Prospective Randomized Evaluation of the Watchman Left Atrial Appendage Closure Device in Patients with Atrial Fibrillation Versus Long-term Warfarin Therapy

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Introduction

- Atrial fibrillation is the most common type of cardiac arrhythmia. It affects 800,000 people in the UK and causes a five times increase in the risk of stroke.
- It is estimated that the cause of stroke in 90% of these patients are due to a clot forming in the left atrial appendage that travels to the blood vessels that supply the brain.
- Currently, anticoagulants like warfarin are used to treat at-risk patients. However, there are many side effects associated with its long-term use, which has led to issues in the management of stroke prevention; resulting in only 50% of eligible patients to take warfarin.

Methods

- In this randomized control trial, all the participants had atrial fibrillation and were at high risk of getting stroke. The CHA2DS2-VASc scoring method was used to identify these high risk patients. It is used to assess whether patients have congestive heart failure, hypertension, age>75 years, diabetes or had previously episode of stroke. The patients are considered high risk if they score ≥2.
- The patients were randomly assigned either the device group or the warfarin therapy group. The LAA group had 269 participants and the chronic warfarin therapy had 138 participants. The participants and clinicians were aware of which treatment they were assigned, so it was not a blind trial which might cause bias.

Exclusion Criteria

- Long term anticoagulant therapy for reasons other than AF
- Contraindications to warfarin/ aspirin
- Previous stroke/transient ischemic attack within 90 of enrolment
- Symptomatic carotid disease
- Patient fornalen amputee
- Atrial septal defect requiring treatment
- Clopidogrel therapy

Results

- **Primary Efficacy**: The rate of the first co primary endpoint of this trial (stroke, death) at 18 months was 0.064 in the device group and 0.063 in the warfarin group. The rate ratio calculated was 1.07 with a 95% confidence interval. The results show that there is a 95% certainty that the true value of the rate ratio lies between 0.57 to 1.89. This however did not meet the predefined non-inferiority criterion, as the upper boundary (1.89) crosses the pre-defined non-inferiority margin of 1.75.

Table 1: Summary of the exclusion criteria in the Preval trial

| In this trial, patients with certain conditions were not selected to exclude interference with the results, summarized in Table 1. The mean demographics in both groups such as age, height, sex and ethnicity were very similar, which helps reduce any bias that might be caused by these factors. The average CHAD2 score in both groups was 2.6±1, which also help improve the reliability of the results.
| **Participants** in the LAA occlusion group had the device inserted and guided by transesophageal echocardiography (TEE). They also had to take warfarin and aspirin for 48 days after the implantation to prevent the risk of a thrombus forming before the device fully implants in the walls of the atrium. To assess the stability of the device, a TEE was performed at 45 days, 6 days and 12 months.
| **The control patients** received warfarin treatment and were monitored to check that their international normalized ratio is between 2.0 and 3.0. This measurement was taken every 2 weeks for 6 months and then every month after that.
| **Follow up** were made at 45 days, 6 months and 9 months then twice a year after that. A neurologic assessment was also made at 12 months and 24 months and whenever a neurologic event was suspected.
| There were 4 patients from the LAA occlusion group in which the device implantation was not attempted because either the device was not a suitable size for the patient’s LAA, a thrombus was found or the patient didn’t stop taking anticoagulation before the procedure.

Discussion

- **This trial has provided vital additional evidence that closure of the left atrial appendage is a reasonable alternative to chronic warfarin therapy in stroke prevention in patients with atrial fibrillation.**

Conclusion

- **Participants** randomly chosen to get the Watchman implant have to take warfarin for a few days as a safety precaution until the device fully implants. Therefore, this trial does not consider patients that have an absolute contraindications to warfarin.
- Event rates were lower than expected in the warfarin group, so non-inferiority was not established. Repetition of the trial with a larger number of participants would be useful in achieving a non-inferiority for the overall all rate of stroke and death in the device group.
- **This trial** has not compared the safety of the watchman device to other oral anticoagulants, such as rivaroxaban. It has also not looked into the clinical significance of occluding the left atrial appendage. It might interfere with hormonal regulation of blood pressure as LAA is the main site that produces atrial natriuretic peptide.
- Participants in this trial also had to be candidates for chronic anticoagulants, to make it easier to randomize against the control group. This might have affected the reliability of the results. Perhaps a longer study with more participants would be useful to address and evaluate these issues.

References