

Gastrointestinal Bleeding and Association with Oral Anticoagulant Use at Abbotsford Regional Hospital



Geraldine Gabriel, B.Sc.(Pharm)., Gordon Klammer, B.Sc.(Pharm)., ACPR, BCPS, Caitlin Lang B.Sc.(Pharm)., ACPR, Dale Toews, B.Sc.(Pharm)., ACPR, Arden Barry, B.Sc., B.Sc.(Pharm)., ACPR, Pharm.D.

Background

- Oral anticoagulants are recommended for numerous medical conditions such as venous thromboembolism, mechanical heart valves, left ventricular thrombus and atrial fibrillation.
- Warfarin was the mainstay of therapy, but had several drawbacks. As a result, the direct oral anticoagulants (DOACs) were developed.
- Post-marketing studies have shown conflicting evidence regarding safety concerns with DOACs, specifically their risk of gastrointestinal (GI) bleeding, as compared to warfarin¹⁻⁴.

Objectives

- Primary objective:** in adult patients admitted to ARH with a major GI bleed and taking an oral anticoagulant prior to admission, what is the percentage of patients taking warfarin as compared to a DOAC?
- Secondary objective:** of the patients taking warfarin or a DOAC prior to admission, to determine: a) baseline characteristics; b) total number of patients also taking an antiplatelet agent, SSRI or NSAID prior to admission; and c) if an anticoagulant reversal agent was administered for the GI bleed.

Methods

- Design:** single-centre retrospective electronic medical record review at ARH from September 1, 2016 to August 31, 2019.
- Inclusion criteria:** patients aged ≥ 18 years admitted to ARH with a major GI bleed who were taking warfarin or a DOAC prior to admission.
- Exclusion criteria:** patients who were pregnant or had major surgery or trauma involving the upper torso in the month prior to admission.

Results

- The majority of patients, 423 of 476 (89%), admitted for a GI bleed were not on an oral anticoagulant (Figure 1).
- Of the 47 patients with a major GI bleed who were taking an oral anticoagulant prior to admission, 31 (66%) were on a DOAC. Among the patients on a DOAC, 21 of 31 (68%) were on rivaroxaban (Figure 2).
- Patient baseline characteristics are shown in Table 1. More warfarin patients were on a concomitant SSRI or NSAID, which increases a patient's bleed risk.
- Among warfarin patients, the highest INR was 8.2 and the lowest was 1.7.
- Of the patients on warfarin, 15/16 (94%) were administered a reversal agent. The patient on dabigatran was not administered idarucizumab.
- The appropriate dose of the DOACs were assessed in 18 of the 31 patients (58%) and it showed that 3 patients on rivaroxaban were dosed incorrectly at a higher dose.

Table 1: Patient baseline characteristics (N=47)

Characteristic*	Warfarin (N=16)	DOAC (N=31)
Mean age (years)	79.8 \pm 9.9	80.2 \pm 9.1
Male (%)	50	41.9
Mean weight (kg)	68.8 \pm 14.8	80.7 \pm 28.5
Obesity (BMI ≥ 30 kg/m ²) (%)	6.3	22.6
eGFR (mL/min)	38.3 \pm 23.1	48.1 \pm 20.5
HASBLED score	2 (2,2)	1.5 (1,2)
Liver disease (%)	6.3	3.2
Gastric or esophageal varices (%)	0	3.2
Gastritis (%)	6.3	12.9
Chemotherapy that affects GI epithelium (%)	6.3	0
Prior GI bleed (%)	18.8	35.5
Cancer (%)	12.5	6.5
Medication PTA (%):		
Antiplatelet agent (includes ASA)	31.3	32.3
SSRI	31.3	12.9
NSAID	18.8	6.5
Alcohol use disorder (%)	0	3.2
Indication (%):		
Atrial fibrillation	56.3	96.8
Mechanical heart valve	12.5	0
VTE	31.3	0
Other	0	3.2
CHADS2 score	3 (3,3)	2.5 (2,3.75)
INR on admission	4 \pm 1.9	–
INR >3 (%)	68.8	–
Vitamin K, fresh frozen plasma, or PCC (%)	93.8	–
PRBC given (units)	2.8 \pm 1.9	2.2 \pm 1.5
Death (%)	6.3	6.5
Length of stay (days)	11.5 \pm 13.4	13.6 \pm 16.5

