Availability of direct oral anticoagulants testing among Italian anticoagulation clinics: a rapid evolution of clinical practice

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ABSTRACT

Background: Direct oral anticoagulants (DOACs) are largely prescribed, and the lack of need for a laboratory monitoring was the main reason for their large diffusion. However, a wide inter-individual variability has been described, and the need for blood levels measurement when a thrombotic or hemorrhagic event occurred has been suggested.

Materials and methods: In 2022, a survey was conducted among the Italian centers affiliated with the Italian Federation of Centers for the Diagnosis of Thrombotic Disorders and the Surveillance of the Antithrombotic Therapies - FCSA, recording that only few centers provided DOACs testing. In 2025, a second survey was performed to evaluate if a change in that area have occurred.

Results: We observed a rapid increase in the number of centers providing DOAC testing, from 39/124 (31.0%) in 2022 to 72/122 (59.0%) in 2025; 26% of centers not providing DOAC testing, claimed no funding for testing. In 70/72 (97.2%) of centers, DOAC testing was limited to selected conditions, such as thrombotic or hemorrhagic complications.

Conclusions: Data derived from our survey are relevant in developing adequate anticoagulation stewardship programs, that are increasingly required.

Key words: direct oral anticoagulants; laboratory test; anticoagulation management.

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Dedication: this paper is dedicated to the memory of Armando D'Angelo.

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Introduction

Direct oral anticoagulants (DOACs) have been introduced to the market fifteen years ago, after the demonstration of non-inferiority for efficacy and safety with respect to warfarin in patients with atrial fibrillation and acute venous thromboembolism. Since their approval, despite the higher costs, a large diffusion in their use has been recorded due to the fixed dosage and the independence from laboratory monitoring. In particular, the lack of need for laboratory monitoring was the main reason for the large diffusion of these drugs in clinical practice. However, after marketing, several data were published indicating that a wide inter-individual variability was present,[1,2] and the need for blood levels measurements when a thrombotic or hemorrhagic event occurred has been outlined by several authors.[3-8] After many years of DOACs use in clinical practice, the need for DOACs measuring has progressively increased. However, clinicians seem largely not aware of the opportunity of measuring these drugs to manage adverse events or invasive procedures. Moreover, laboratories are frequently not interested in implementing these new tests. Therefore, in many hospitals DOAC testing is still not available. The International Council for Standardization

in Hematology (ICSH) in 2021 redacted a Consensus Recommendation to collect information on DOACs testing availability around the world with the aim of helping the working parties to provide guidelines.[9]

Therefore, in 2022 we performed a survey among the Italian centers affiliated with the Italian Federation of Centers for the Diagnosis of Thrombotic Disorders and the Surveillance of the Antithrombotic Therapies (FCSA), which recorded a limited number of centers that provided DOACs testing.[10] During the last years, FCSA has promoted the adoption of DOAC testing by the affiliated centers, in the frame of the educational program conducted by the Federation, including webinars, meetings, the publication of an annually-updated guide for the management of antithrombotic therapies, and the use of an app specifically developed for mobile phones.[11] After 3 years from the first survey, we decided to ask again the FCSA affiliated centers to evaluate if a change in that area had occurred.

Materials and methods

The survey was available on a dedicated online form, guaranteeing anonymity. An e-mail invitation was sent to all 251 FCSA Centers affiliated with FCSA in February 2025, followed by two reminders in the subsequent weeks.

The survey included a request for general information about: i) characteristics of the center: ii) number of patients, patients on Vitamin K Antagonists

(VKAs) and/or patients on DOACs; iii) availability of DOAC testing; reasons why testing is not available; median number of DOAC tests performed monthly; indication for testing; timing of test availability (twenty-four hours or daily working hours); modality of collecting results in relation to the safety cut-off.

The results were analyzed using only descriptive statistics: categorical data were reported as counts and percentages.

