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Letter to the Editor

Cancer and atrial fibrillation. Author's reply

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To the Editor

We appreciate the interest of Sorigue in our paper [1,2]. In his comments [2], he underlines several interesting points relevant to the management of atrial fibrillation (AF) in cancer patients.

The first comment is about the representativeness of our population compared to the whole population of the AF patients with active malignancy, with a potential overrepresentation of the patients with hematological malignancies, since hemolymphopoietic cancers affected one third of our population [1].

In a meta-analysis of AF patients with malignancy treated with direct oral anticoagulants (DOACs) the proportion of patients with hemolymphopoietic disease ranged between 3 and 15% [3], but these data are derived from a selected group of studies. Indeed, any analysis of in-hospital patients with cancer is highly dependent on local specialties and in our setting hematological cancers cover a relatively high proportion of oncological care.

For a more general view, the epidemiologic picture of AF patients is likely to show some changes related to the wider use in oncology of new drugs that are associated with an increased risk of AF [4]. As one example, the risk of AF associated with ibrutinib, used in some hematological malignancies, has been highlighted [5] with consequent need for appropriate decision making on thromboprophylaxis.

Our paper shows that in the subset of patients with hemolymphopoietic cancer, as well as in other type of malignancies, anticoagulation did not show disadvantages in terms of mortality [1], thus suggesting the need for future studies that could reassure physicians about its use in this potentially risky group of patients.

Other observational data indicate that patients with Philadelphia negative myeloproliferative neoplasm have a 33% chance of developing deep venous thrombosis, acute coronary syndrome or stroke and approximately 8% risk of bleeding, especially from the upper gastrointestinal tract [6]. In view of the complexity of managing anticoagulants in AF patients with hematological malignancies, the neutral effect of anticoagulants on mortality may better address decision making, taking into account patient preferences and values, including the potential for disability associated with a severe stroke [7].

Hence, we do not share the views of Sorigue that a reduction in mortality has to be demonstrated in order to sustain the need for anticoagulation in this complex subset of patients with AF and cancer. Indeed, a reduction in all-cause mortality has never been considered as a primary end-point of the anticoagulation trials in patients with non-valvular AF, especially since stroke-related deaths actually represent less than 10% of the total mortality in anticoagulated patients [8].

In our article we acknowledged the limitations related to the retrospective nature of our analysis, including potential bias and effect of confounding, however with the advantage of a small percentage of patients lost to follow-up. In view of the type of approach our data on follow up were limited to survival, and should be considered as exploratory [1]. On the other hand, active cancer constituted a specific exclusion criterion for enrolment in randomized controlled trials that evaluated DOACs in non-valvular AF and only few data related to variable antithrombotic regimens are currently available to estimate the outcome of this selected sub-group of AF patients [1,9–11].

We fully agree that widespread use of low molecular weight heparin (LMWH) in such AF patients is expensive and clinically unjustified since no evidence is available about the efficacy and safety of these agents about long-term prevention of stroke or systemic embolism in this population. Lack of confidence in use of DOACs in the setting of active cancer, fear of adverse outcomes and a widespread tendency to transfer the standard use of LMWH for venous thromboembolism (VTE) complicating cancer to the AF setting may explain our findings, consistent with that reported by Sorigue [12].

In our study, the prescription of LMWH for AF largely occurred between 2011 and 2015, before the wide implementation in daily practice of DOACs. Evidence that DOACs can replace the standard treatment with LMWH in most cases of cancer-associated VTE [13–15] may be the basis for an improved familiarity of oncologists in the use of DOACs also in cancer patients with AF. It is important to recognise that a bidirectional relationship between AF and VTE [16–18].

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Another complex area is the management of so called “secondary AF” i.e. cases of AF triggered by surgery or other facilitating conditions or illnesses. In an analysis of Framingham cohort, AF due to secondary precipitants showed a tendency to recur over time [19], with an increased risk of morbidity and mortality. Post-operative AF was associated to an increased risk of stroke (HR 2.0, 95% Confidence Interval 1.7–2.3), even if the increase in risk appears lower than that demonstrated for “primary” AF. A recent position paper [20] of the European Heart Rhythm Association suggests anticoagulation should also be considered in patients with AF occurring in the context of transient factors (i.e. surgery) or illnesses, provided that absolute contraindications are excluded.

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