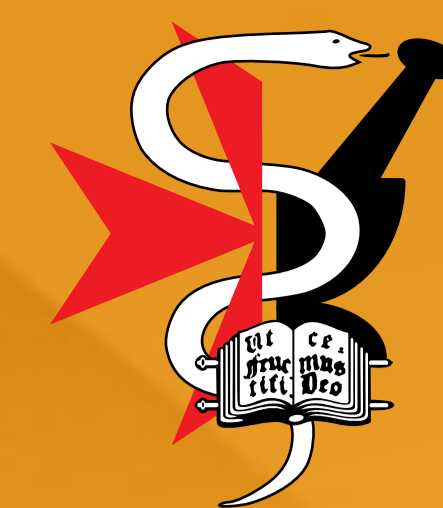


DRUG INTERACTIONS AND BLEEDING COMPLICATIONS WITH RIVAROXABAN COMPARED TO WARFARIN

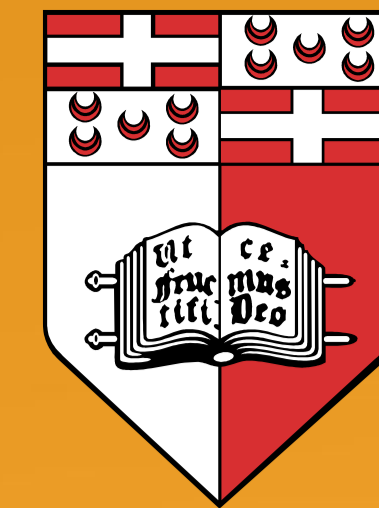
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INTRODUCTION

Compared to warfarin, the novel oral anticoagulant (NOAC) rivaroxaban has the advantages of a fixed dosing regimen with no need for INR monitoring and fewer potential drug-drug interactions (DDIs).¹ However, there is conflicting evidence regarding bleeding complications.²

AIMS

- To determine INR control for patients on warfarin
- To compare warfarin to rivaroxaban with respect to potential DDIs and incidence and severity of bleeding

METHOD

- Following ethics approval, 100 patients (50 on warfarin, 50 on rivaroxaban) were recruited by convenience sampling from hospital outpatient clinics and community pharmacies. Patient recruitment was undertaken between July 1, and December 31, 2016.
- Informed written consent was obtained and data collection was completed via a semi-structured interview and information from patient hospital-related documentation.

- The Rosendaal Linear Interpolation Method was used to measure time in therapeutic range (TTR) for patients on warfarin.³
- Bleeding complications were classified according to the Bleeding Academic Research Consortium (BARC) criteria.⁴
- Micromedex complete drug interactions and Medscape multidrug interaction checker tools were used to identify and analyse potential DDIs.^{5,6}

RESULTS

- The mean age of the 100 patients recruited was 65 ±12.91 years, 53 patients were female and 47 were male, and the mean duration of anticoagulation use was 10 ±5.97 months.
- Over a 6-month period, 768 INR tests were processed (mean 2.56 ±1.58 tests/patient/month), of which 37% were not in TTR.
- 91 (mean 1.8 ±1.03/patient) and 19 (mean 0.4 ±0.52/patient) potential DDIs were identified in patients on warfarin and rivaroxaban, respectively (p<0.001) (Figure 1). Simvastatin (23) was implicated in the highest number of DDIs with warfarin while amiodarone (7) was implicated in the highest number of DDIs with rivaroxaban.
- 24 patients reported BARC Type 1 bleeding (18 warfarin, 6 rivaroxaban) and 10 patients reported Type 2 bleeding (6 warfarin, 4 rivaroxaban) (p<0.001) (Figure 2).

