

DOACs for Stroke Prevention in Cancer Patients with Atrial Fibrillation

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Background

Atrial fibrillation (AF) has been shown to occur at an increased frequency in patients with cancer, with approximately 4% of cancer patients having a diagnosis of AF (1,2). The link between cancer and AF is not fully understood, however possible explanations include increased sympathetic drive, anaemia, paraneoplastic processes and therapeutic interventions including chemotherapy and surgery (3). Specific examples include drugs such as ibrutinib - a tyrosine kinase inhibitor used in haematological malignancies which has been shown to increase the risk of developing new AF (4).

Stroke prevention is an important aspect of management in patients with AF, however this can prove challenging in the setting of active malignancy which predisposes to an increased risk of haemorrhage as well as thrombosis. Direct tumour invasion (especially gastrointestinal and genitourinary cancers), cancer-related thrombocytopenia, and post-operative bleeding are but a few reasons to explain the bleeding pathogenesis in cancer (3). With this in mind, anti-coagulation decisions become much more difficult. Traditionally low molecular weight heparin (LMWH) and warfarin have been used in this setting.

The recent introduction of DOACs for stroke prophylaxis in AF (SPAF) has bolstered the options available, although there remains limited evidence for their use in cancer patients. However, small prospective studies and subgroup analyses have demonstrated comparable safety and efficacy profiles against warfarin and LMWH. Shah et al demonstrated similar rates of bleeding in cancer patients with AF taking rivaroxaban or dabigatran compared to warfarin, and a lower rate of bleeding in patients taking apixaban compared to warfarin (5). The same study found no significant difference in rates of ischaemic stroke among anticoagulant users. Subgroup analysis of the ENGAGE AF-TIMI trial found a preserved efficacy and safety of edoxaban compared to warfarin in patients with active malignancy and AF (6). In another retrospective study it was found that there were fewer bleeding events and a preservation of efficacy in cancer patients treated with DOACs compared to enoxaparin (7).

With there being a lack of clear consensus regarding optimal anticoagulation in cancer patients with AF, there remains highly variable clinical practice with the adoption of multiple anti-coagulation strategies. Here we analyse DOAC prescribing in AF and cancer at a single tertiary-care institution over a 6-month period.

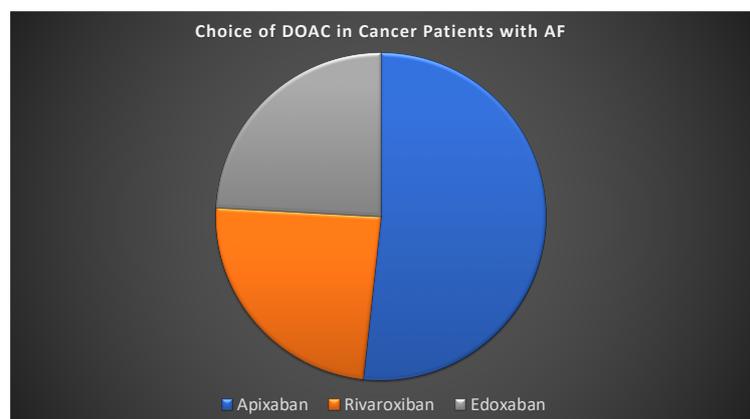
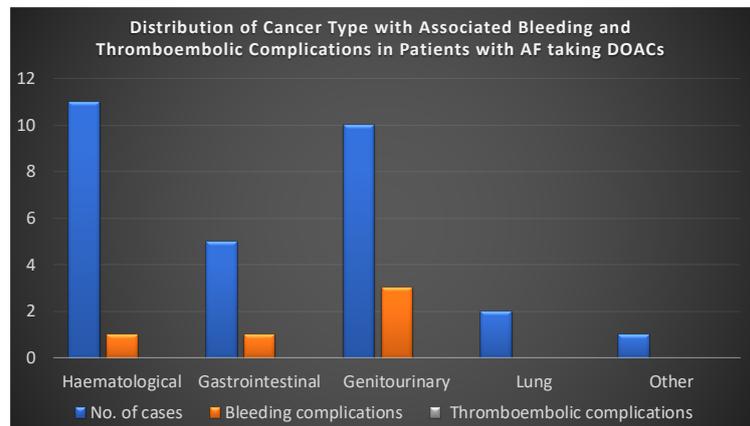
Methods

All outpatient DOAC prescriptions at St Bartholomew's Hospital between November 2018 and April 2019 were reviewed, as well as all inpatient orders of DOACs on the oncology wards. From this, all patients with an active diagnosis of cancer who were prescribed a DOAC for SPAF were identified. Information yielded included type of DOAC, duration of treatment and associated complications with a particular focus on TIAs/embolic strokes, other thromboembolic events and bleeding episodes (major and minor). As well as this, details regarding onset of AF and date of cancer diagnosis were also identified.

Results

29 patients with cancer diagnoses who had received a DOAC for SPAF were identified. 38% of patients had a haematological malignancy and 62% had solid tumour malignancies. The mean duration of DOAC therapy was 10.9 months. DOACs used included apixaban (52%), edoxaban (24%) and rivaroxaban (24%). Patients had a wide range of CHA₂DS₂-VASC scores ranging from 1 to 6 with a mean score of 3.14. The majority of patients developed AF following their cancer diagnosis (59%). 21% of patients were diagnosed with AF before their cancer diagnosis whilst the remainder of patients (21%) had an unknown date of onset of AF.

There were no embolic strokes or transient ischaemic attacks (TIAs) identified in any of the patients following commencement of DOAC. 5 patients suffered from minor bleeding complications including minor gastrointestinal bleeding and haematuria. 4 of these patients had gastrointestinal or genitourinary cancer. There were no major bleeding events identified in any of the patients.



Conclusion

The study population was composed of just 29 patients and the mean duration of DOAC therapy was just under 11 months; however there were no TIAs, embolic strokes or thromboembolic complications and no major bleeding events observed throughout the study period. The bleeding events which were observed included non-major gastrointestinal bleeding and minor haematuria, which as highlighted in the graph above were probably more a result of the underlying cancer than the choice of anti-coagulant.

Cancer is a challenging setting in which to make decisions regarding anti-coagulation. There are factors which are more common and more likely to pose difficulties in the context of cancer such as thrombocytopenia, concurrent renal failure, and limitations to route of administration. Furthermore, drug-drug interactions with less familiar anti-cancer medications must also be borne in mind. It must also be remembered that whilst some patients may develop AF following their cancer diagnosis, there are other patients who already have established AF at the time of their cancer diagnosis. With so many potential complications, an evaluation regarding optimal anti-coagulation is much needed, with randomised controlled trials being especially important.

As discussed before, multiple observational studies have demonstrated a promising role for DOACs in SPAF and cancer, with no negative implications on safety and no compromise in efficacy. This study, albeit with a very small data set, adds to this growing collection of evidence. This study also lends support to the recent guidance issued by the International Society for Thrombosis and Haemostasis suggesting an individualised approach to anticoagulation in cancer based on stroke and bleeding risk, drug-drug interactions and patient values.

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