CASE REPORT

Need of a Revised Bleeding Risk Model in Patients on Warfarin Therapy: Considering Hypertension as an Important Risk Factor

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Introduction

Atrial fibrillation is a well recognized risk factor of stroke.[1] Various risk stratification models have been used but CHADS2 (an acronym for Congestive heart failure, Hypertension, Age over 75, Diabetes mellitus, and prior Stroke or transient ischemic attack) is the most commonly used model, possibly because of its easy scoring.[2] In this system, a point is given for congestive heart failure, hypertension, age over 75 years, and diabetes, and two points for previous history of stroke. CHADS2 scoring places patients in one of three risk categories with a score of 0 as low, 1 as moderate, and more than or equal to 2 as high. Aspirin alone is recommended for low risk, aspirin or oral anticoagulants for moderate risk, and oral anticoagulants for high risk individuals.[3]

Although anticoagulants are superior to aspirin alone or the combination of aspirin and clopidogril, they are associated with a significant risk of intracranial hemorrhage.[4-6] The Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE-W) analysis demonstrated the high efficacy of oral anticoagulation (OAC) over the combination of aspirin and clopidogril in patients with CHADS2 score of 1.[7] Therefore, it is important to keep the balance between risks and benefits of starting warfarin in these patients.

Case Report

An 83-year-old male known to have hypertension, atrial fibrillation, hypothyroidism, parkinsonism, bladder carcinoma (status post resection), diabetes mellitus type 2 on insulin, coronary artery disease (status post coronary artery bypass graph in two vessels) presented with generalized weakness, anorexia, and confusion for the past six months that worsened in the prior two weeks. Review of the rest of systems was non-contributory. He had no allergies. He quit smoking and drinking several years prior.

The patient's father had diabetes mellitus; the rest of the family history was unremarkable. He was taking warfarin 2 mg daily for chronic atrial fibrillation, insulin, levothyroxine, lisinopril, carvedilol, amlodipine, citalopram, levetiracetim, carbidopa/levadopa, and hydrocodone.

On examination, blood pressure was 139/83 mmHg and controlled with medication, heart rate was 75 bpm, respiratory rate was 20 bpm, and temperature was 98°F. Positive physical findings were depressed mood, dry mucous membranes suggestive of mild dehydration, 3/6 holosystolic murmur in the left lower sternal border, and chronic venous stasis changes noted in bilateral lower extremities. The electrocardiogram and chest x-ray were normal.

Blood work was normal except for hemoglobin at 11.4 g/dl and platelets at 96 x 10^9/L. The patient was admitted for IV rehydration. His INR was 2.54 and the following day his brain natriuretic peptide came back 808 pg/mL, therefore careful diuresis with furosemide was started with strict intake and output charting.

On the 5th post admission day, the patient was more confused and disoriented from his baseline mental status. A plain computed tomography (CT) scan of the head revealed intraventricular hemorrhage (Figure 1). His INR that day was 3.5. Therefore, warfarin therapy was discontinued and fresh frozen plasma was given for the reversal of anticoagulation. He was transferred to the neuro-intensive care unit and monitored closely for five days. No improvement in his condition was observed and he was transferred to hospice care. He died a few days later.
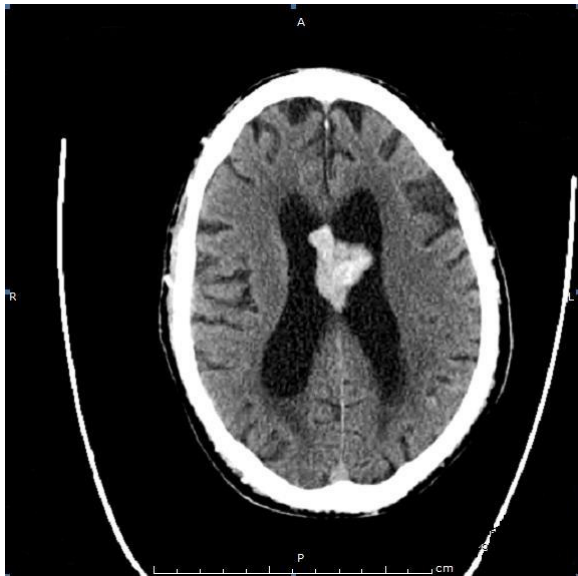

Figure 1. Intraventricular hemorrhage revealed on CT scan.

Discussion

The estimation of bleeding risk related to warfarin therapy is important. Risk is different for individual patients. To help physicians in risk stratification, various bleeding risk models for patients on warfarin have been developed. An early outpatient bleeding risk index for warfarin-treated patients provided an evidence-based starting point for warfarin therapy rather than relying on the physician's prediction.[8] Four risk factors were identified, including age over 65, history of stroke, history of gastrointestinal bleeds, and one of the following: diabetes mellitus, creatinine over 1.5 mg/dL, hematocrit over 30%, or recent myocardial infarction. According to this model, patients were classified as low risk (no risk factor), intermediate risk (1-2 risk factors), and high risk (3-4 risk factors) for bleeding.

Another model predicts the risk of bleeding for patients receiving warfarin.[9] This model considered age over 60, sex, and malignancy in their formula, (1.6 X age) + (1.3 X female sex) + (2.2 X malignancy), to calculate the score and subsequent stratification of the patients as high (more than 3 points), intermediate (1-3 points), or low risk (0 points).

In 2006, Shireman and colleagues[10] proposed a new model to simplify the queries regarding risks of warfarin therapy. Eight factors including age over 70 years, gender, remote bleed, recent bleed, alcohol/drug abuse, diabetes, anemia, and anti-platelet therapy use are considered. Bleeding rates then are compared with rates derived using other models.

All these models have clinical implications. Hypertension was not studied in any of these models. Hypertension is the single most important risk factor for the intracerebral hemorrhage (ICH).[11-13] It is one of the components of CHADS score and a very important risk factor for ICH. A revised bleeding risk model should be designed to address hypertension as one of the risk factors for bleed in patients receiving warfarin.

Conclusion

The risk of intracranial bleeding is associated with oral anticoagulation therapy with warfarin. Multiple risk factors have been associated with the risk of bleeding. Association between hypertension and intracranial bleeding is well established. Various bleeding risk models in patients on warfarin have been developed, but the relationship of high blood pressure with warfarin therapy and the risk of intracranial bleed has not been studied comprehensively. Further studies are needed to guide physicians and avoid grave complications like intracranial bleed.

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