Figure 1: Potential DDIs with warfarin versus rivaroxaban (N=111)
 $X^2(2)=47.81, p<0.001$

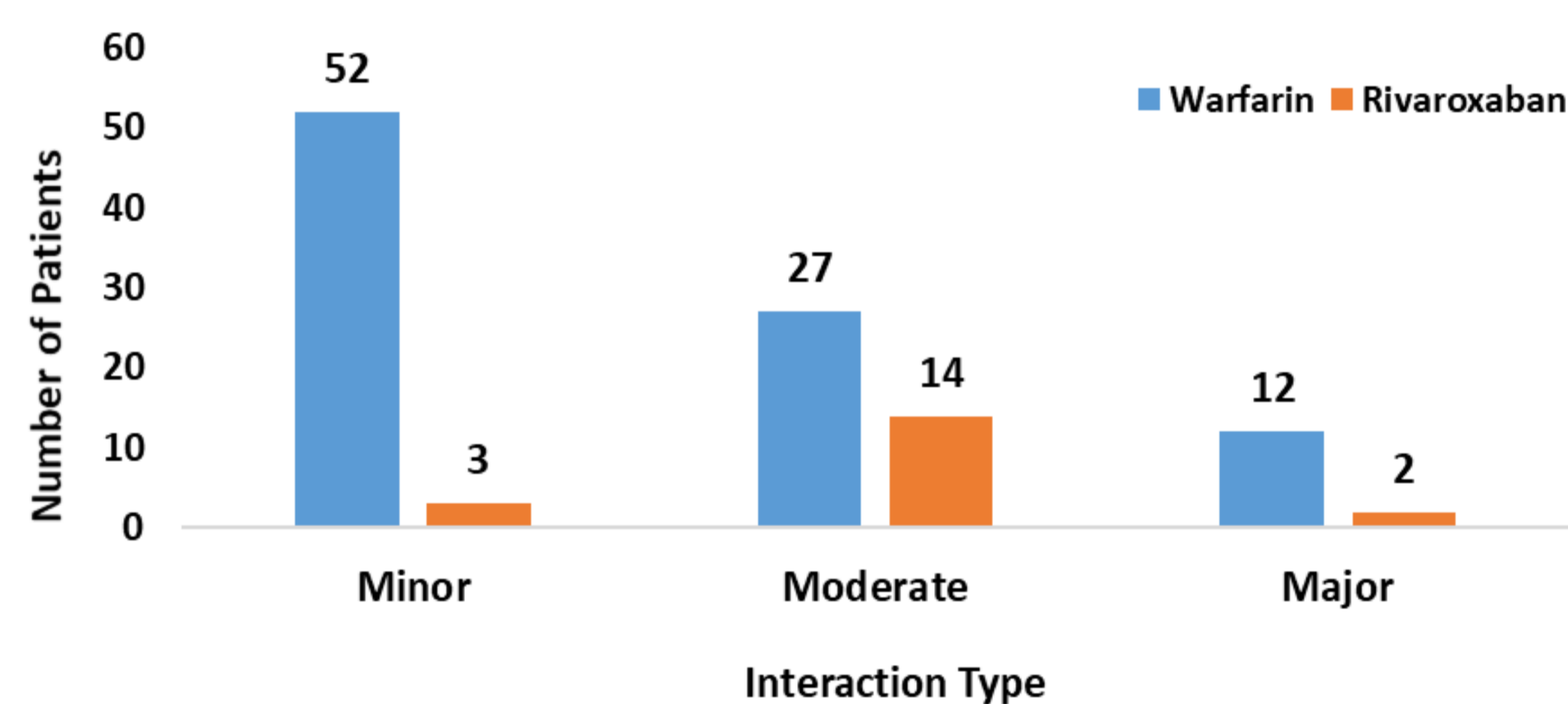
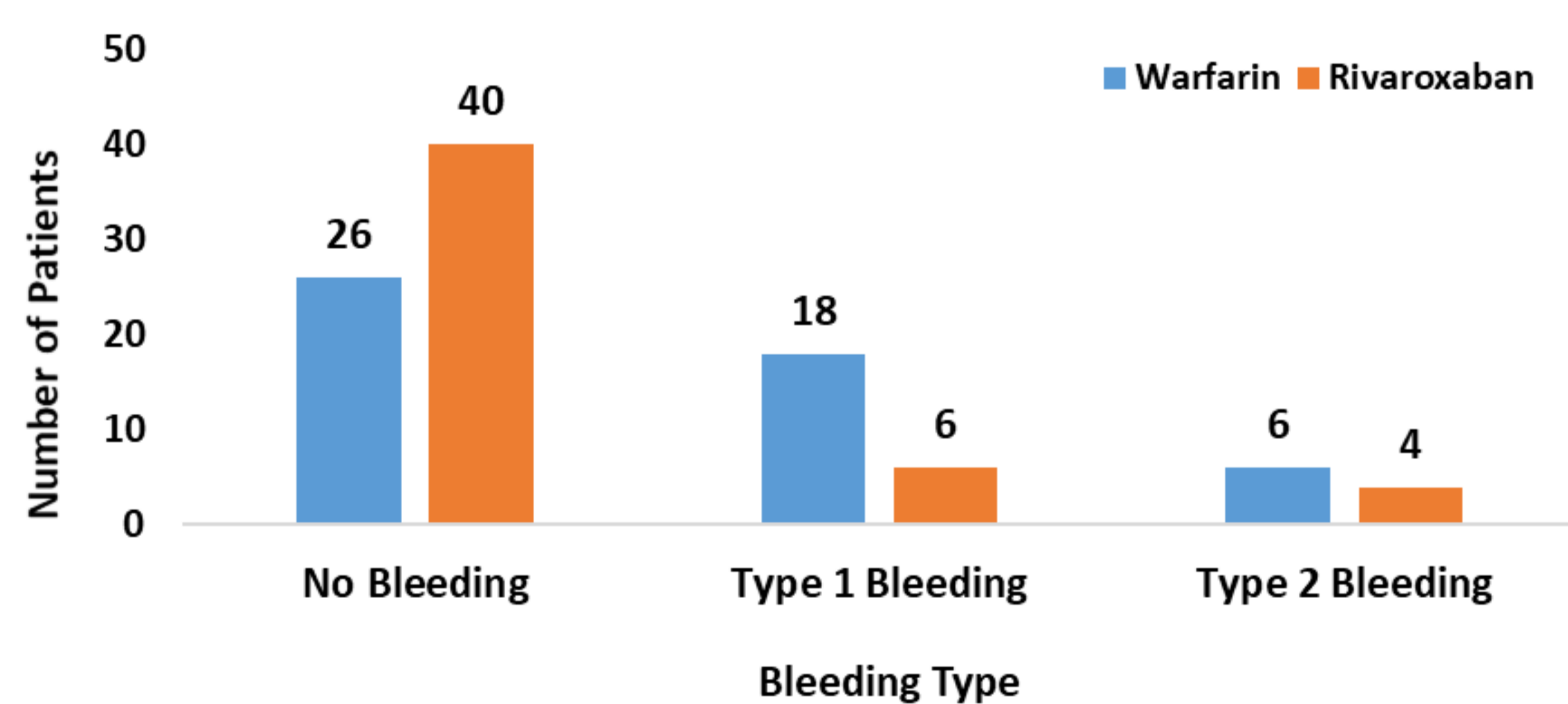