Results

We asked to the 251 federated centers to participate to the online survey, and 122 (48.6%) of them agreed. Participating centers followed in total 168.672 anti-coagulated patients. The online survey performed in 2022 had a similar rate of participation (124 centers, 49.4%). The participating centers were equally distributed among the country: 51 (41.8%) from the northern, 36 (29.5%) from the central, and 35 (28.7%) from the southern Italian regions, and were distributed in 16 of the 21 regions.

Forty-seven centers (38.5%) followed only patients on VKAs treatment, with a median number of 300 patients [interquartile range (IQR) 150-700 pts] regularly managed; 75 centers (61.5%) followed both patients on VKAs and on DOACs treatment, with a median number of 1400 patients regularly managed (IQR 850-2350 pts). A minority of centers (9/122, 7.4%) followed a small group of patients (<100 pts); 115/122 (94.3%) of the centers used dedicated electronic programs for the management of VKAs treatment.

Comparing the results of the survey conducted in 2022 with the results of the survey conducted in 2025, we observed a large difference in the number of affiliated centers that followed patients on DOACs treatment, with an increase from 50 centers (40%) recorded in 2022 to 75 centers (61.5%) recorded in 2025 (Figure 1).

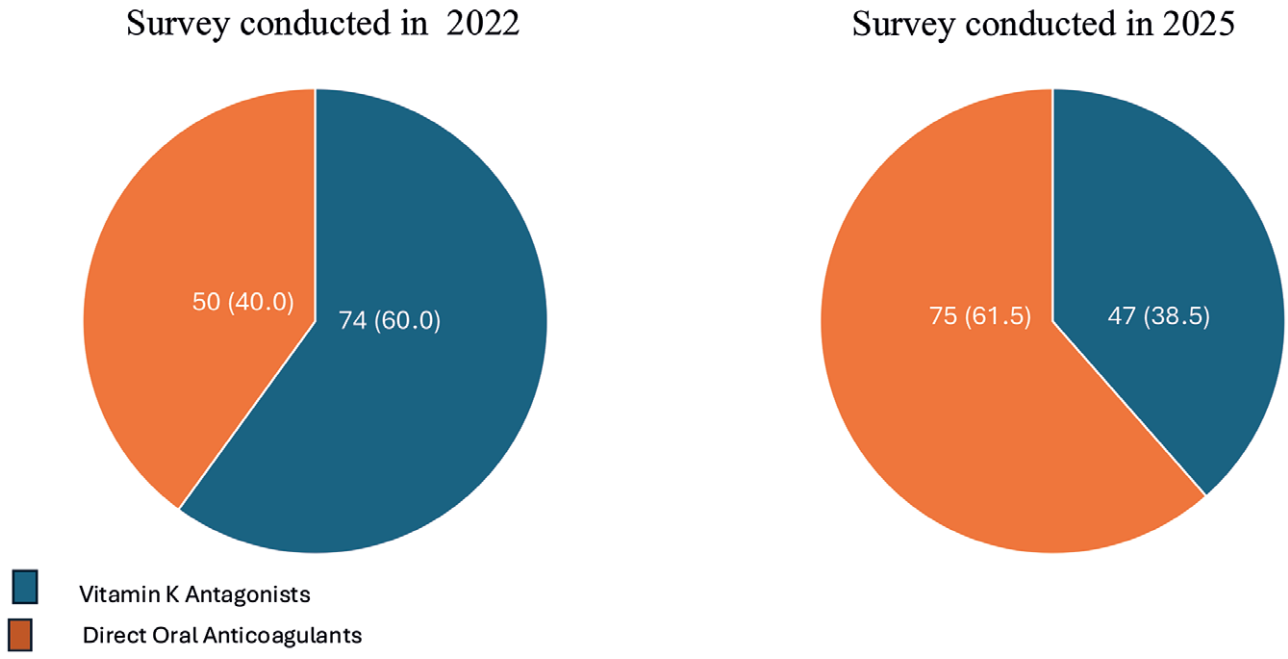


Figure 1. Centers following only patients on vitamin K antagonists and centers following all anticoagulated patients in 2022 compared to 2025.

