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Aim

To determine the usefulness of the in vitro medical device (IVD) DOAC Dipstick in clinical scenarios

Background

Qualitative determination of DOACs is considered as useful by international consensus groups. A 100 % sensitivity and 100 % specificity for qualitative determination of DOAC Dipstick was calculated for DOACs in urine.

A specific and sensitive detection of DOACs in urine by a point of care test may support rapid diagnosis in emergency medicine.

Reduced renal function and urine colour may influence the performance of the DOAC Dipstick test.

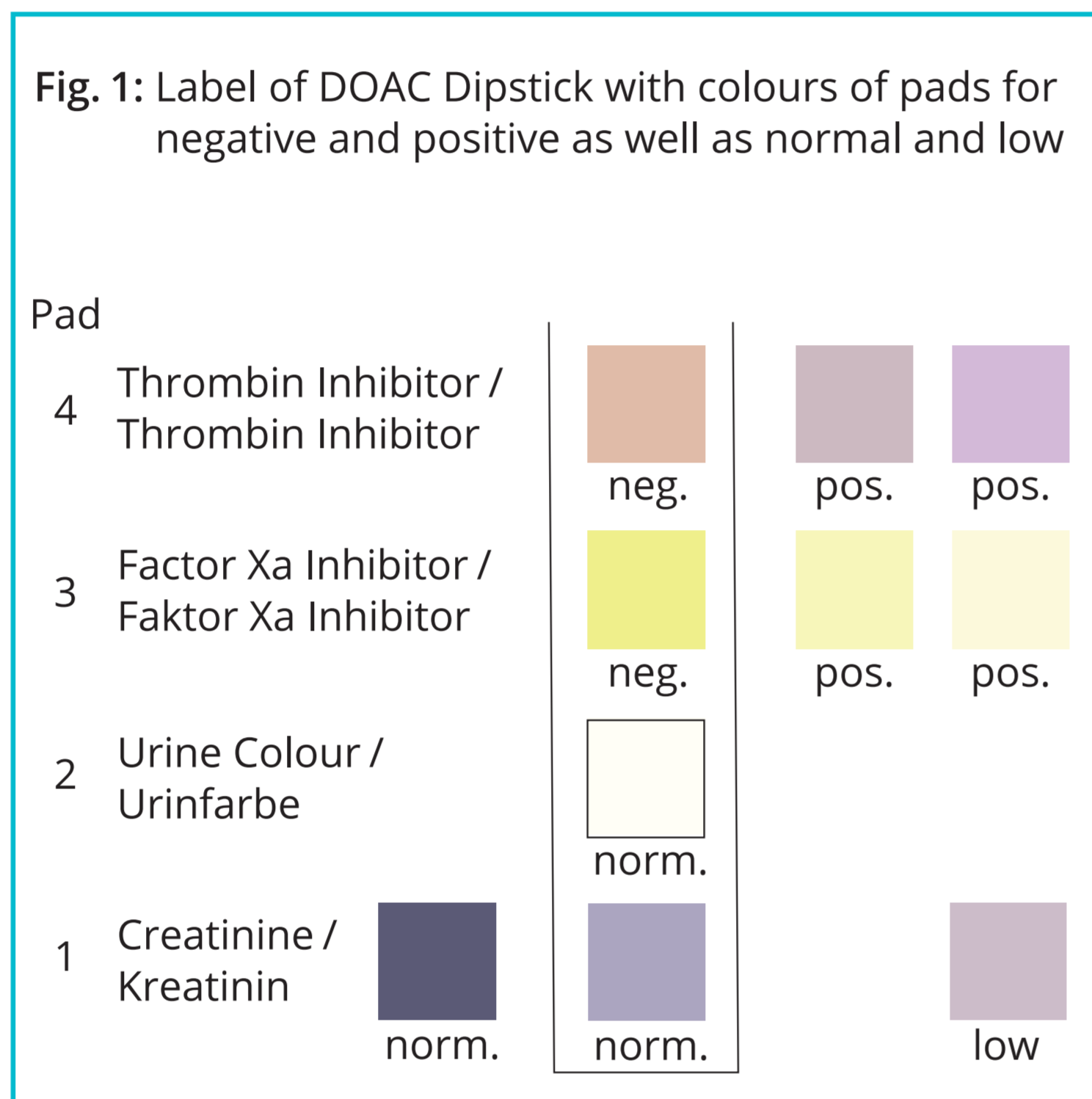
When every minute counts ...



