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EDITORIAL COMMENT

CHA_2DS_2-VASc Score in Cardio-Oncology

Sharpening the Rules*

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Atrial fibrillation (AF) is the most common cardiac arrhythmia in patients with cancer.[1] Its prevalence is highly variable, ranging from 2% to 16%, according to the cancer type[2] and stage,[3] anticancer therapies,[4] and pre-existing comorbidities that predispose patients to AF.[5] The 2022 European Society of Cardiology guidelines on cardio-oncology[1] recommend an integrated approach to patients with cancer presenting with AF based on the "ABC pathway" (A: anticoagulation to avoid stroke/systemic embolism (S/SE); B: better symptom control with rate- and/or rhythm-control drugs and interventions; C: comorbidities and cardiovascular risk factors management).[6] However, the ESC-EHRA EORP-AF General Long-Term (ESC-European Heart Rhythm Association EURObserva-tional Research Programme AF General Long-Term) registry has recently shown suboptimal adherence to this strategy.[7] One of the main reasons is because specific evidence on how to improve cancer patients' cardiovascular outcomes is scare, and most therapeutic decisions are extrapolated from general population guidelines[6] or based on retrospective data.

Anticoagulation decision making is the ABC pathway Achilles' heel, and suboptimal anticoagulation therapy prescription has been reported in patients with active cancer and AF.[8,9] Because the coexistence of cancer increases both thromboembolic and major bleeding risks,[10,11] to make appropriate treatment choices, a multidisciplinary team discussion is needed to balance the sensitive equilibrium between thromboembolic (T) and bleeding (B) risks, interactions (I) among drugs, and patient (P) preferences included in the "TBIP" strategy.[1,12]

The CHA_2DS_2-VASc score has been recognized as the most reliable tool to guide anticoagulant treatment decisions.[1,6] In patients with cancer presenting with AF and a CHA_2DS_2-VASc score ≥2 in men or ≥3 in women, anticoagulant therapy is recommended, and in those with a CHA_2DS_2-VASc score ≥1 in men or ≥2 in women, anticoagulant therapy should be considered.[1] However, the CHA_2DS_2-VASc score is designed to identify low-risk patients in whom anticoagulant treatment should be avoided, and there is little evidence in the literature on its predictive value in patients with cancer,[13,14] particularly in those with low CHA_2DS_2-VASc scores (0-2). D'Souza et al[15] showed in a large Danish cohort that bleeding risks exceed S/SE risks in patients with recent cancer and a CHA_2DS_2-VASc score of 0, whereas both S/SE and bleeding risks were higher in patients with cancer and a CHA_2DS_2-VASc score of 1 compared with noncancer patients.

In this issue of *JACC: CardioOncology*, Leader et al[16] report the results of a population-based retrospective cohort of patients with a CHA_2DS_2-VASc score of 0 to 2 and not receiving anticoagulation at the time of the cancer diagnosis. Patients were categorized into 4 subgroups: AF and cancer (n = 1,411), AF and no cancer (n = 4,233), no AF and cancer (n = 4,233), and no AF and no cancer (n = 19,421). The primary outcome was arterial thromboembolism (ATE) at 12 months, and the secondary outcomes included ATE at 6 and 36 months as well as bleeding and venous thromboembolism at

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6, 12, and 36 months. The median follow-up time was 3 years. The strength of this study is the large series of patients and the robust methodology implemented in the selection of the 4 cohorts. The fact that only patients with a recent cancer diagnosis and without anticoagulant treatment were included reduces potential bias in the assessment of S/SE and bleeding risks related with advanced cancer status and/or antithrombotic therapies. The authors concluded that the 12-month cumulative incidence of ATE was highest in the AF and cancer cohort (2.13%; 95% CI: 1.47-2.99) than in the AF and no cancer cohort (0.8%, 95% CI: 0.56-1.10) with an HR of 2.70 (95% CI: 1.65-4.41). Interestingly, the risk is highest in AF men with a CHA_2DS_2-VASc score = 1 and women with a CHA_2DS_2-VASc score = 2. Another remarkable finding is that the overall ATE incidence was higher than the bleeding incidence in these patients with newly diagnosed cancer in the absence of anticoagulation. Venous thromboembolism risk at 12 months was higher in the cancer cohorts but comparable between the AF and no AF cohorts without cancer. The 36-month overall survival was significantly lower in the cancer population with AF compared with those without AF.

The CardioCHUVI-AF[17] (Retrospective Observational Registry of Patients With Atrial Fibrillation From Vigo's Health Area) registry confirmed these results. This is a retrospective observational Spanish cohort including 16,056 patients with AF (1,137 patients with AF and cancer); the median follow-up was 4.9 years. The authors concluded that in patients with AF and cancer who were not treated with anticoagulation the CHA_2DS_2-VASc score had a limited discriminative capacity and underestimated the S/SE risk. The S/SE risk of cancer patients with a CHA_2DS_2-VASc score = 1 was similar to patients with a CHA_2DS_2-VASc score ≥2, and only patients with a CHA_2DS_2-VASc score = 0 presented with a very low risk of embolic events. In addition, a HASBLED score >3 was not associated with a higher bleeding risk in patients with cancer compared with a noncancer population.

In summary, patients with cancer and a low CHA_2DS_2VASc score are left with a higher residual stroke rate, which is partially explained by our nonspecific characterization of AF. The paper by Leader et al[16] sharpens the profile of patients with a CHA_2DS_2-VASc score of 0 to 2 who will benefit from the use of anticoagulation. This study supports the use of anticoagulant therapy in men with a CHA_2DS_2-VASc score =1 and women with a CHA_2DS_2-VASc score = 2 presenting with cancer and AF in the absence of a prohibitive bleeding risk. Future studies are needed to prospectively identify cancer-specific stroke prediction scores in patients at low risk that include cardiac biomarkers, advanced cardiac imaging, and cancer-related factors.

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