Ross for Valve Replacement in Adults (ReViVAL) Trial & Registry

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Background

- Aortic valve disease is the most common form of valvular heart disease in the developed world
- Aortic valve replacement is considered to be the standard of care
- Current conventional options include mechanical and biological valves:

  Mechanical valves require lifelong anticoagulation and patients remain at increased risk for thromboembolism and life-threatening bleeding
  Biological valves have limited prosthesis durability and a 63% lifetime risk of reoperation

Background

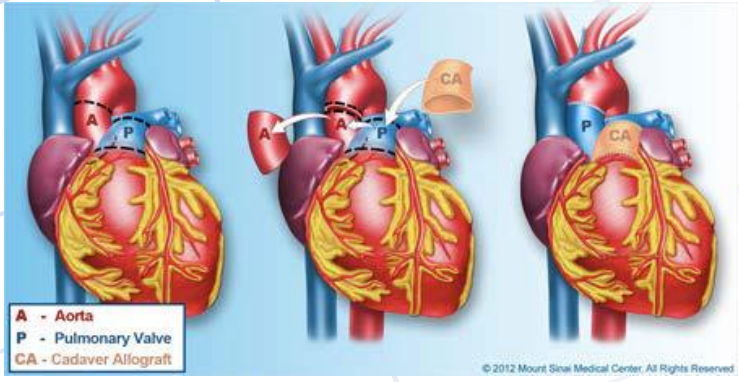
- Patients < 65 face unique challenges
  - Prolonged life expectancy = prolonged exposure to valve related complications

- Current management of aortic valve disease in the young is palliative, not curative.

- Life expectancy in non-elderly adults after AVR is decreased when compared to general population. **The younger the patients are, the higher excess mortality is**. *Kvidalet al, 2000.*

Background

- Limited studies suggest that long term outcomes with the Ross Procedure may be superior to conventional aortic replacement:
    - Avoids need for lifelong anticoagulation
    - Provides a more durable aortic valve substitute (vs. bioprostheses)
    - Reduces long term mortality
    - Provides outcomes comparable to age matched controls
- However, the complexity of the procedure may increase operative risk and converts a single valve disease into a two-valve disease.



Hypothesis: The Ross procedure will decrease rates of life-threatening valve complications, conferring significant benefit over conventional AVR

Research Question

REVIVAL pilot trial: Is it feasible to conduct a large randomized controlled trial (RCT) evaluating the efficacy and safety of the Ross procedure compared to conventional aortic valve replacement (AVR)? Specifically, can participating centres recruit an average of 6 patients per year using the expertise-based RCT protocol we have developed with acceptable compliance to allocation?

Full trial: The primary objective is to determine if the Ross procedure results in superior outcomes when compared to conventional AVR techniques, including stented or stentless bioprostheses and mechanical aortic valves, with respect to survival free of life-threatening valve-related complications (life-threatening bleeding, systemic thromboembolism, valve thrombosis, and operated-on valve re-intervention) over the duration of follow-up in patients undergoing AVR for the treatment of aortic valve disease.

Trial Design

- A multi-centre, expertise-based, randomized controlled trial evaluating the efficacy and safety of the Ross procedure compared to conventional aortic valve replacement in nonelderly patients with aortic valve disease.
- The first 60 patients will be considered the pilot trial patients and will be rolled into the full trial, should the pilot demonstrate feasibility.
- The sample size for the full trial is a total of 1,047 patients recruited from 40-50 international centres.
- All patients who meet eligibility criteria of the REVIVAL trial but are not included due to patient or clinician factors will be approached to participate in the concurrent REVIVAL registry.

