

## Cardiovascular disease

### Concomitant steroid therapy raises GI bleeding risk in AF patients on DOACs

Oral glucocorticoids are associated with an increased risk of gastrointestinal (GI) bleeding in patients with atrial fibrillation (AF) concomitantly treated with direct acting oral anticoagulants (DOACs), a nationwide study from Denmark has found.

Patients with AF, aged 18-100 years, who redeemed a first prescription for a DOAC between 2012 and 2018 were identified from national registers. Patients were defined as exposed to oral glucocorticoids if they claimed a prescription within 60 days prior to a GI bleed.

The authors investigated the association between GI bleeding and oral glucocorticoid exposure, reporting hazard ratios (HR) via a nested case-control design and absolute risk (AR) via a cohort design. The variables used for matching were: age group, sex, calendar year of the first redeemed prescription for a DOAC, follow-up time and type of DOAC.

A total of 98,376 patients on DOACs, median age 75 years, 44% female, were included in the study. Of these, 15,971 (16%) had redeemed at least one oral glucocorticoid prescription (70% with a dose of  $\geq 20$  mg/day) within three years.

Most patients were treated with rivaroxaban (36%), apixaban (35%) or dabigatran (27%), and a small number with edoxaban (2%).

The HR of a GI bleed was increased in patients exposed to glucocorticoids compared with non-exposed patients. A dose-response relationship was

seen with a higher HR at higher doses:

- Patients treated with  $< 20$  mg/day; HR 1.54 (95% CI: 1.29-1.84)
- Patients treated with  $\geq 20$  mg/day; HR 2.19 (95% CI: 1.81-2.65)

Likewise, a dose-response relationship was seen for case fatality rates for GI bleeding. The rate was highest (27%) in those patients exposed to a glucocorticoid dose  $\geq 20$  mg/day.

The 60-day AR of GI bleeding following a first redeemed oral glucocorticoid prescription was also increased compared with non-exposed patients:

- 60-day AR 0.71% (95% CI: 0.58-0.85%) vs 0.38% (95% CI: 0.32-0.43%)
- The risk ratio was also elevated at 1.89 (95% CI: 1.43-2.36)

Oral glucocorticoids are frequently prescribed for a wide range of medical conditions and have been associated with an increased risk of bleeding in patients concomitantly treated with warfarin and other vitamin K antagonists. However, to date no major studies had investigated a similar association with DOACs.

The authors state: 'We found a doubling in both HR and AR of GI bleeding following concomitant treatment with oral glucocorticoids within 60 days of the GI bleeding incident. This could have implications for clinical management, necessitating closer monitoring or other risk mitigation strategies during episodes of cotreatment with oral glucocorticoids.'

'The risk increase was associated with short-term exposure, begging the question how long-term or repeated glucocorticoid exposure might influence GI bleed risk. These considerations, along with comorbidity and concomitant medication known to elevate the risk of GI bleed, underscore the importance of evaluating each patient separately when assessing benefit versus harm in relation to immediate glucocorticoid treatment,' they say.

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Holt A, Blanche P, Zareini B et al. Gastrointestinal bleeding risk following concomitant treatment with oral glucocorticoids in patients on non-vitamin K oral anticoagulants. *Heart* 2022;108:626-32