* Values presented as mean \pm standard deviation for continuous variables and median (25th percentile, 75th percentile) for categorical variables. BMI= body mass index; GFR= glomerular filtration rate; GI= gastrointestinal; PTA= prior to admission; ASA= acetylsalicylic acid; SSRI= selective serotonin reuptake inhibitor; NSAID= non-steroidal anti-inflammatory drug; VTE= venous thromboembolism; INR= international normalized ratio; PCC= prothrombin complex concentrate; PRBC= packed red blood cells

Figure 1: Percentage of GI bleeds associated with oral anticoagulants (N=476)

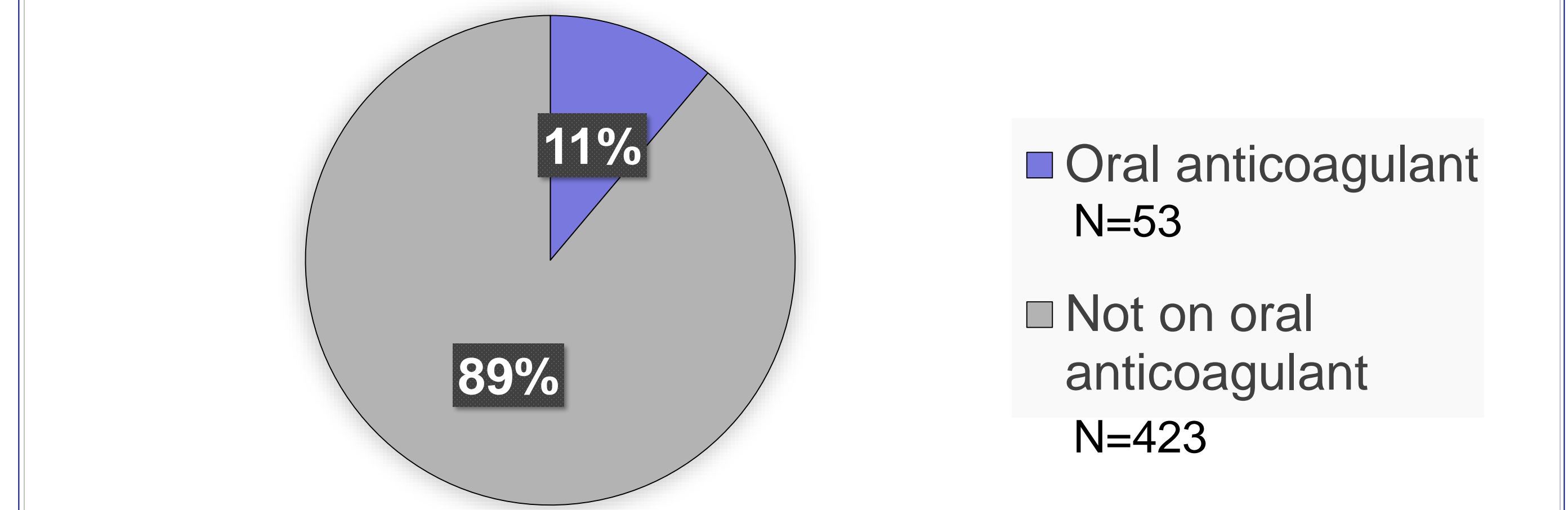
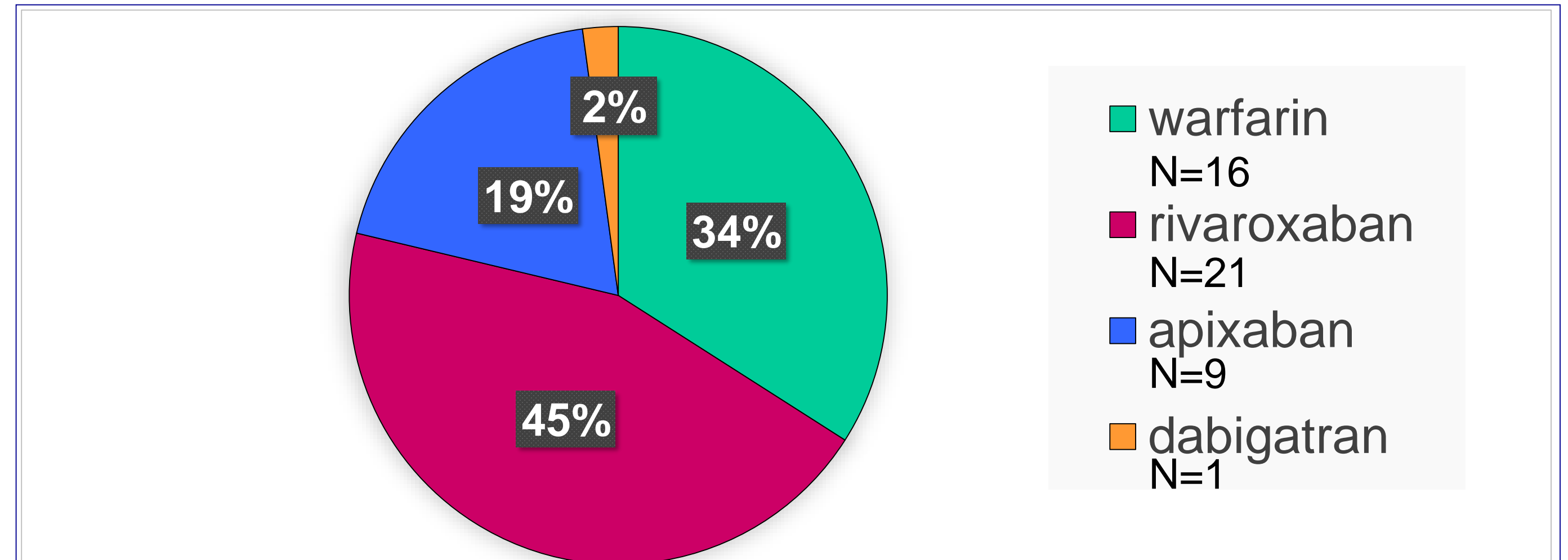


