

Management of oral anticoagulant reversal prior to emergency surgery: are we following guidelines in the United States?

Jerrold H Levy¹, Marie E Steiner²,
Jean M Connors³

¹Division of Cardiothoracic Anesthesiology and Critical Care, Department of Anesthesiology, Duke University School of Medicine, Durham, NC, USA; ²University of Minnesota Department of Pediatrics, Hematology, and Critical Care, Minneapolis, MN, USA; ³Hematology Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Introduction

- Patients receiving anticoagulant therapies such as vitamin K antagonists (VKAs) or nonvitamin K oral agents (NOACs) are at increased risk of bleeding during emergency surgery, as there is often insufficient time to allow the anticoagulant effect to dissipate. Therefore, strategies are needed to reduce bleeding risk.
- Potential anticoagulation reversal strategies include oral/intravenous vitamin K, fresh frozen plasma (FFP), activated prothrombin complex concentrates (PCCs), 3- or 4-factor PCCs (3F-PCC and 4F-PCC, respectively) and recombinant (r) factor concentrates such as rFVIIa.^{1,2}
- The American College of Cardiology and American College of Chest Physicians recommend the use of PCCs as first-line therapy for urgent VKA reversal in adults requiring an emergency surgical/invasive procedure.^{1,3,4} PCCs are also recommended for non-specific reversal of NOAC anticoagulation in this patient population when specific reversal agents (e.g. idarucizumab, andexanet alfa) are unavailable.^{1,3}
- Various factors may prevent anesthesiologists from administering anticoagulation reversal agents in a timely fashion in an emergency surgery setting; these include lack of product availability, lack of understanding, inefficient hematology approval systems in hospitals, and other potentially unexplored issues.
- To address this uncertainty, we created a survey to determine current clinical practices and clinician understanding of the recommended use of these anticoagulation reversal agents in emergency surgery. We hope that the results of the survey will help to provide improved education and knowledge among clinicians who manage emergency situations.

Methods

- A 22-question survey covering aspects of clinical practice relating to oral anticoagulant reversal was sent to American Society of Anesthesiology members. Weekly reminders were sent during data collection from 22 October to 4 December 2018. Responses were collected using the Survey Monkey platform and are presented descriptively here.

Results

- Responses were received from 2315 anesthesiologists; key demographic details are shown in **Table 1**.
- The majority of respondents were aged >30 years (97.2%; n=2246/2310), US-based (85.5%; n=1969/2302) and community practitioners (60.1%; n=1384/2304).

Table 1. Key demographic details of respondents

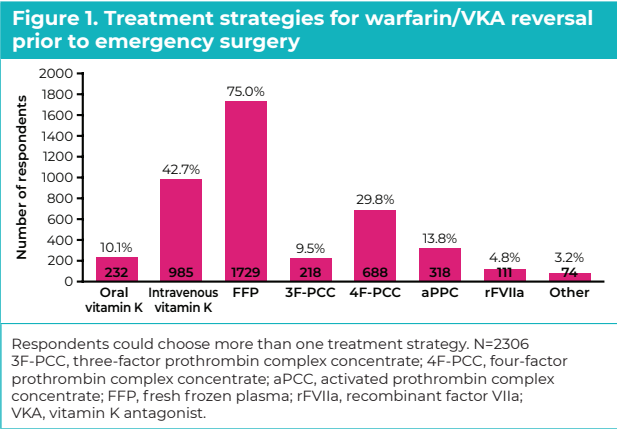
Characteristic	Proportion of respondents (%)
Age*	
≤30 years	2.8
31–40 years	24.4
41–50 years	24.7
51–60 years	31.1
61–70 years	15.3
≥70 years	1.8
Country [†]	
USA	85.5
Non-USA	14.6
Area of clinical focus [‡]	
General anesthesia	36.2
No specific area of focus	24.3
Cardiothoracic	17.5
Other	11.2
Practice setting [§]	
Community hospital	60.1
Academic teaching institution	39.9

Participants could select ≥1 country or area of clinical focus. Areas including >5% of respondents are listed. *N=2310; [†]N=2299; [‡]N=2251; [§]N=2304.

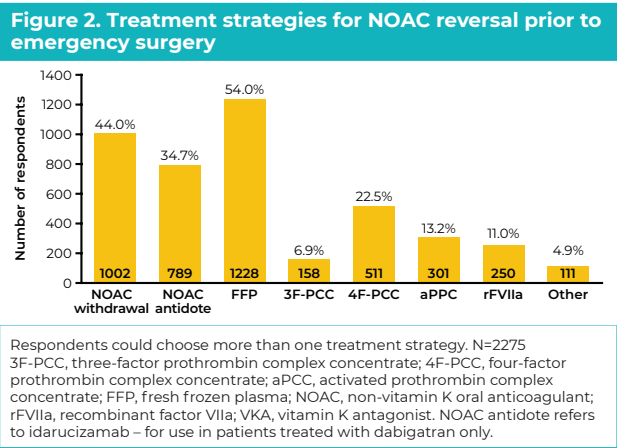
References

- Tomaselli GF, et al. J Am Coll Cardiol 2017;70(24):3042–3067.
- Agno W, et al. Chest 2012;141(2 Suppl):e44S–e88S.
- American College of Cardiology, 2018. Guidance for anticoagulation reversal. Available from: https://www.acc.org/-/media/Non-Clinical/Images/Tools%20and%20Practice%20Support/Mobile%20Resources/ManageAnticoag/B18120_ManageAnticoag_App_Fact_Sheet.pdf.
- Holbrook A, et al. Chest 2012;141(2 Suppl):e152S–e84S.

