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Effectiveness of Anticoagulants in Atrial Fibrillation in Patients with Chronic Heart Failure

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Effective treatment of atrial fibrillation (AF) must begin with the initiation of anticoagulant therapy (ACT) [1]. A key component of managing patients with both AF and heart failure (HF)—especially with the growing prevalence of procedures like cardioversion or catheter ablation (CA)—is the accurate prescription of ACT and continuous monitoring throughout the treatment process.

The coexistence of AF and HF significantly increases the risk of stroke, irrespective of left ventricular ejection fraction (LVEF), leading to higher mortality rates [30, 31]. An irregular ventricular rhythm during AF can elevate pressure in the pulmonary capillaries, disturb homeostasis, and impair overall hemodynamics. The activation of the renin-angiotensin-aldosterone system and cytokines during HF plays a major role in this process. Together, these hemodynamic, neurohormonal, and electrophysiological factors worsen the pathological conditions in patients with both AF and HF, thereby activating all components of Virchow's triad and increasing the risk of thrombosis [5].

The ORBIT-AF registry [4] has demonstrated that in patients with both AF and HF, the prognosis is further worsened by the risk of bleeding. For patients with HF, anticoagulants (ACs) are recommended to prevent stroke, with direct oral anticoagulants (DOACs) being the first-line choice [1]. Russian guidelines for managing HF patients with anticoagulation therapy in the presence of AF favor the use of DOACs due to their lower risk of stroke, intracranial hemorrhages, and mortality [3].

Clinical studies on the use of DOACs in AF have included HF patients, and numerous analyses on anticoagulant therapy for this group have been published [7,8]. The efficacy and safety of DOACs in HF patients remain under active investigation. A recent meta-analysis, which included nine studies on the use of DOACs in AF and HF patients, found that compared to warfarin, DOACs were associated with a similar or lower risk of thromboembolic events and bleeding in HF patients [8].

For HF patients, the safety profile of ACs in terms of bleeding risk is especially important. An observational study in the United States, which followed 45,361 patients over one year, assessed the safety of ACT with apixaban, dabigatran, rivaroxaban, and warfarin. Major bleeding was defined as requiring hospitalization. The risk of major bleeding was lower with apixaban and dabigatran while rivaroxaban did not show a statistically significant difference compared to warfarin [9].

When comparing the safety of three DOACs, apixaban outperformed rivaroxaban in reducing major bleeding risk , and showed a slightly lower but non-significant bleeding risk compared to dabigatran. There was no significant difference between dabigatran and rivaroxaban.

In the ARISTOTLE study, the presence of HF increased the risk of cardiovascular complications or death. The risk reduction with apixaban compared to warfarin was similar for both HF and non-HF patients [10]. Apixaban proved to be more effective and safer than warfarin, with the greatest absolute benefit in patients with left ventricular dysfunction.

Given that age is a significant risk factor affecting prognosis in AF and HF patients, the safety of ACT in elderly patients is critical when choosing an anticoagulant. A retrospective study of AF patients over 65 years enrolled in the Medicare program in the United States compared warfarin (n=183,318), dabigatran (n=86,198), rivaroxaban (n=106,389), and apixaban (n=73,039). The study analyzed outcomes such as stroke, intracranial hemorrhage, major extracranial bleeding, and all-cause mortality. Stroke, intracranial hemorrhage, and mortality rates were highest in the warfarin group, while major extracranial bleeding was most frequent with rivaroxaban.

Apixaban significantly reduced the risk of major extracranial bleeding, and dabigatran had similar rates to warfarin. The gastrointestinal bleeding risk, which made up 82% of extracranial bleeding, increased with dabigatran and rivaroxaban but decreased with apixaban compared to warfarin. The rates of stroke and all-cause mortality were comparable among DOACs, with rivaroxaban showing a higher risk compared to apixaban and dabigatran . Dabigatran was associated with a reduced risk of intracranial hemorrhage but an increased risk of major extracranial bleeding compared to apixaban. A post-hoc analysis favored apixaban over dabigatran in terms of efficacy and safety [11].

A large observational study (ARISTOPHANES) involving 434,046 AF patients assessed stroke/systemic thromboembolism and major bleeding rates. The use of DOACs resulted in fewer stroke/systemic thromboembolism events compared to warfarin, with apixaban and dabigatran showing lower bleeding rates and rivaroxaban showing higher rates [12]. Apixaban demonstrated the lowest rates of stroke/systemic thromboembolism and major bleeding compared to dabigatran and rivaroxaban.

Kidney function must be considered when prescribing DOACs in patients with HF, as kidney dysfunction, common in this group, increases the bleeding risk and may reduce the advantages of DOACs over warfarin. A study evaluating bleeding events in AF and HF patients found that apixaban and dabigatran were associated with a lower risk of major bleeding and death compared to warfarin, while rivaroxaban did not show similar outcomes.

Chronic kidney disease increased the bleeding risk with DOACs but did not affect warfarin similarly. Overall, mortality and bleeding rates were lower with DOACs than with warfarin, regardless of kidney function [13].

In AF and HF patients, when initiating ACT, both bleeding risk and the efficacy/safety ratio of the drug should be considered. A meta-analysis comparing four DOACs in HF patients confirmed that dabigatran 150 mg twice daily and apixaban were the most effective, while edoxaban 30 mg twice daily was the safest in terms of bleeding prevention [14]. The recommended sequence for choosing a DOAC in these patients is: apixaban, edoxaban 60 mg twice daily, and dabigatran 150 mg twice daily.

Given the prognostic significance of sinus rhythm in HF patients, anticoagulation therapy during procedures like cardioversion and catheter ablation (CA) plays a crucial role. All DOACs have been well studied for use during these interventions. A meta-analysis involving 7,588 patients found that DOACs and warfarin had similar efficacy and safety in AF patients undergoing cardioversion [14]. Modern guidelines recommend using DOACs when preparing for cardioversion in patients who have not previously received anticoagulation and continuing DOAC therapy during the procedure [1, 12].

Catheter ablation, while effective, carries a risk of both bleeding and thromboembolic complications. Studies have shown that DOACs are at least non-inferior to warfarin in AF patients undergoing CA, with apixaban being particularly well-studied [45]. For planned CA, the procedure should be performed without stopping DOACs or by discontinuing one or two doses before the procedure, resuming the medication afterward [1, 12].

In AF patients with HF, additional bleeding risks related to HF must be considered, and the safest therapy should be selected. A recent prospective study on continuous apixaban use during CA found it to be as safe and effective as warfarin [46].

Conclusion. Patients with both AF and HF represent a significant portion of cardiology patients, and as the population ages, their numbers will continue to rise. Given the poor prognosis for this group, refining treatment approaches is essential to reducing mortality. Studies emphasize the importance of rhythm control in HF patients. The prevention of thromboembolic complications is critical for the lifespan of AF patients. For those with AF and HF, the priority in anticoagulant therapy should be effective stroke prevention, mortality reduction, and safety. Based on meta-analyses, apixaban appears to be the optimal choice for this patient group.

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