... fast DOAC testing matters.

Methods and results

- The reagents are immobilized on the surface of the DOAC Dipstick pads.
- When the reagents react with urine, specific colours develop according to the action of factor Xa or thrombin on the release of a chromophore bound to a substrate.
- Chromophore release is negatively related to the amount of DOAC in urine and different chromophore colours indicate the absence or presence of factor Xa and thrombin inhibitors on the same test strip.
- Yellow indicates the absence of factor Xa inhibitors and white indicates the presence of factor Xa inhibitors.
- Ochre indicates the absence of thrombin inhibitors and rose indicates the presence of thrombin inhibitors.
- The pad colours can be visually identified as early as 10 min. after incubation of test strip with a urine sample. Pad colours are printed on the test tube for comparison (Fig. 1).



Creatinine (pad 1)

If the colour of pad 1 corresponds to the "normal" colour ("norm") or is between the "norm" or "low" colours on the tube label, then creatinine in the urine is normal, indicating normal renal function (Fig. 2, examples A and B).

If the colour of pad 1 corresponds to the "low" colour or is lighter than the respective colour on the tube label, then creatinine in the urine is low, indicating renal insufficiency. The results of pads 3 and 4 may be false negative (Fig. 2, example C).

Urine colour (pad 2)

If the pad colour is white like the respective colour marked "norm" on the tube label, then the colours of pads 1, 3,

and 4 can be visually evaluated (Fig. 2, examples A, B and C).

If the colour of the pad is darker than the colour "norm" on the tube label, the colours of pads 1, 3, and 4 may be falsified (Fig. 3, example D).

Direct oral factor Xa inhibitors (pad 3)

The test pad detects all currently licensed direct oral factor Xa inhibitors, i.e. apixaban, edoxaban, and rivaroxaban. The different inhibitors cannot be distinguished.

If the colour of pad 3 is yellow like the colour marked "neg." (negative) on the tube label, then direct oral factor Xa inhibitors are not present in the urine sample (Fig. 2 B).

If the colour of pad 3 is less yellow than the colour marked "neg." or is white like the colour marked "pos." (positive) on the tube label, then one direct oral factor Xa inhibitor is present in the urine (Fig. 2, example A).

Direct oral thrombin inhibitors (pad 4)

If the colour of test pad 4 is ochre like the colour marked "neg." on the tube label, then a direct oral thrombin inhibitor is not present in the urine sample (Fig. 2, example A).

If the colour of pad 4 is between the ochre colour marked "neg." and the rose colour marked "pos.", or rose like the colour marked "pos." on the tube label, then a direct oral thrombin inhibitor is present in the urine (Fig. 2, example B).