Similarly, in the short period of three years, we recorded an increase in the number of centers where laboratories provide DOAC testing. In 2022, only 39/124 centers (31.0%) declared to have dedicated test for DOACs, while in 2025 72/122 (59.0%) of the centers declared to have availability for DOAC testing (Figure 2). Only in 8/122 centers (11.1%) the number of tests performed per month was elevated (≥80). Among the 50 centers where DOACs testing was not available, 16 (26.0%) declared that hospital administration did not provide funding to purchase reagents for testing. This reason for not testing was reported in the 16% of cases in 2022; 20 centers (40.0%) declared that clinicians do not prescribe DOAC testing.

In the great majority of the centers, 70/72 (97.2%), DOAC testing was limited to selected conditions such as: thrombotic or hemorrhagic complications, suspected drug-drug interaction, reduced renal function, extreme body weight. The safety cut-off used in the different centers was reported by 60/72 centers (83.3%) (Table 1). Only 15/122 centers (12.3%) were able to provide a twenty-four hours testing. Three centers provided urine qualitative test for DOACs detection, one center provided the urinary test and blood DOAC testing, the other two centers provided only urinary test.

Discussion

The main result of the survey conducted among Italian Centers affiliated with FCSA in 2025 is the large increase in the number of centers that started to provide DOAC testing with respect to the survey conducted in 2022.[10] The rapid increase in the number of centers starting to provide DOAC testing, suggests an enhanced awareness of this clinical needing. In the great majority of cases, measurement is limited to specific clinical conditions, such as bleeding or thrombotic events, extreme body weight, need for high bleeding risk surgery or procedures, or suspected drug-drug interference. Only in a minority of cases (5 centers, 6.9%) the large number of measurements suggests a use of the tests for a sort of 'monitoring' of the treatment.

The need for availability of DOAC testing has been outlined by international guidelines, in particular for the management of bleeding complications.[9-12] Moreover, the management of patients on DOACs undergoing surgery or invasive procedures requires attention when the patient or the type of procedure are at high risk for bleeding.[13,14] Therefore, our results suggest that centers generally provide an adequate use of DOAC testing, avoiding measurements that are aimed at monitoring blood concentrations and eventually adapting the dosage accordingly. The ICSH Working Party suggests to use testing in the context of patients history, taken into account DOAC type, DOAC dose and timing of assumption of the last dose and the potential impact on patients management, especially in relation to surgery, bleeding and use of reversal strategies.[9]

Moreover, the survey recorded that when DOAC testing is provided, the results are given with the indication of the safety cut-off. In patients with severe bleeding, a drug concentration of >50 ng/mL is considered to require an active reversal strategy. Instead, when a patient requires surgery at high bleeding risk, drug blood concentration should be <30 ng/mL.[14-16] In patients with acute stroke occurring during DOAC treatment, intravenous thrombolysis is contraindicated and a safety cut-off is

Table 1. Safety cut-off of direct oral anticoagulants blood levels indicated by the centers.

Safety cut-off	N. of centers (%)
<20 ng/mL	30 (41.7)
<30 ng/mL	10 (13.9)
<40 ng/mL	2 (2.8)
<50 ng/mL	18 (25.0)
Not available	16 (16.6)