Figure 2: Breakdown of oral anticoagulants in patients with major GI bleeds (N=47)



Limitations

- Retrospective review with a limited number of patients.
- Does not account for frequency of prescribing of DOACs and warfarin in the population.
- Adherence to oral anticoagulant therapy prior to admission could not be confirmed.

Conclusions

- Only 11% of patients admitted to ARH with a GI bleed were on an oral anticoagulant.
- Among adult patients with a major GI bleed who were on an oral anticoagulant prior to admission, the majority were on a DOAC.
- Among the patients on a DOAC, the majority were on rivaroxaban.

References

- Villines TC, Peacock WF. Safety of direct oral anticoagulants: insights from postmarketing studies. Am J Emerg Med 2016 Nov;34(11S):9-13.
- Graham DJ, Reichman ME, Wernecke M, Zhang R, Southworth MR, Levenson M, et al. Cardiovascular, bleeding, and mortality risks in elderly Medicare patients treated with dabigatran or warfarin for nonvalvular atrial fibrillation. Circulation 2015 Jan 13;131(2):157-164.
- Halvorsen S, Ghanima W, Fride Tvete I, Hoxmark C, Falck P, Solli O, et al. A nationwide registry study to compare bleeding rates in patients with atrial fibrillation being prescribed oral anticoagulants. Eur Heart J Cardiovasc Pharmacother 2017 Jan;3(1):28-36.
- Abraham NS, Singh S, Alexander GC, Heien H, Haas LR, Crown W, et al. Comparative risk of gastrointestinal bleeding with dabigatran, rivaroxaban, and warfarin: population based cohort study. BMJ 2015 Apr 24;350:h1857.