BSH 2020 VIRTUAL
9 -14 NOVEMBER
British Society for Haematology
60 1960–2020
Listening • Learning • Leading

Effects of Rivaroxaban on thrombophilia screening tests – results from a UK National External Quality Assessment Scheme for Blood Coagulation (UK NEQAS BC) exercise.

UK NEQAS Blood Coagulation

I Jennings, S Kitchen, DP Kitchen, S Munroe-Peart, A Lowe, L Brown, ID Walker
UK NEQAS BC, Sheffield, UK
ian.jennings@nhs.net

INTRODUCTION

Many studies have investigated the effects of anticoagulants on thrombophilia screening tests; current recommendations suggest testing for heritable thrombophilia should not be carried out on patients receiving anticoagulation (Baker et al, 2020, Moore et al 2019), or should be repeated after suspension of treatment with direct oral anticoagulants (DOACs) (van Cott et al, 2020). However, information about the effects of DOACs on thrombophilia screening tests is useful, as clinical information is not always available when samples are received in the laboratory for testing.

AIM

To investigate effects of rivaroxaban on a wide range of methods used in thrombophilia screening in an external quality assessment (EQA) exercise.

METHOD

A sample from a patient with protein S deficiency and taking rivaroxaban (level 93ng/ml) was sent to UK NEQAS BC laboratories for thrombophilia testing, without relevant clinical information. Participants were asked to perform their thrombophilia screen (Protein C (PC), Protein S (PS), Antithrombin (AT) and activated protein C resistance (APCR)) on the sample and interpret their results. The sample was sent to a total of 370 centres enrolled in the UK NEQAS (Blood Coagulation) thrombophilia screening programme. Results were collated and median, range and coefficient of variation (CV) were determined based on methodology used by participants.

RESULTS

347 centres returned results. Table 1 shows results from the 3 most widely used chromogenic PC assays, and the 2 most widely used clot-based assays. All results are shown in fig 1. Clot-based PC activity assay results were significantly higher than chromogenic-based assay results (122.7u/dl vs 101.7u/dl, p<0.001).

Table 1. Protein C activity assays – most widely used assay medians and all method medians

Method	n	Median (u/dl)
Chrom: IL HemosIL	164	102.0
Chrom: Siemens	70	101.6
Chrom: Stago	39	100.0
Clotting: IL HemosIL ProClot	5	115.6
Clotting: Stago Staclot	6	125.5
All Chrom. Assays	291	101.7
All Clotting Assays	11	122.7

Fig 1. Protein C activity assays

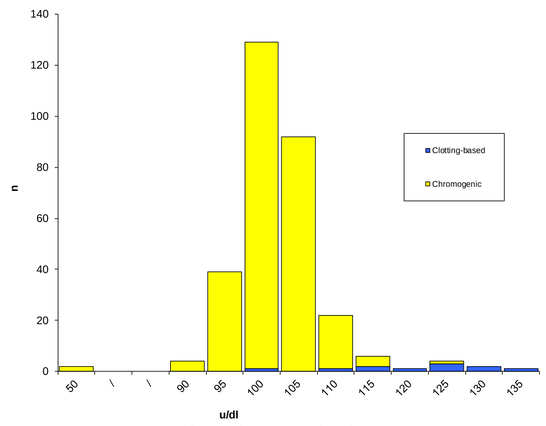


Table 2 shows results from the 3 most widely used free PS antigen methods and the 3 most widely used PS activity methods. PS activity assay results were higher than free PS antigen results (24.4u/dl vs 11u/dl, p<0.001). All results are shown in fig 2.

Table 2. Protein S free antigen and activity assays – most widely used assay medians and all method medians

Method	n	Median (u/dl)
HemosIL Protein S (latex)	158	10.0
Siemens Innovance Free PS	63	16.0
Stago Liatest	35	17.0
All PS free antigen results	**271**	**11.0**
IL HemosIL	19	30.0
Siemens	11	22.4
Stago	21	23.0
All PS activity results	**54**	**24.4**

Fig 2. Protein S free antigen and activity assays

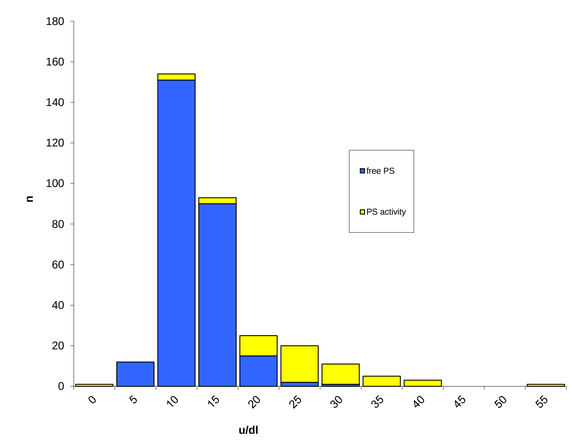
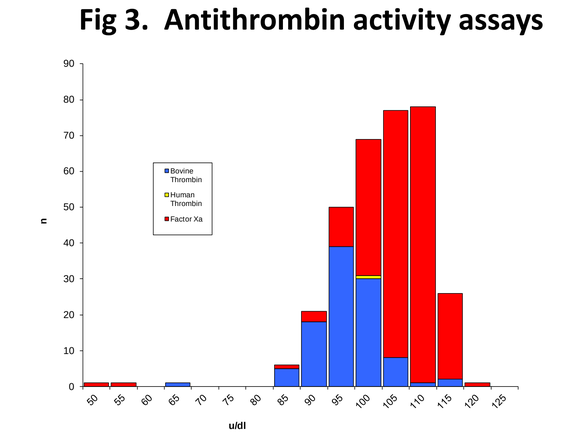


Table 3 shows results obtained with the most widely used antithrombin activity assay methods. Thrombin-based antithrombin assays gave lower results than Xa-based methods (96.0u/dl vs 107.0u/dl, p<0.001). All results are shown in fig 3.

Table 3. Antithrombin activity assays – most widely used assay medians and all method medians

Methoda	n	Median (u/dl)
Chrom: Siemens	58	95.8
Chrom: Stago Stachrom	39	97.0
Overall Bovine Thrombin Assays	104	96.0
Chrom: HemosIL	41	108.0
Chrom: HemosIL (Xa) (liquid)	131	107.5
Chrom: Siemens Innovance (Xa)	30	105.0
Overall Factor Xa Assays	226	107.0

Fig 3. Antithrombin activity assays



CONCLUSIONS

Anticoagulation with DOACs is not reported to affect chromogenic PC assays or free PS assays, so false negative results are unlikely if these tests are employed in a thrombophilia screen, as they are by the large majority of UK NEQAS participants. However, AT assays may be affected by either thrombin- or Xa-based inhibitors dependent on the substrate used, and false positive results may arise in patients with mild AT deficiency – our data show both these methods are widely used. These differences were seen across the range of methods employed by participants, confirming that a direct Xa inhibitor caused over estimation of AT when the method is based on Xa inhibition. Despite this, all centres performing a full thrombophilia screen obtained the correct interpretation of PS deficiency in this exercise, although a small proportion additionally reported APC resistance.