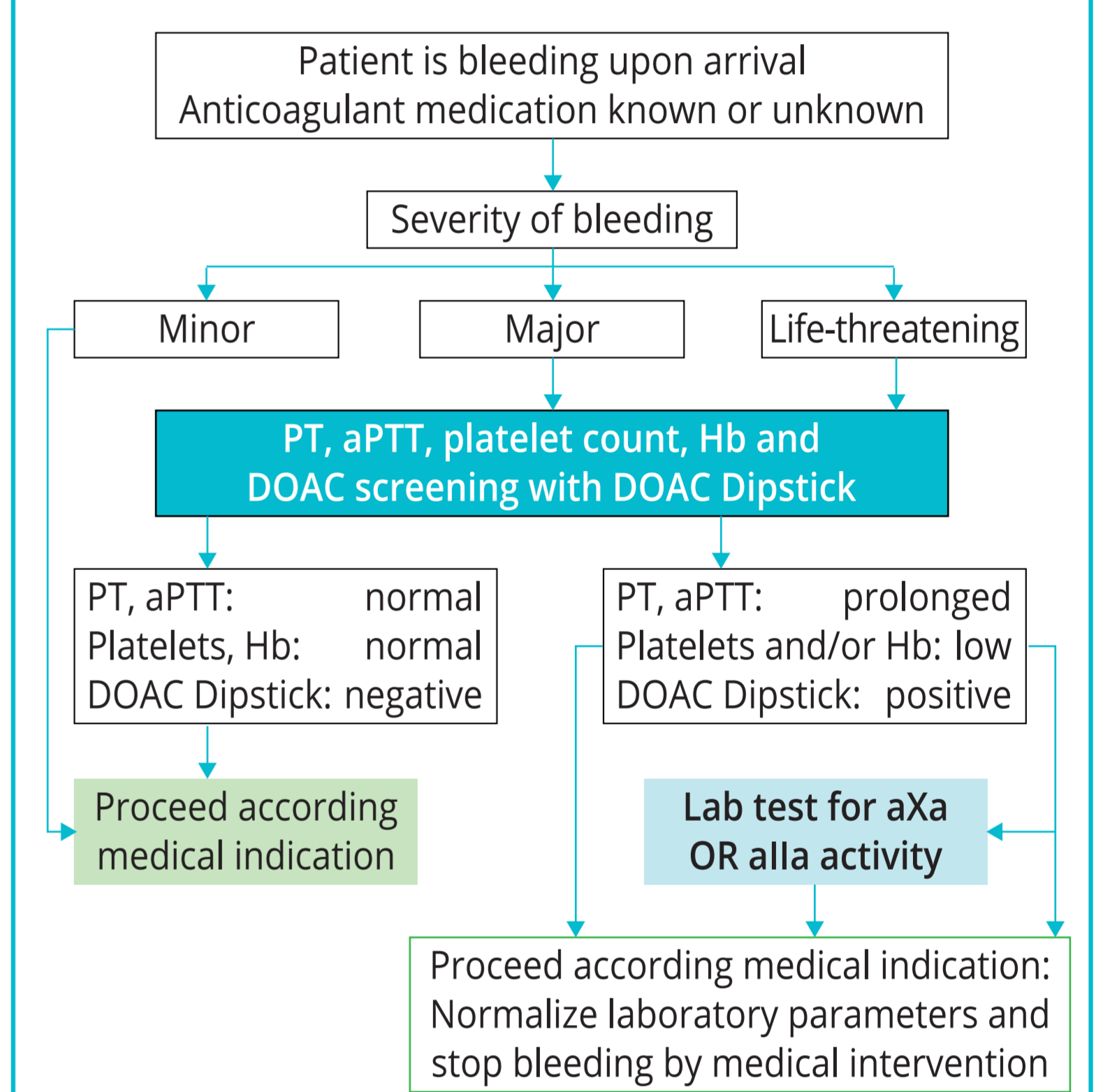
Fig. 2: Results of colours of pads 1 to 4 of DOAC Dipstick. Examples A and B represent colours of pads the presence or absence of direct oral Factor Xa and Thrombin inhibitors in urine. Example C shows results of a urine samples with low creatinine and false negative results of pads 3 and 4. Example D shows results of colours of pads when colour of urine sample (pad 2) is not-normal.

Pad	Example A	Example B	Example C	Example D
4	Thrombin Inhibitor: negative	Thrombin Inhibitor: positive	Thrombin Inhibitor: not evaluable	Thrombin Inhibitor: not evaluable
3	Factor Xa Inhibitor: positive	Factor Xa Inhibitor: negative	Factor Xa Inhibitor: not evaluable	Factor Xa Inhibitor: not evaluable
2	Urine Colour: normal	Urine Colour: normal	Urine Colour: normal	Urine Colour: not-normal
1	Creatinine: normal	Creatinine: normal	Creatinine: low	Creatinine: not evaluable

