

Direct Oral Anticoagulant monitoring: real world utilisation of rivaroxaban plasma level monitoring

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Background

Rivaroxaban, a direct oral anticoagulant (DOAC), is approved for prevention of stroke and systemic embolism in atrial fibrillation (AF) and prevention and treatment of venous thromboembolism (VTE)¹. Routine therapeutic drug monitoring is not recommended due to their more predictable anticoagulant effect¹.

DOACs are high risk medications due to bleeding risk. Additionally DOACs, including rivaroxaban, have known inter and intra-patient drug plasma level variability¹. These factors have resulted in discussion of potential utility of drug plasma level monitoring in the clinical management of DOAC prescription.

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation², have suggested that measurement of DOAC plasma levels may have some benefit in specific clinical scenarios; including emergencies (bleeding, surgery or VTE), elective procedure management, extremes of body weight and drug interactions. The Clinical Excellence Commission NOAC guidelines: Non-Vitamin K Antagonist Oral Anticoagulant³ 2017 and The National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Diagnosis and Management of Atrial Fibrillation⁴ 2018, both recommend measurement of DOAC plasma levels in the clinical management of bleeding patients on a DOAC. However, there is limited evidence regarding interpretation of plasma levels.

Expected rivaroxaban plasma ranges have been published, however there is poor correlation between plasma levels and outcomes. In practice, clinical management decisions may be made in response to plasma levels despite limited evidence on interpretation of results. Published retrospective audits of DOAC plasma levels have been conducted in small sample sizes^{5,6}. These have indicated low rates of DOAC plasma level monitoring and limited impact on drug dosing decisions and conclude further work is required to determine impact on clinical outcomes. Prior studies have not reported pathology turn-around-time (TAT) for plasma levels which may impact the clinical utility of results.

Aim

To investigate the utilisation of rivaroxaban plasma levels, including the rationale, timing and resulting clinical decision-making in adult patients.

Methods

A retrospective audit was undertaken of all rivaroxaban plasma levels at a metropolitan health network between 2015–2018.

Inclusion criteria was all rivaroxaban plasma levels taken in adults (>18 years) presenting to our institution (emergency, inpatient and outpatient settings). The exclusion criteria was paediatric patients (<18 years) and external institution results.

Electronic medical records, clinical patient notes and pathology data were reviewed for the following data points; patient demographics, indication for rivaroxaban, dose, documented rationale for ordering rivaroxaban plasma level, time of dose, time of level and time of pathology result availability, rivaroxaban plasma level, clinical management outcome, and clinical changes around DOAC management.

Data was analysed to determine trends in the ordering requests, TAT and subsequent clinical decisions due to interpretation of rivaroxaban levels.

Figure 1.

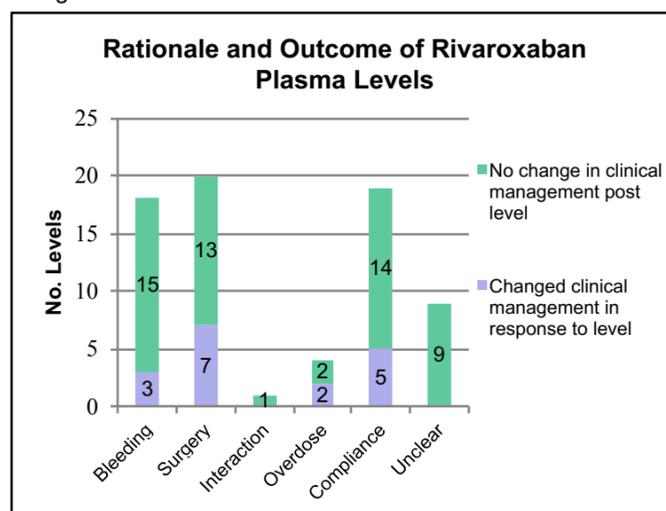


Figure 2.

