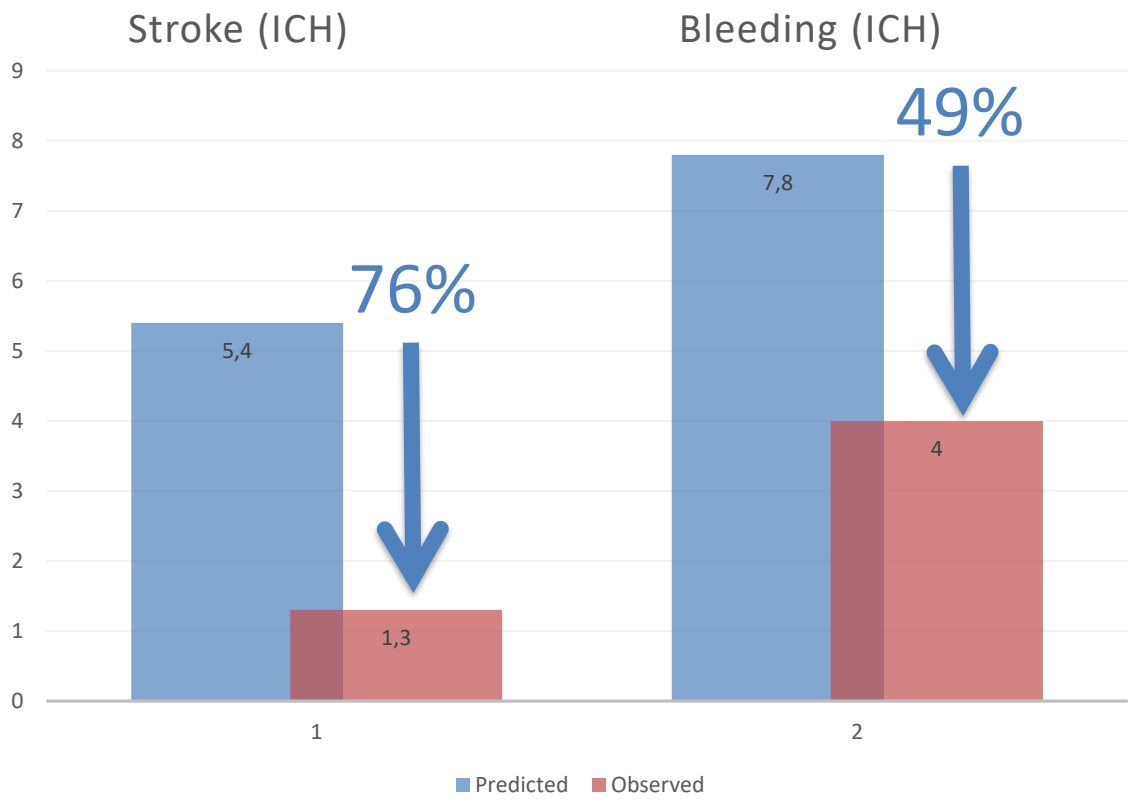
Aim of the study:

- To assess the effect of LAAO to reduce the incidence of stroke, bleeding and mortality in patients with NVAF and prior ICH

Background

- N=109 LAAO procedures March 2010 to March 2015 at AUH, Skejby
- N=49 AF patients with a prior ICH
- Promising results → Nordic Propensity Score Matched Study



