Dr. Moriyama and colleagues highlighted the need to evaluate for amyloid cardiomyopathy among patients before they developed overt decompensated heart failure. Evaluation for amyloid cardiomyopathy may be particularly relevant for patients with concerning clinical features, such as a history of carpal tunnel syndrome, echocardiographic findings suggestive of infiltrative cardiomyopathy, aortic stenosis, or low stroke volume despite a normal ejection fraction (2-4). Similarly, other studies also demonstrated a high burden of amyloid cardiomyopathy in patients with heart failure and highlighted the need for early evaluation for amyloid among such patients (5). There is an unmet need for practical screening algorithms that use the available demographic, clinical, and imaging data among patients with heart failure and identify those most likely to have underlying amyloid cardiomyopathy. Once identified, such patients could be evaluated with more detailed amyloid-specific phenotyping, including serum and urine electrophoresis, cardiac magnetic resonance imaging, technetium pyrophosphate scintigraphy scan, and myocardial biopsy, if needed. Considering the rapid advancement in therapies for amyloidosis, a screening strategy to identify subjects with amyloid cardiomyopathy early in the disease course is critical to ensure maximal clinical benefits from these effective therapies.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

#### REFERENCES

1. Arora S, Patil N, Strassle PD, et al. Amyloidosis and 30-day outcomes among patients with heart failure: a nationwide readmissions database study. J Am Coll Cardiol CardioOnc 2021;2:710–8.

**2.** Sperry BW, Reyes BA, Ikram A, et al. Tenosynovial and cardiac amyloidosis in patients undergoing carpal tunnel release. J Am Coll Cardiol 2018;72: 2040-50.

**3.** Pagourelias ED, Mirea O, Duchenne J, et al. Echo parameters for differential diagnosis in cardiac amyloidosis: a head-to-head comparison of

deformation and nondeformation parameters. Circ Cardiovasc Imaging 2017; 10:e005588.

**4.** Ternacle J, Krapf L, Mohty D, et al. Aortic stenosis and cardiac amyloidosis: JACC review topic of the week. J Am Coll Cardiol 2019;74:2638-51.

**5.** Hahn VS, Yanek LR, Vaishnav J, et al. Endomyocardial biopsy characterization of heart failure with preserved ejection fraction and prevalence of cardiac amyloidosis. J Am Coll Cardiol HF 2020;8:712-24.

# Anticoagulation Challenges in Cancer Patients



The study by Fradley et al. (1) suggested that anticoagulant therapy is withheld from patients with cancer and atrial fibrillation/flutter, with 54.9% of their patients not prescribed anticoagulation. However, in the context of previously published literature, we have several considerations and suggestions for future analysis.

Other studies have demonstrated that bleeding risk is dependent on cancer type. In the study by Pastori et al. (2), the incidence of major bleeding was higher in myeloma, leukemia, and liver cancer with reported incidences of 11.6%, 12.4%, and 12.7% per year, respectively. Leukemia, myeloma, and liver cancer were inversely associated with an increase in ischemic stroke, with incidences of 2.0%, 2.0%, and 1.9% per year, respectively, compared with 2.4% per year in the noncancer group. The cancer types with the highest bleeding risk had the highest mortality risk. Therefore, it would be interesting to see longer-term data in the Fradley et al. (1) study with anticoagulation prescription and bleeding incidence defined.

Livneh et al. (3) showed that 30-day bleeding risks were higher than arterial thromboembolism rates in patients with hematologic malignancy and atrial fibrillation. It would be informative to compare the 24 patients with a hematologic malignancy prescribed anticoagulation with other groups in the Fradley et al. study (1).

Boriani et al. (4) also showed significant heterogeneity in anticoagulation choice where direct oral anticoagulants were preferred by 62.6%, with lower numbers (24.1% and 7.3%, respectively) for lowmolecular-weight heparin and warfarin. That study also demonstrated differing levels of expertise in making anticoagulation decisions. It would be interesting to know how many patients in the Fradley et al. (1) cohort were referred to cardiologists for anticoagulation decisions. A survey could provide important insight.

In conclusion, Fradley et al. (1) have importantly demonstrated heterogeneity in anticoagulation

decisions for these patients; however, more detailed data regarding these decisions are important. We suggest further analysis of their data, and in particular, more detailed insight into cancer type may be useful. This might help us in developing a cancerspecific risk tool for this important patient population.

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#### REFERENCES

**1.** Fradley M, Ellenberg K, Alomar M, et al. 2020 patterns of anticoagulation use in patients with cancer with atrial fibrillation and/or atrial flutter. J Am Coll Cardiol CardioOnc 2020;2:747-54.

**2.** Pastori D, Marang A, Bisson A, et al. Thromboembolism, mortality, and bleeding in 2,435,541 atrial fibrillation patients with and without cancer: a nationwide cohort study. Cancer 2021 Feb 25 [E-pub ahead of print].

**3.** Livneh N, Braeken D, Drozdinsky G, et al. Anticoagulation in patients with atrial fibrillation, thrombocytopenia and hematological malignancy. J Thromb Thrombolysis 2021 Feb 1 [E-pub ahead of print].

**4.** Boriani G, Lee G, Parrini I, et al. Anticoagulation in patients with atrial fibrillation and active cancer: an international survey on patient management. Eur J Prev Cardiol 2021;28:611–21.

# **REPLY:** Anticoagulation Challenges in Cancer Patients



We thank Drs. Khan and Ahmad for their interest in our study (1). The authors cite several studies that that demonstrate challenges in anticoagulation decision making in cancer patients. Our study was designed to evaluate anticoagulation prescribing patterns based on stroke and bleeding risk and not to evaluate outcomes. However, our data are complementary to other analyses that indicate heterogeneity in bleeding and stroke risk stratified by cancer type. We agree that following our cohort for long-term bleeding and thromboembolic events would be of significant interest.

In our analyses, we evaluated rates of anticoagulation based on 9 cancer categories: hematologic, gastrointestinal, cutaneous, genitourinary, lung, breast, gynecologic, sarcoma, and other. While performing subgroup analyses of the 24 patients with hematologic malignancies that were prescribed anticoagulation would be interesting, we think that the small number of patients would make interpretation of the results challenging. We did perform multivariable analyses to identify factors independently associated with the prescription of anticoagulation in patients with cancer and atrial fibrillation, and all cancer subtypes were included to control for confounding. However, using a larger dataset of hematologic malignancy patients to evaluate this specific question would be of value. We also agree that a survey of the anticoagulation decision makers in our cohort would be a useful future study and would expand upon the data recently published by Boriani et al. (2), specifically to determine the frequency of cardiology evaluation and to identify any inherent biases that may exist among the various practitioners caring for cancer patients with atrial fibrillation.

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#### REFERENCES

**1.** Fradley MG, Ellenberg K, Alomar M, et al. Patterns of anticoagulation use in patients with cancer with atrial fibrillation and/or atrial flutter. J Am Coll Cardiol CardioOnc 2020;2:747-54.

**2.** Boriani G, Lee G, Parrini I, et al. Anticoagulation in patients with atrial fibrillation and active cancer: an international survey on patient management. Eur J Prev Cardiol 2021;28:611-21.