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Letter to the Editor

On cancer and atrial fibrillation: Nuances and limitations

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In a recent study, Malavasi et al. [1] describe the prevalence and predictive factors for anticoagulant use in a cohort of patients with atrial fibrillation (AF) and cancer admitted into an oncology unit. Their main findings are that 1) 8.4% of the more than 4500 patients had AF. 2) that only 41% of patients received full-dose anticoagulation and, of those, almost 80% received low molecular weight heparin (LMWH) while an additional 35% received prophylactic-dose LMWH. 3) that anticoagulant use was not predicted by either cancer type or stage or CHA_2DS_2VASC and 4) that the use of anticoagulants did not impact overall survival.

AF in patients with cancer is currently an area of active research, yet the heterogeneity of "patients with cancer," particularly in terms of life-expectancy and risk of bleeding under anticoagulation, has made any conclusions regarding their optimal management elusive to-date. Malavasi et al. [1] deserve praise for their effort which involves a large sample size, prospectively gathered data and a specific population.

However, we would like to point out relevant limitations to the more broad application of their results as well as some disagreements with some of their conclusions.

Based on the short median survival (8 months) and the disproportionately large percentage of patients with hematologic malignancies (33% of the cohort), we believe their data may not be representative of most cancer patients. Furthermore, given that the patients were admitted to a ward, it is possible that a large proportion of AF episodes would be secondary to a triggering event, which may perhaps have a lower risk of stroke than primary AF [2] (especially once one the trigger [most commonly sepsis, anemia, surgery] is resolved) and, especially in patients with cancer, a high associated risk of death, likely because it reflects a low homeostatic reserve [3–5]. This would be in line with the very short survival of the cohort. Although the formal treatment of secondary AF may not differ from that of primary AF, some physicians may be less inclined to recommend indefinite anticoagulation, especially in a cohort of patients with such short life-expectancy. This may partly justify the low rates of anticoagulation reported by Malavasi et al. [1] and may, again, make their results not entirely applicable to patients with new-onset AF under other circumstances or to patients with AF at the time of cancer diagnosis.

The authors underscore the similar survival between anticoagulated and non-anticoagulated patients as a sign of the relative safety of their approach to anticoagulation, as patients with cancer are known to be at increased risk of bleeding [6,7]. Yet, we believe a lack of improvement in mortality should also make the authors consider that these patients may not benefit from the inconvenience, increased bleeding risk and expense of LMWH. Admittedly, the study is not powered to establish either the efficacy or safety of their approach to anticoagulation (as the authors recognize), the anticoagulation and no anticoagulation groups are not comparable, and, sadly, there is no data on hemorrhagic or ischemic events, but a lack of a mortality increase can hardly be considered an encouraging sign. In addition, as the authors point out, the competing risk of death is high, so the use of Kaplan-Meier estimations to determine survival may not have been ideal. A competing risk model might be more appropriate [8].

Finally, and perhaps more importantly, we would hesitate to call the use of LMWH "reasonable," especially if this treatment is continued indefinitely after discharge. The report shows that LMWH for AF is common practice in their cohort (therapeutic doses in 121 and prophylactic doses in 134 of the 380 patients), which may well be representative of AF and cancer more broadly, probably based on the evidence with LMWH in VTE, as the authors argue. But we would like to point out that there is, to our knowledge, no evidence supporting the use of LMWH in patients with AF, with or without cancer, for the prevention of stroke and that the incidence of bleeding with LMWH is not lower than that of vitamin K antagonists in patients with cancer [7,9]. While one may argue that LMWH was given to these patients for the prevention of VTE rather than that of stroke, and indeed the mentioned link between AF and VTE is credible, AF is not an established risk factor for VTE and LMWH (at any dose) is not recommended to prevent VTE based solely on the presence or absence of AF (and the authors do not provide any data on whether patients receiving prophylactic-dose LMWH in their cohort were at a higher risk of VTE judged by better-established risk factors [10]). Therefore, we consider there are no grounds to call the reported use of LMWH "reasonable" and we do not believe the prescription of LMWH merely on the basis of AF should be encouraged.

In conclusion, and despite our minor quibbles, the report by Malavasi et al. [1] is a new and relevant datapoint on the how this

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subset of patients with AF and cancer are being managed. We hope future research will shed further light on the optimal anticoagulant strategy for each individual patient with cancer and AF.

Conflict of interest

The author report no conflict of interest.

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