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Letter to the Editor

Starting anticoagulation with vitamin k antagonists alone or with concomitant low-molecular weight heparin for non-valvular atrial fibrillation

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It is well known that a majority of patients with non-valvular atrial fibrillation (NVAF) treated with vitamin K antagonists (VKA) do not benefit from bridging anticoagulation for ambulatory procedures [1–3]. Conversely, there is little evidence around overlapping low-molecular weight heparin (LMWH) with VKA when starting anticoagulation, despite it being common practice. The present study aimed to describe the frequency of use of an overlapping strategy and determine the incidence of bleeding and thrombotic events based on whether this strategy or VKA were used.

This is a single-center, observational study including patients starting anticoagulation with VKA for NVAF or auricular flutter in an outpatient setting from December 2016 until June 2018. Patients undergoing electrical cardioversion in the emergency room, those suffering stroke or transient ischemic attack (TIA) as well as those admitted to hospital were excluded.

Patients were divided into those starting VKA alone and those starting VKA overlapped with LMWH (VKA + LMWH). The latter group included patients receiving any dose of LMWH higher than that approved for venous thromboembolism (VTE) prophylaxis simultaneously with VKA for at least one day. The incidence of stroke/TIA (a sudden and focal neurological deficit corresponding to a vascular territory) and that of major bleeding (a lethal bleeding, one in a critical organ or one leading to a drop in hemoglobin of > 20 g/L or to the transfusion of at least 2 red cell units, according to the international society of thrombosis and haemostasis [4]) were determined at 30 days, as recommended [5]. For quantitative variables, median and interquartile range (IR) are given and, for qualitative variables, frequencies and percentages. Fisher's exact test, the chi-squared test and the Mann-Whitney *U* test were used for comparisons between groups.

Three-hundred and eleven patients, with a median of 74 years (IR 69–82) and a CHA_2DS_2VASc of 3 (IR 2–4), were included. Ninety-eight (32%) started anticoagulation with VKA + LMWH and 213 (68%) VKA alone. CHA_2DS_2VASc was similar in the two groups (median 3 [IR 2–4] in the VKA + LMWH group vs. 3 [IR 3–4] in the VKA alone p = 0.54) but there was a difference in the medical specialty starting anticoagulation. The VKA + LMWH strategy was more common when anticoagulation was prescribed in the emergency department (Table 1). In a subanalysis of these patients, there were no differences in terms of CHA_2DS_2VASc between patients starting VKA alone vs. VKA + LMWH (median 3 [IR 2–4] in both groups, p = 0.74) or in time from the start of symptoms (25/50 [50%] with recent onset [< 48 h] of symptoms vs. 66/116 [57%] with onset > 48 h or unknown received overlapping LMWH [p = 0.5]).

Table 1
Differences in anticoagulation strategy (vitamin K antagonists [VKA] alone or with concomitant low-molecular weight heparin [LMWH]) for non-valvular atrial fibrillation based on the medical specialty of the prescribing physician.

	Prescribing specialty				
	Emergency department	Hematology	Cardiology	Primary care	Other
VKA alone	75	58	47	26	7
VKA + LMWH	91	0	2	0	5

At 30 days from the start of anticoagulation, there was 1 TIA (1/213, 0.5%) and no major bleeds among patients starting VKA alone and 1 ischemic stroke (1/98, 1%) and two major bleeds (2/98, 2%), both intracranial, in the VKA + LMWH group. These differences were not significant (p = 0.53 for stroke/TIA and p = 0.1 for major bleeding).

This study found that the incidence of ischemic and hemorrhagic events at 30 days from beginning anticoagulation for NVAF with VKA was low, regardless of the overlapping use of LMWH.

Importantly, the use of LMWH did not lower the incidence of stroke, in accordance with what Bouillon et al. [6] described in a large cohort, although in their study, in contrast to ours, the increase in bleeding with the overlapping use of LMWH reached statistical significance (0.47% vs. 0.30% at 30 days). These results are similar to those seen in perioperative bridging, where the use of LMWH increases major bleeding without a benefit in stroke protection [1–3,7].

In our study, the use of LMWH appeared to depend on the medical specialty of the prescribing physician rather than on the characteristics of the patient. These findings are also in line with some studies in the setting of perioperative bridging [7–9]. We hypothesize that the use of LMWH when starting anticoagulation for NVAF could be due to extrapolation of the evidence for VTE, where early antithrombotic activity is essential to decrease the risk of recurrence. This does not appear to be

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needed in NVAF.

In conclusion, this study does not support the overlapping use of LMWH and VKA when starting anticoagulation for NVAF in the ambulatory setting.

Conflict of interest

The authors declare no potential conflict of interests.

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