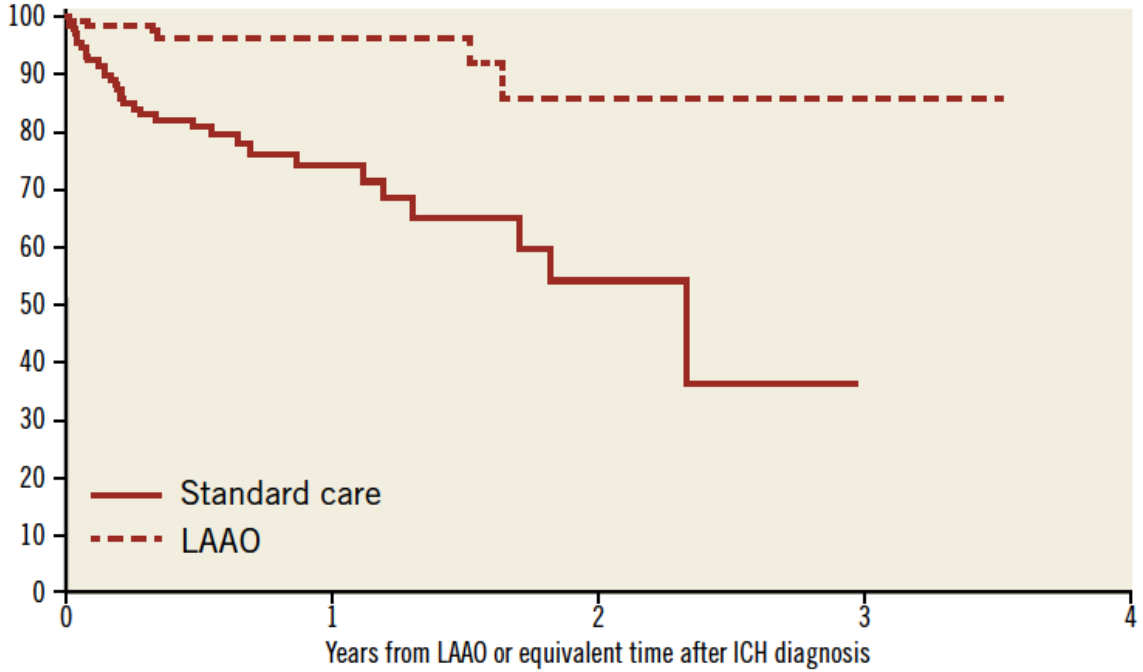
Nordic PS match study

Aim of the study:

- To **compare** the clinical outcome of **LAAO** versus **standard medical care** in patients with AF and a prior ICH 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).

Nordic PS match study

Composite outcome: ischemic stroke, major bleeding, all-cause deaths (N=302)



Nielsen-Kudsk et al. Eurointervention 2017;13:371-378

Nordic PS match study

Outcome	Standard care (n=151)	LAAO (n=151)
Ischaemic stroke/major bleeding/all-cause mortality		
Event	33	6
Patient time (years)	90.0	112.6
Event rate (95% CI)	366.7 (298.2-450.9)	53.3 (44.3-64.1)
Ischaemic stroke		
Event	8	2
Patient time (years)	98.5	115.8
Event rate (95% CI)	81.2 (66.6-98.9)	17.3 (14.4-20.8)
Major bleeding (including recurrent ICH)		
Event	13	4
Patient time (years)	95.3	113.4
Event rate (95% CI)	136.4 (111.6-166.7)	35.3 (29.4-42.4)
Recurrent ICH		
Event	9	1
Patient time (years)	95.1	116.4
Event rate (95% CI)	94.6 (77.4-115.7)	8.6 (7.2-10.3)
All-cause mortality		
Event	16	2
Patient time (years)	102.5	116.6
Event rate (95% CI)	156.2 (128.7-189.6)	17.2 (14.3-20.6)

ICH: intracerebral haemorrhage; LAAO: left atrial appendage occlusion

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Nordic PS match study

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	

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Nordic PS match study

Additional PS analysis.
All patients in the standard care group treated by OAC
N=206

Outcome	Hazard ratio (95% CI)
Ischaemic stroke/major bleeding/all-cause mortality	0.26 (0.09-0.80)
Ischaemic stroke	0.32 (0.06-1.56)
Major bleeding	0.66 (0.11-3.94)
Recurrent ICH	0.51 (0.05-5.65)
All-cause mortality	0.28 (0.06-1.36)

ICH: intracerebral haemorrhage; LAAO: left atrial appendage occlusion; OAC: oral anticoagulant therapy

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STROKECLOSE; 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 1-6 months after the ICH and followed for a minimum of two years
- Primary outcome a composite endpoint of
  - stroke (ischemic or hemorrhagic)
  - systemic embolism
  - life-threatening or major bleeding
  - all-cause mortality

STROKECLOSE; Study design

- Secondary outcomes
  - ischemic stroke
  - hemorrhagic stroke
  - systemic embolism
  - life-threatening or major bleeding

  - all-cause mortality
  - other intracranial hemorrhage
  - all-cause mortality
  - cardiovascular mortality
  - unplanned hospitalization
  - mRS
  - neurological and cognitive status
  - QoL

STROKECLOSE; Study design

- Endpoints related to LAAO:
  - Device success
  - Technical success
  - Procedural success
- Adverse events will be documented throughout the study, irrespective of the assigned treatment.
  - This includes, but is not limited to, complications related to the LAAO procedure and device-related complications.

STROKECLOSE; Inclusion criteria

- A diagnosis of paroxysmal, persistent or long-standing NVAF with CHA2DS2VASc score >2.
- Clinical and CT/MRI evidence of intracerebral hemorrhage within 1-6 months prior to enrollment.
- Age > 18 years.
- Signed informed consent.