Figure 2: BARC bleeding with warfarin versus rivaroxaban (N=100)
 $X^2(2)=9.37, p<0.001$



CONCLUSION

A higher risk of DDIs and increased bleeding complications were observed in patients on warfarin. NOACs may provide a personalised treatment option for patients not stable on warfarin.

References

1. Mekaj YH, Mekaj AY, Duci SB, Miftari EI. New oral anticoagulants: Their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events. *Ther Clin Risk Manag.* 2015;11:967-77.
2. Vilchez JA, Gallego P, Lip GY. Safety of new oral anticoagulant drugs: a perspective. *Ther Adv Drug Saf.* 2014;5(1):8-20.
3. Rosendaal FR, Cannegieter SC, Van der Meer FJ, Briet E. A method to determine the optimal intensity of oral anticoagulant therapy. *J Thromb Haemost.* 1993; 69(3): 236-9.
4. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J et al. Standardized bleeding definitions for cardiovascular clinical trials: Consensus report from the Bleeding Academic Research Consortium. *Circulation.* 2011; 123 (23): 2736-47.
5. Micromedex® 2.0. DRUG-REAX System [Online]; 2017 [cited 2017 Jul 12]. Available from: URL: www.micromedexsolutions.com/micromedex2/4.14.0/WebHelp/Tools/Interactions/Drug_Interactions.htm.
6. Medscape. Drug Interaction Checker [Online]; 2017 [cited 2017 Jul 12]. Available from: URL: www.reference.medscape.com/drug-interactionchecker.