Recurrent Stroke Prevention in Atrial Fibrillation Patients

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Abstract

Stroke patients diagnosed with Atrial Fibrillation are at a significantly increased risk of recurrent strokes secondary to this abnormal heart rhythm. The standard first-line treatment for atrial fibrillation and stroke prevention includes anticoagulation therapy, such as warfarin or novel oral anticoagulants.. Novel oral anticoagulants have become the preferred choice of anticoagulation in recent years , however the question still remains if they are superior at preventing recurrent strokes when compared to warfarin. This research hopes to determine in stroke patients diagnosed with atrial fibrillation (P), are novel oral anticoagulants (NOACs) (I) actually more effective at preventing recurrent strokes (O) when compared to warfarin(C)?

Introduction

- Stroke is the 3rd leading cause of death and the 1st leading cause of long-term disability in the US
- Occurs when blood supply to the brain is interrupted and leads to lack of oxygen and nutrients to the brain
- Major risk factor for developing strokes is an abnormal heart rhythm called Atrial Fibrillation (AF)
- Stroke patients with a cardioembolic etiology, such as AF are at a significantly higher risk of recurrent strokes
- For many years, warfarin has been the anticoagulation therapy of choice for recurrent stroke prevention in AF patients
- However, with novel oral anticoagulants (NOACs) now on the market, there has been a significant deterrence in the use of warfarin as stroke prevention therapy
- Although NOACs have been said to have a more desirable side effect profile and are associated with less bleeding risks than warfarin, it is still unclear if NOACs are superior to warfarin in preventing subsequent cardioembolic strokes

Methods

A literature search was performed in November 2019 using Pubmed, Google Scholar, and Academic Search Ultimate to compile six articles with the most relevant and applicable research. Inclusion and exclusion criteria were applied to the search in order to compile the most appropriate articles in regards to the proposing question.

Results

1. **Arihiro S, Todo K, Koga M, et al. Three-month risk-benefit profile of anticoagulation after stroke with atrial fibrillation: The SAMURAI-Nonvalvular Atrial Fibrillation (NVAF) study. *International Journal of Stroke*. 2016;11(5):565-574. doi:10.1177/1747493016632239**
   - Researchers looked at 1,137 patients who were hospitalized with ischemic stroke/TIA and diagnosed with AF who were started on different anticoagulation, and compared number of recurrent ischemic events in those started on warfarin, dabigatran, rivaroxaban, or apixaban
2. **Diener H-C, Connolly SJ, Ezekowitz MD, et al. Dabigatran compared with warfarin in patients with atrial fibrillation and previous transient ischaemic attack or stroke: a subgroup analysis of the RE-LY trial. *The Lancet Neurology*. 2010;9(12):1157-1163. doi:10.1016/s1474-4422(10)70274-x**
   -RCT of 18, 113 AF patients assigned to receive dabigatran or warfarin and followed for 2 years to assess for recurrent strokes
3. **Garcia DA, Wallentin L, Lopes RD, et al. Apixaban versus warfarin in patients with atrial fibrillation according to prior warfarin use: Results from the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation trial. *American Heart Journal*. 2013;166(3):549-558. doi:10.1016/j.ahj.2013.05.016**
   - RCT of 18, 201 patients with AF assigned to take apixaban, warfarin, or placebo to test efficacy in preventing stroke or systemic embolism
4. **Hong K-S, Kwon SU, Lee SH, et al. Rivaroxaban vs Warfarin Sodium in the Ultra-Early Period After Atrial Fibrillation–Related Mild Ischemic Stroke. *JAMA Neurology*. 2017;74(10):1206. doi:10.1001/jamaneurol.2017.2161**
   - RCT of 195 patients with acute cardioembolic strokes secondary to AF designed to determine whether rivaroxaban or warfarin was more effective at preventing subsequent strokes
5. **Kanai Y, Oguro H, Tahara N, et al. Analysis of Recurrent Stroke Volume and Prognosis between Warfarin and Four Non–Vitamin K Antagonist Oral Anticoagulants' Administration for Secondary Prevention of Stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2018;27(2):338-345. doi:10.1016/j.jstrokecerebrovasdis.2017.09.007**
   - Investigated the volume and number of recurrent strokes in 101 patients with nonvalvular atrial fibrillation who were treated with non-vitamin K antagonist oral anticoagulants and compared outcomes to patients receiving warfarin
6. **Rost NS, Giugliano RP, Ruff CT, et al. Outcomes With Edoxaban Versus Warfarin in Patients With Previous Cerebrovascular Events. *Stroke*. 2016;47(8):2075-2082. doi:10.1161/strokeaha.116.013540**
   - RCT of 5,973 AF patients with previous ischemic stroke/TIA designed to investigate and compare the efficacy of edoxaban with warfarin in reducing the risk of recurrent stroke

Study	Reduction in Recurrent Stroke	Reduction in Major Bleeding	Overall Efficacy and Safety of NOAC over Warfarin
1	NS	S	NS
2	S	S	S
3	S	S	S
4	NS	NS	NS
5	NS	NA	NA
6	NS	S	NS

Key: S= Significant, NS= Not Significant

Discussion

On the basis of these results, all 6 of the studies found that the efficacy of novel oral anticoagulation was comparable to that of warfarin. However, only two of the studies provided enough statistical evidence to determine that novel oral anticoagulation was significantly more effective at preventing strokes when compared to warfarin (Diener and Garcia.) The study conducted by Kanai suggested that administering NOACs after a stroke event may not reduce infarct recurrence, but it may reduce recurrent infarct volume when compared to warfarin. One major deficit across all studies was the timeline and duration of intervention. The stroke risk associated with AF and prior cerebrovascular accidents is a lifelong risk and requires long term follow up and management.

Conclusion

The studies compiled for this meta-analysis all demonstrated that warfarin and novel oral anticoagulation are comparable in regards to efficacy in recurrent stroke prevention. Some research showed promising evidence that NOAC patients experienced less recurrent ischemic stroke events and lower volumes of strokes. Though the evidence is not overwhelming enough to determine that NOACs should be the drug of choice, it provides insight for further research for more definitive data. Future studies would have much more power and significance if they could obtain a larger, more diverse sample population, as well as longer follow up. Ultimately, this analysis demonstrated that no one anticoagulant can be determined the “gold standard” when reducing stroke risk in patients with AF. While warfarin and NOACs are comparable in regards to efficacy, there are many other factors that must be considered on a case by case basis. The choice of anticoagulant should be individualized to the patient, based on their individual risk factors, comorbidities, insurance, and personal preference.