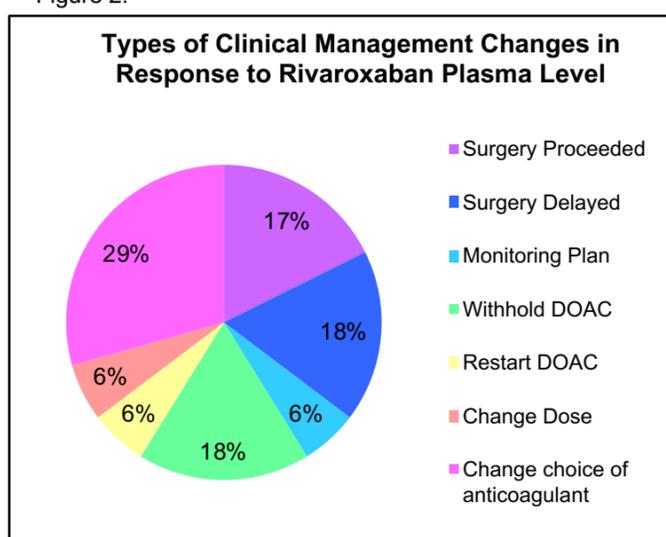
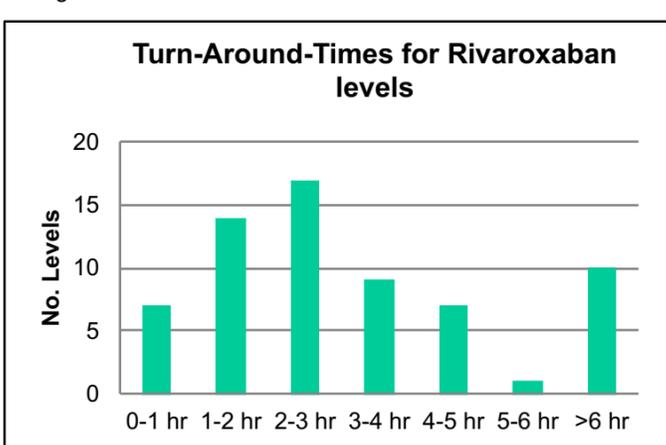


Figure 3.



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Results

A total of 88 rivaroxaban levels were included, representing 71 patients, of which 63% were male and the median age was 72 years (range 25-97).

Rivaroxaban indications were AF (49%) and VTE prevention or treatment (51%).

Rationale for ordering plasma levels included pre-operative assessment (28%), compliance (27%), bleeding (25%), overdose (6%) and drug interaction (1%). Rationale was unclear for the remainder (13%). In 17 patients (19.3%), the rivaroxaban level resulted in a change in clinical management (Figure 1).

In the pre-operative setting, clinical management decisions were made on the basis of results in 7/20 patients (35%). In this setting, the levels either reassured clinicians that surgery could proceed or needed to be delayed. (Figure 2)

The median TAT for results was 2.9 hours (range 1.7-4.6 hours). It is unclear whether TATs impacted on number of plasma levels that resulted in a change in clinical management. A significant proportion of result TATs were delayed and clinical decisions may have already been made in time-critical situations. (Figure 3)

Implications for practice

This audit demonstrated that rivaroxaban plasma levels are not routinely utilised within our network, with only 88 taken over a thirty-eight month period.

Rivaroxaban plasma levels resulted in a change of management in 1 out of 5 patients. In many patients where management was not changed it appeared that the results were used to reassure clinicians about current clinical management rather than to alter future prescribing.

Overall, documentation regarding the plasma levels was poor. It was frequently unclear how significant a role the results played in decision making. In some cases the haematology team were contacted, however in most no expert advice was documented.

Timing of last rivaroxaban dose was also poorly documented. Therefore, it was not possible to determine if the rivaroxaban level was a peak or trough.

Based on this audit, TAT varied with the majority being available within 3 hours. However in time-critical situations results may not be available soon enough to inform clinical decision making.

Rivaroxaban levels appeared to have the greatest impact on pre-surgical patients. Results allowed reassurance that surgery could proceed or if further delay of surgical intervention was required. This has the potential to reduce unnecessary delays and bleeding risk in some patients and may represent a patient cohort where rivaroxaban levels could be better utilised.

Conclusions

Rivaroxaban plasma levels resulted in a change of clinical management in 19.3% of patients where a level was measured. This audit demonstrates rivaroxaban plasma levels may have an important role in patient clinical management, and further studies are required to develop guidelines for appropriate utilisation and interpretation of DOAC testing.

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