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EDITORIAL

Atrial Fibrillation and Hemodialysis – Should we Anticoagulate These Patients? Ischemic Versus Hemorrhagic Risk

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Editorial referring to the article: Hemorrhagic Versus Ischemic Risk In Patients With Atrial Fibrillation On Hemodialysis

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide, and it is a very frequent cause of increased morbidity and mortality in adults. This arrhythmia favors the formation of thrombi, which can lead to systemic embolism, such as ischemic stroke.

To identify patients with thromboembolic risk, the most used score is the CHA2DS2VASC, which takes the following factors in consideration: heart failure, arterial hypertension, age, diabetes, previous stroke, vascular disease, and sex. It is worth emphasizing that this score does not take renal function or dialysis treatment into consideration.

Oral anticoagulation (OAC) is indicated in the majority of patients to decrease embolic events; however, it increases hemorrhagic events. Therefore, we must assess the patient's individual risk of both thromboembolic and hemorrhagic events, when indicating OAC. The most used score for assessing the risk of bleeding is the HAS-BLED, which takes the following factors in consideration: arterial hypertension, renal and hepatic dysfunction, previous stroke, bleeding, international normalized ratio (INR) lability, age, and drug and alcohol use. In this score, renal dysfunction receives 1 point for risk of bleeding.

It is important to highlight that OAC is indicated using the CHA2DS2VASC score. If it is 0 for men and 1 for women, OAC is not indicated; if it is 1 for men and 2 for women, OAC should be considered; if it is greater than or equal to 2 for men and 3 for women, OAC should be recommended.

Keywords

Atrial Fibrillation; Heart Disease, Ischemic; Hemorrhage; Renal Dialysis; Anticoagulants; Stroke.

High HAS-BLED scores do not contraindicate OAC; nevertheless, a high score identifies patients with greater risk of bleeding, who require special care to minimize the hemorrhagic risk.

There is a population that has been poorly studied in research, namely, patients with chronic kidney disease (CKD), especially those on dialysis. Currently, there are no multicenter randomized studies on the use of OAC in patients on dialysis, either with warfarin or direct-acting anticoagulants.

In patients with CKD, AF is more frequent than in the general population, and it is even higher in patients on hemodialysis; additionally, it is associated with greater morbidity and mortality. This group of patients deserves individualized attention, seeing that they have been excluded from several studies with OAC, and the use of OAC in this population is still controversial.

CKD increases thromboembolic risk, but it is also associated with increased bleeding, regardless of the presence of AF. Patients on hemodialysis demand special attention, because the hemorrhagic risk is even greater than in patients not on dialysis. Therefore, we must consider the risk versus the benefit when recommending OAC treatment in this population.

For many patients with CKD, the general recommendation for OAC according to the CHA2DS2VASC score should be followed,[1] especially for patients who are not on dialysis. However, there are few data on patients with advanced-stage CKD, especially those undergoing dialysis; therefore, the approach should be individualized, as the benefit of anticoagulation in these patients is not evident. The HAS-BLED score is also used in this population, even though its performance is lower in patients on dialysis.[2]

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We must consider the possibility that warfarin does not have the same efficacy in reducing thromboembolic events in patients with CKD, when compared to the population without CKD.[3] This may be due to several factors, especially to the difficulty of adjusting the INR in these patients.[4]

The results have been divergent in different studies in relation to the indication of OAC in patients with AF and chronic renal failure.

Sousa et al.,[5] in a study recently published in this journal, evaluated the ischemic versus hemorrhagic risk in patients with AF on hemodialysis, and they did not observe any difference between the incidence of ischemic and hemorrhagic events, notwithstanding the use of OAC. The study was observational and retrospective, and there was no correlation between the CHA2DS2VASC score and the risk of ischemic events. Nevertheless, patients who had previous stroke or thromboembolic events appear to have a greater risk of new events and may benefit from OAC.[5]

Other authors have observed a relationship between increased CHA2DS2VASC score values and the risk of ischemic stroke in patients with AF on hemodialysis, such as Chao et al.,[6] and Wang et al.,[7]