- Emergency surgery was defined as within 4 hours by 60.4% (n=1392/2304) of respondents.
- FFP was selected by 75.0% (n=1729/2306) of respondents for warfarin/VKA reversal prior to emergency surgery (**Figure 1**).



- 41.0% (n=945/2306) of respondents selected a single treatment strategy for warfarin/VKA reversal prior to emergency surgery.
 - 24.8% (n=573/2306) selected FFP alone and 8.8% (n=203/2306) selected 4F-PCC alone.
- 59.0% (n=1361/2306) of respondents selected two treatments or more.
 - 34.6% (n=797/2306) selected both FFP and intravenous vitamin K.
 - 14.5% (n=334/2306) selected both FFP and 4F-PCC.
 - 13.1% (n=301/2306) selected both 4F-PCC and intravenous vitamin K.
- FFP was also a preferred treatment for NOAC reversal prior to emergency surgery (selected by 54% [n=1228/2275] of respondents) (**Figure 2**).

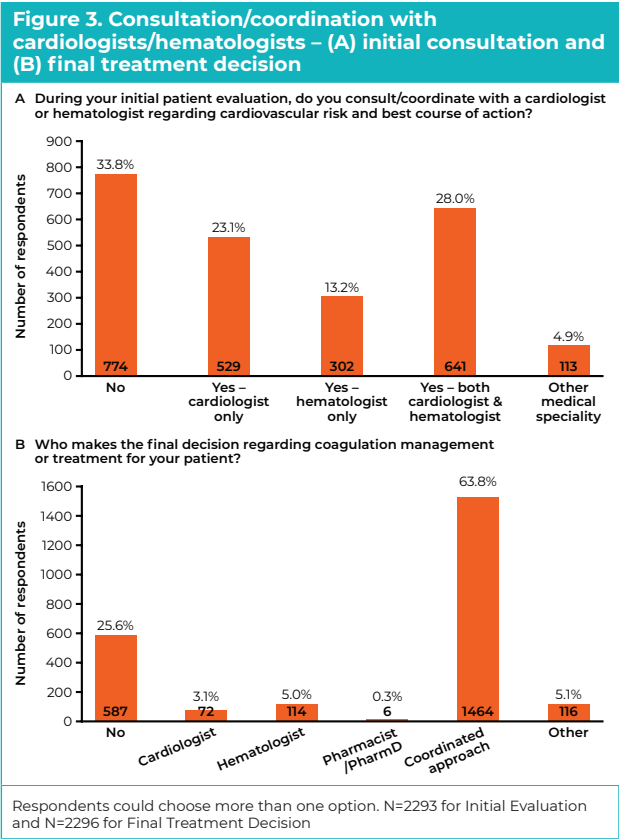


- 44.6% (n=1014/2275) of respondents selected a single treatment strategy for NOAC reversal prior to emergency surgery.
 - 20.5% (n=466/2275) selected FFP alone and 9.7% (n=220/2275) selected NOAC withdrawal alone.
- 55.4% (n=1261/2275) selected two or more treatment strategies.
 - 20.6% (n=468/2275) of respondents selected both NOAC withdrawal and NOAC antidote; 8.0% (n=183/2275) selected these agents and also FFP.
 - 9.1% (n=207/2275) selected both FFP and 4F-PCC.
- Overall, 68.3% (n=1572/2300) of institutions did not have a standardized protocol for emergency warfarin/VKA reversal.

Disclosures

JHL: serves on research steering committees or advisory boards for Boehringer-Ingelheim, CSL Behring, Instrumentation Laboratories, and Merck.
MES: none.
JMC: Bristol-Myers Squibb: scientific advisory boards, consultant; Portola: scientific advisory boards; CSL Behring: research funding to the institution.

- The majority of respondents preferred an International Normalized Ratio (INR) goal of ≤1.5 for VKA reversal; 12.6% (n=290/2244) of respondents selected an INR goal of ≤1.3, 16.3% (n=376/2244) selected ≤1.4 and 53.8% (n=1238/2244) selected ≤1.5.
- Approaches to initial patient management were variable (**Figure 3A**); 33.8% (n=774/2293) of respondents did not consult with either a cardiologist or a hematologist during their initial consultation, while 28.0% (n=641/2293) consulted with both.
- The majority of respondents (63.8%; n=1464/2296) noted that the final decision regarding coagulation management was a coordinated approach (**Figure 3B**); 25.6% (n=587/2296) made the decision themselves.



- Less than half of the respondents (48.6%; n=1095/2252) were able to prescribe 4F-PCC for emergency surgery without requiring approval from a hematologist consultation.
- PCCs were primarily obtained from the pharmacy (60.6%; n=1225/2021) and the blood bank (32.6%; n=659/2021).

Conclusions

- These results indicate that FFP is still extensively used for emergency VKA and NOAC reversal in the USA, despite guideline recommendations that PCCs should be used as first-line therapy in this setting.
- Many respondents did not consult or coordinate emergency anticoagulation management with hematologists during initial patient management, yet nearly half required hematologist approval to proceed with PCC administration.
- There is a need to improve communication between anesthesiologists and other specialty areas when making decisions on patient care; improved education and guideline review are essential for preoperative optimization of anticoagulated patients who require emergency surgery.

Acknowledgments

Medical writing support was provided by Hanna Mourad-Agha of Fishawack Communications Ltd, Abingdon, UK, funded by CSL Behring.

Funding: This study was supported by CSL Behring.