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Can We Improve on the Rapid Assessment of Clinically Relevant Levels of Direct Acting Oral Anticoagulants (DOAC)?

Jeanine M. Walenga, PhD[1]

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The use of direct acting oral anticoagulants (DOACs) dabigatran, rivaroxaban, apixaban, and edoxaban has changed the management and prevention of ischemic stroke in patients with atrial fibrillation, treatment of venous thromboembolism (VTE), prophylaxis for prevention of VTE following elective surgery, and management of acute coronary syndrome.[1] DOACs are inhibitors of either thrombin or coagulation factor Xa.

DOACs, in contrast to traditional warfarin, are administered in fixed dosing and do not require routine dose adjustment or level monitoring.[1] However, measuring circulating levels can help patient management in those undergoing surgery, requiring dose interruption, with worsening renal function, and to confirm adherence to prescribed therapy.[2,3] Detection of the presence of a DOAC when an emergency reversal may be potentially needed to prevent serious bleeding would also be useful as DOAC antidotes are expensive and associated with thrombotic complications.[2,3]

Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) is the standard assay for DOAC quantitative assessment,[4–6] but this technology is not available in most hospital settings. Clinical test systems for anticoagulant testing such as the PT, APTT, and ACT provide highly variable results with DOACs or they fail to detect the DOAC due to lack of sensitivity.[5] The chromogenic substrate anti-FXa test used for heparin is one acceptable assay for the factor Xa inhibitor DOACs, and thrombin clotting assays or ecarin-based assays are being used for thrombin inhibitor DOACs. However, these tests are not suitable for quick point-of-care (near-patient) use, require standardization and calibration for specific DOAC, and the performance and interpretation of these tests require a specialist; all of which limit their use.

A rapid test that can be reliably and remotely interpreted is currently an unmet clinical need. The DOAC Dipstick (DOASENSE GmbH, Germany) was developed based on the knowledge that DOACs are excreted into the urine.[7] The DOASENSE test provides qualitative results reporting the absence or presence of a DOAC (both factor Xa inhibitors and thrombin inhibitors) in a patient's urine sample.[8] The testing procedure is relatively simple, being similar to that used for a routine urinalysis with reaction pads on a dipstick and results obtained within minutes.

Since the concept paper published in 2013 by Harenberg, et al,[7] studies have been published describing the performance characteristics of the DOAC Dipstick test.[9–11] Evidence of the clinical applications of this novel test system have been published with other clinical investigations.[12,13] Two recently published papers in *Clinical and Applied Thrombosis/Hemostasis* provide further detail to support the clinical utility of the DOAC Dipstick test.[14,15] The publication by Örd, *et al*[14] confirms that the DOAC urine Dipstick test detects DOACs at the clinically relevant plasma level of ≥30 ng/mL, the threshold determined in clinical trials[6,16] during development of the DOACs. The second paper by Harenberg, *et al* clarified that heparin and low-molecular-weight heparin will not interfere in the DOAC Dipstick test.[15] Both of the published papers in this journal provide data validating the functionality and analytical performance, demonstrate inter-operator agreement, and lack of color interferences in the dipstick reading.[14,15]

DOACs have become a mainstay option for anticoagulant management. The challenges that the clinical community has faced with the laboratory assessment of DOACs may now be improving with the development of new test systems. The DOAC Dipstick test has potential for aiding in patient care as the rapid, near-patient result reporting, classifying type of DOAC and above/below threshold levels, can assist clinical decision making in multiple settings. The potential to have such a test system available for urgent surgical, serious bleeding, and other acute indications is of particular value.

[1] Cardiovascular Institute, Loyola University Chicago, Chicago, Illinois, United States

Corresponding Author:
Jeanine M. Walenga, Cardiovascular Institute, Loyola University Chicago, Chicago, Illinois, United States. Email: jwaleng@luc.edu

ORCID iD

Jeanine M. Walenga https://orcid.org/0000-0002-1418-7369

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