Pokorney et al.,[8] evaluated patients with severe chronic renal failure and AF. Their cohort included 8410 patients, and they did not observe any association between the use of OAC and reduced stroke or death in this group, although OAC was associated with increased hospitalization for bleeding or intracranial hemorrhagic.[8]

In another study, Yang et al.,[9] suggested that patients with AF on hemodialysis would not benefit from warfarin use to prevent ischemic events; moreover, it increased the risk of hemorrhagic events and was associated with vascular calcification in this population. The authors recommend that the routine use of warfarin should be discouraged, and it should only be used in patients at a high risk of thromboembolic stroke.[9]

In contrast, Abbott et al.,[10] evaluated 3374 patients with AF on dialysis, concluding that the use of warfarin was associated with improved survival in patients hospitalized for AF.[10]

Chan et al.,[11] assessed whether the use of warfarin, clopidogrel, or acetylsalicylic acid was associated with outcomes in a retrospective cohort of 1671 patients with AF and severe CKD. The authors concluded that warfarin was associated with increased stroke, whereas clopidogrel and acetylsalicylic acid were not. The greatest risk related to warfarin was in patients who did not undergo strict INR adjustment. Nonetheless, warfarin was not associated with greater risk of mortality or hospitalization.[11]

Several studies have found similar results, and they suggest that warfarin is not a safe medication for patients with AF on hemodialysis, seeing that it increases the hemorrhagic risk, without adequately protecting against the thromboembolic risk.

A large observational study indicated a benefit of OAC. In this study, Bonde et al.,[12] evaluated a national Danish cohort and analyzed patients with CKD and AF. They observed a benefit of OAC with warfarin for stroke prevention in patients with CHA2DS2VASC score greater than or equal to 2.[12]

In a systematic review and meta-analysis, Tan et al.,[13] evaluated 2709 references and 20 studies, including more than 56,000 patients with severe CKD and AF, who were evaluated for warfarin, direct-acting anticoagulants, non-use of medication, or acetylsalicylic acid. The results with direct-acting anticoagulants were inconclusive; warfarin was not effective in protecting against stroke, and it was related to increased bleeding.[13]

A meta-analysis published in 2020 included 15 studies, evaluating nearly 50,000 patients with AF and severe chronic renal failure. The study evaluated patients using warfarin, who were compared to those who were not using this medication. The authors did not observe any difference in the risk of ischemic stroke. They demonstrated an increased risk of hemorrhagic stroke in patients using warfarin, and they did not observe any difference in mortality or major bleeding. A criticism of this study is in relation to adequate anticoagulation time, which was not evaluated in many studies and may have had an impact on the results.[3]

Therefore, even though there are several major studies on the use of OAC, patients with CKD on hemodialysis were not included; therefore, the benefit of OAC remains questionable in these patients.

In this population, in order to indicate OAC, in addition to the CHA2DS2VASC score, perhaps prior thromboembolic events or stroke should be considered more relevant, as they appear to present a greater risk of new events, and these patients may benefit more from OAC. When considering use of OAC in patients on dialysis, we should always have a discussion with the patient for careful assessment of the risks and benefits, with the goal of making the best shared decision in each case.

Once OAC has been indicated, it is important to maintain strict follow-up, with frequent review of the INR, if the patient is using warfarin.

It is important to consider not using OAC in patients who have uncontrolled arterial hypertension, patients who have had important or recurrent bleeding, and patients who are very frail, because the benefit versus risk is not evident in these patients.

We understand that OAC should not be routinely indicated for all patients with AF on hemodialysis; the decision must be individualized with the goal of obtaining the best reduction in the risk of embolism, with the lowest hemorrhagic risk possible.

Perhaps, we should consider alternative strategies to OAC for preventing thromboembolism in patients with AF on hemodialysis.

The benefit of OAC in patients with AF on hemodialysis is very controversial; observational studies have suggested a possible reduction in the hemorrhagic risk with the use of direct-acting anticoagulants when compared to warfarin.[14]

It is worth emphasizing that we do not have robust evidence for OAC in patients with AF on hemodialysis, with warfarin or with direct-acting anticoagulants.[15]

We need further studies for management of patients with AF on hemodialysis, in order to identify this population's "sweet spot" for adequate prevention of thromboembolic phenomena.

There are ongoing studies evaluating this population, which should help substantially in future decision making.

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