Clinical Scenarios

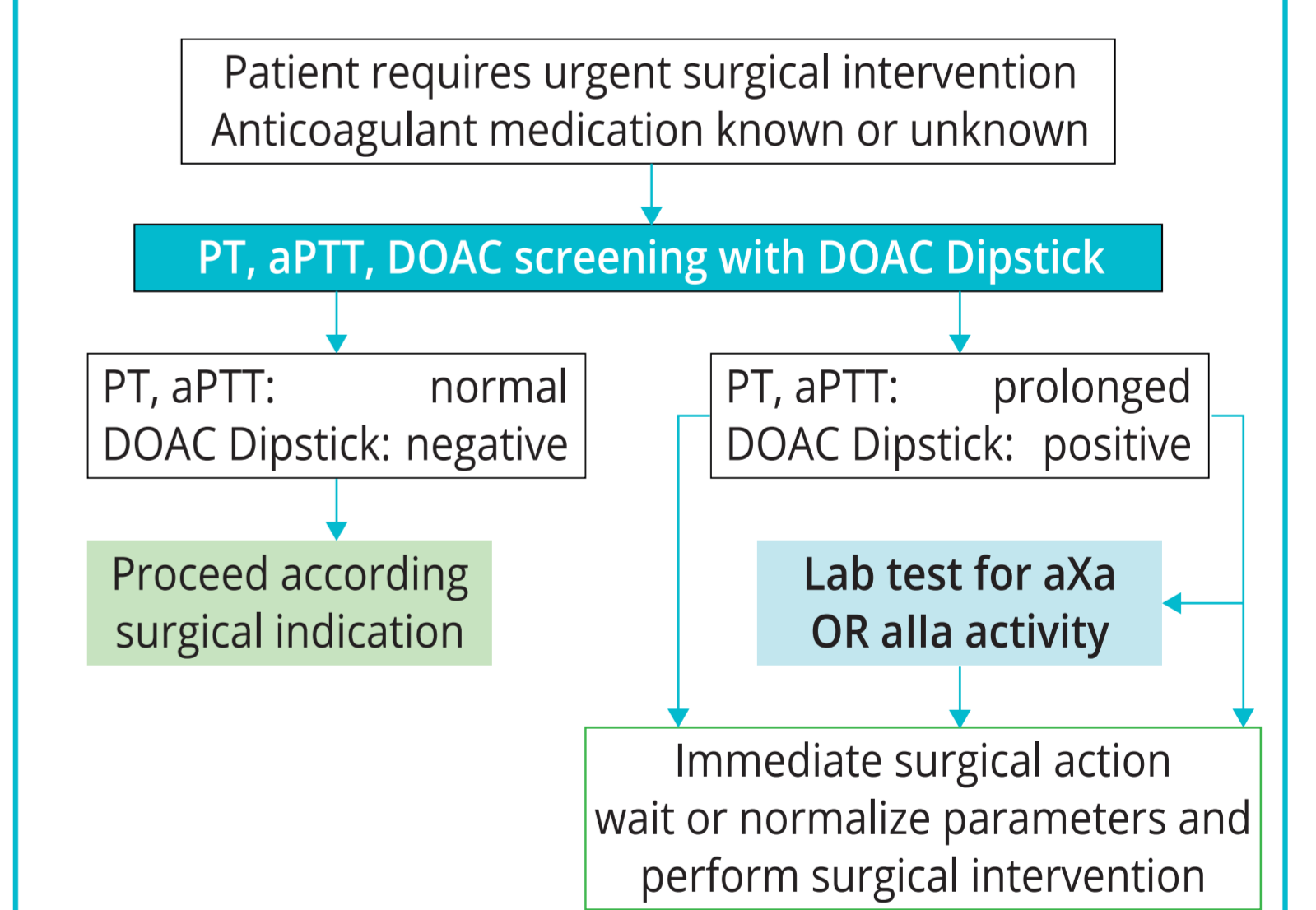
Scenario 1:

Usefulness of DOAC Dipstick in a patient with an acute bleeding event and known or unknown DOAC medication



Scenario 2:

Usefulness of DOAC Dipstick in a patient about to receive an acute major surgical intervention with known or unknown DOAC medication



Potential position of IVD DOAC Dipstick in clinical management:

In a patient with an unknown medication/anticoagulant history, the result obtained with the IVD DOAC Dipstick reduces the number of coagulation assays needed to identify the two types of DOACs from two to one, i.e. factor Xa- or thrombin inhibitors.

The authors thank Ulrich Warttinger for the electronic photographs, and Simone Mangold for preparation of scenarios.

Conclusions

- The qualitative determination of anti-IIa and anti-Xa DOACs by the IVD DOAC Dipstick in urine samples may offer a way

for healthcare professionals to detect DOACs in specific patient populations.

- The test results may substantially shorten clinical decision-making.
- The limitations of renal insufficiency and not-normal urine colour are eliminated to detect DOACs in urine by the IVD DOAC Dipstick.

Conflict of interest / address

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