Patient Population

Inclusion Criteria

1. Age 18-60 years
2. Undergoing clinically-indicated AVR with a primary indication for surgery of correction of aortic valve pathology
3. Written informed consent from either the patient or substitute decision maker

Exclusion Criteria

1. Previous valve replacement not in the aortic position
2. Patients undergoing concomitant CABG or other valve procedure during AVR
3. Known connective tissue disease
4. Severe (grade 3 or 4) right or left ventricular dysfunction
5. Pulmonary valve dysfunction or anomalies noncompatible with the Ross procedure (as determined by the consulting cardiac surgeon)
6. Life expectancy less than 5 years (as determined by the consulting cardiac surgeon)
7. Documented severe aortic insufficiency not solely based on leaflet problem
8. Previous intervention on the pulmonary valve

Primary Outcomes

The primary outcome of the **Pilot** is the feasibility of a large-scale trial as defined by:

1. To evaluate the capacity to enroll a mean of 6 patients per year per centre;
2. To validate the assumption of greater than 90% compliance with allocation;
3. To validate the proportion of mechanical (at least 65%) versus biological (at most 35%) valves in the conventional arm.

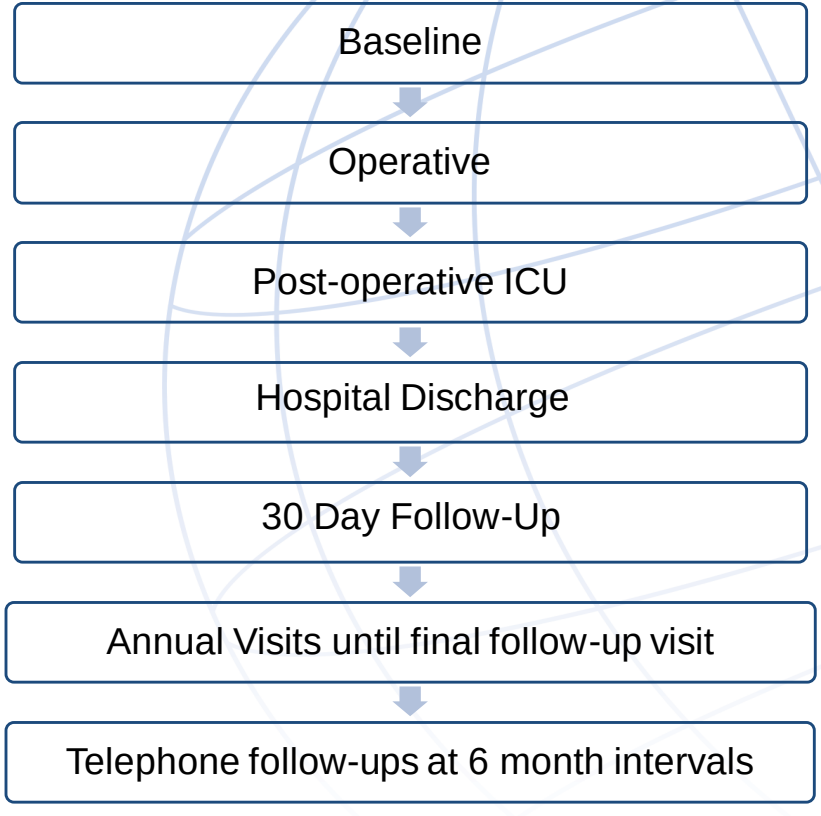
The primary outcome of the **Full trial** is survival free of life-threatening valve-related complications (life-threatening bleeding, systemic thromboembolism, valve thrombosis, and operated-on valve reoperation) over duration of follow-up.

Secondary Outcomes

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

1. The individual components of the primary outcome (major bleeding, stroke or systemic thromboembolism, valve thrombosis, and operated-on valve reintervention)
2. Mortality within 30 days post-operatively
3. Health-related quality of life (assessed using the SF-36 questionnaire)
4. Operated-valve endocarditis
5. Aortic valve re-intervention
6. Pulmonary valve re-intervention
7. Echocardiographic parameters
8. Pregnancy free of valve-related complications
9. Live births

Patient follow-up



(The common study end date will be determined once at least 155 patients have experience a primary outcome event)