STROKECLOSE; Exclusion criteria

- Intracerebral hemorrhage secondary to vascular malformation or tumors.
- Estimated life expectancy of less than 1 year at eligibility assessment.
- mRS > 3 at enrollment.
- Contraindications to LAAO known at the time of enrollment, such as prior surgical LAA excision.
- Planned combined interventional procedures at the time of enrollment

STROKECLOSE; Intervention group

- The device (Amplatzer Amulet) will be implanted as soon as possible after randomization (≤2 months)
  - could in certain cases be prolonged up to 4 months in case of a resolvable contraindication such as an LAAO thrombus that resolves after antithrombotic treatment

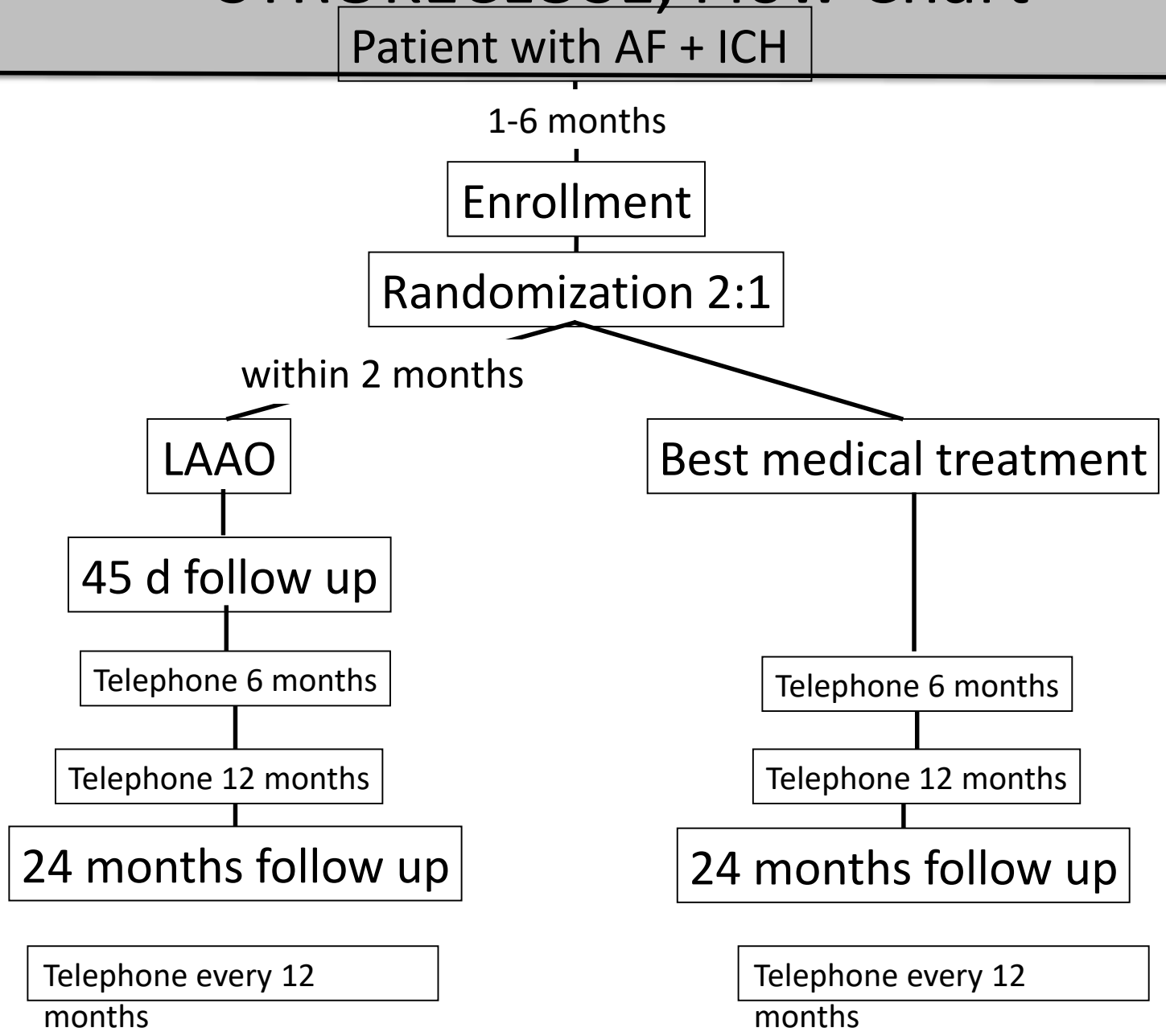
- Device implantation
  - catheterization venous access and a transseptal puncture to obtain access to the LA.
  - procedure performed under general anesthesia or local anesthesia in combination with sedation.
  - procedural imaging guidance is left to the physician's discretion and may include several techniques such as angiography/fluoroscopy, TEE and/or ICE.

- Post-implant antithrombotic therapy
  - ASA therapy for at least 6 months
  - may be combined with clopidogrel for the first 45 days after implantation.

STROKECLOSE; Medical group

- The optimal medical therapy of stroke prevention in NVAF after intracerebral hemorrhage is not known.
- Therefore, it will be left to the discretion of the treating physician to decide if, when, and which pharmacological therapy will be prescribed.
- Available options include anticoagulation with
  - OAC or NOAC or
  - antiplatelet therapy (including monotherapy and dual antiplatelet therapy) or
  - no pharmacological antithrombotic therapy.

STROKECLOSE, Flow Chart



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Thanks for your attention!