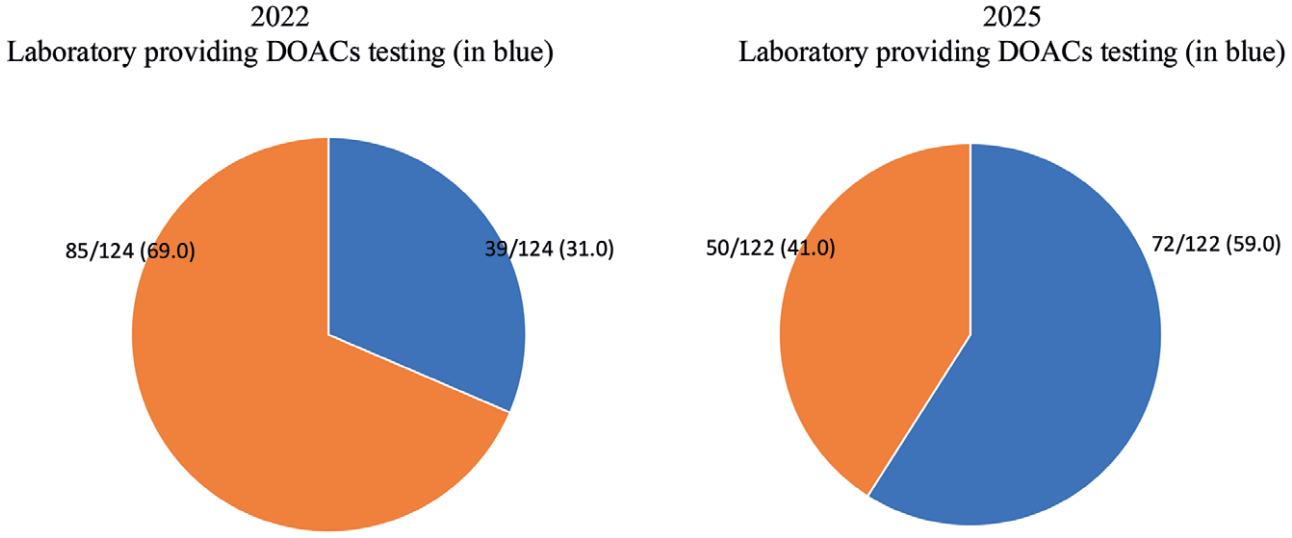


Figure 2. Centers providing direct oral anticoagulants (DOACs) testing recorded in 2022 compared to that recorded in 2025.

indicated in blood concentrations <20 ng/mL.[17] However, no specific recommendation by international guidelines is yet available. In the survey we recorded that more than 90% of centers declared to report a safety cut-off in the laboratory report. In 33.4% of cases the safety threshold was indicated as a concentration <50 ng/mL, whereas it was indicated <30 ng/mL from the majority of the centers. These results indicate that safety is the main objective of DOAC testing, according to the guidelines.

Analyzing centers where no DOAC testing was available, 26% of them declared that the reason for not testing was due to hospital administration, that did not provide funds to purchase reagents. The progressive reduction in economic resources provided by the National Health Service is a serious limitation to update the level of medical and laboratory services to the increasing clinical needs. Accordingly, with the reduced resources available, only 15/122 centers (12.3%) were able to provide a twenty-four hours testing. We are aware of the limitations of our study. Firstly, only 48.6% of affiliated centers participated in the survey. However, it should be noted that among centers affiliated with FCSA, 32 are laboratories that limit their interest to VKAs management, therefore with less interest in managing patients on DOACs. Moreover, in recent years several centers have undergone a reduction in the number of healthcare operators, with a substantial weakening of their activity. Secondly, we do not have information on the diffusion of DOACs testing in hospitals not adhering to the Federation. However, due to the specific role of FCSA in anticoagulation management, we can reasonably hypothesize that centers affiliated to FCSA are more interested and motivated to implement their performance with respect to not affiliated centers.

Conclusions

Anticoagulation management experts should continue to outline the need for adequate laboratory monitoring to manage adverse events in anticoagulated patients, to minimize risks and optimize resources.[18] The use of reversal strategies and antidotes requires the objective demonstration of anticoagulants effects to limit thrombotic risks and treatment costs. Data derived from our survey are of relevance in adequating anticoagulation stewardship programs that are increasingly required.

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