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HEALTH THROUGH KNOWLEDGE

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Background

- Atrial fibrillation (AF) is an important cause of stroke
- Most strokes (70%) in AF patients are cardio-embolic originating from the left atrial appendage (LAA)

Background

- 3 main approaches to stroke prevention in AF patients:
  1. Elimination of AF itself
     - No AF therapy to date has been able to suppress all AF episodes
  2. Prevention of clot formation by medical therapy (either antiplatelet or anticoagulant)
     - Very effective but is limited by potential for serious bleeding and by the general problem of continuity of treatment (under-prescription, non-compliance, sub-optimal anticoagulation control, treatment withdrawal)
  3. Physical elimination of the LAA
     - Results from smaller trials are encouraging , but not definitive

Background

- Cardiac surgery provides an excellent opportunity to remove/occlude the LAA at low risk:
  - LAA is exposed and readily accessible
  - LAA removal only takes a few extra minutes
- Hypothesized that LAA occlusion will reduce stroke and will benefit virtually all AF patients if completed at the time of routine cardiac surgery

Study Design

- A multicentre, international, randomized controlled trial of left atrial appendage occlusion or no occlusion in adult atrial fibrillation patients undergoing cardiac surgery with the use of CPB
- Double-blinded (only assigned surgeon/operating room staff aware of allocation, all others blinded)
- Follows the intention-to-treat principle
- 4,700 patients in approximately 108 centres

Intervention

- Patients randomly allocated through IWRS to LAA occlusion or no LAA occlusion
- Approved LAA occlusion techniques:
  - Amputation and closure (preferred technique)
  - Stapler closure
  - Use of regulatory approved atrial appendage closure device
  - Double layer linear closure from within the atrium (acceptable for mini thoracotomy procedures, must be confirmed by TEE)
  - Other LAA interventions proven to be efficacious may be approved by LAAOS III Operations Committee
- Note: use of simple purse string closure is strictly prohibited

Patient Population

Inclusion Criteria

- Age ≥ 18 years
- Undergoing a clinically indicated cardiac surgical procedure with the use of CPB
- A documented history of atrial fibrillation or atrial flutter
- CHA_2DS_2-VASc score ≥ 2
- Written informed consent

Patient Population

Exclusion Criteria

- Patients undergoing any of the following procedures:
  - Off-pump cardiac surgery
  - Heart transplant
  - Complex congenital heart surgery
  - Sole indication for surgery is ventricular assist device insertion
  - Re-do cardiac surgery if prior surgery required opening of the pericardium
  - Mechanical valve implantation

- Patients who have had previous placement of a percutaneous LAA closure device

Objectives

Primary Objective

- Incidence of ischemic stroke* or transient ischemic attack (TIA) with positive neuroimaging or systemic arterial embolism over duration of follow-up

Secondary Objectives

- Incidence of all cause stroke or TIA with positive neuroimaging or systemic arterial embolism
- Incidence of ischemic stroke* or TIA with positive neuroimaging or systemic arterial embolism or death
- Incidence of ischemic stroke* or TIA with positive neuroimaging or systemic arterial embolism > 30 days after surgery
- Incidence of all cause death

**Ischemic stroke is defined as any stroke that is not documented as primary hemorrhagic.*

Objectives

Safety Objectives

- Incidence of hospitalization for heart failure
- Post-operative safety outcomes
- Chest tube output in first post-operative 24 hours
- Re-operation for bleeding within 48 hours post-surgery
- 30-day mortality
- Incidence of major bleeding
- Incidence of myocardial infarction

Outcomes

Primary Outcome

- The first occurrence of ischemic stroke* or transient ischemic attack with positive neuroimaging or systemic arterial embolism over the duration of follow-up.

* Ischemic stroke is defined as any stroke that is not documented as primary hemorrhagic.
† All components of composite outcomes will also be reported individually.

Outcomes

Secondary Outcomes

- The secondary outcomes over the duration of follow-up (unless otherwise specified) are:

1. All cause stroke or transient ischemic attack with positive neuroimaging or systemic arterial embolism
2. Composite of ischemic stroke* or transient ischemic attack with positive neuroimaging or systemic arterial embolism or death
3. Ischemic stroke* or transient ischemic attack with positive neuroimaging or systemic arterial embolism occurring > 30 days after surgery
4. All cause death

Outcomes

Safety Outcomes

1. Hospitalization for heart failure
2. Operative safety outcomes
   a) Chest tube output in the first post-operative 24 hours
   b) Re-operation for bleeding within the first 48 hours post-surgery
   c) 30-day mortality
3. Major bleed
4. Myocardial infarction

Follow-Up

Eligibility Assessment

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Written Informed Consent

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Randomization

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Baseline Data Collection

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Cardiac Surgery with LAA Occlusion vs. No LAA Occlusion

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ICU & Hospital Discharge

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30-Day Follow-Up Visit (may be done by telephone)

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Telephone calls at 6 month intervals
Annual visits until final follow-up visit (may be done by telephone)

*Patients will be followed to an event-driven common end date (estimated to be a median follow up of 4 years)