



# Timing of anticoagulant re-initiation following intracerebral hemorrhage in mechanical heart valves: Survey of neurosurgeons and thrombosis experts

Fahad AlKherayf<sup>a,e,\*</sup>, Yan Xu<sup>b,d</sup>, Harrison Westwick<sup>c</sup>, Ioana Doina Moldovan<sup>a</sup>, Philip S. Wells<sup>d,e</sup>

<sup>a</sup> Division of Neurosurgery, Department of Surgery, University of Ottawa, Ottawa, Canada

<sup>b</sup> School of Medicine, Queen's University, Kingston, Canada

<sup>c</sup> Division of Neurosurgery, Department of Surgery, Hôpital du Sacré-Coeur de Montréal, Montreal, Canada

<sup>d</sup> Division of Hematology, Department of Medicine, Ottawa, Canada

<sup>e</sup> The Ottawa Hospital Research Institute, Ottawa, Canada

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## ABSTRACT

**Background:** While oral anticoagulation (OAC) is universally indicated for patients with mechanical heart valves (MHVs), OAC resumption following anticoagulant-associated intracerebral hemorrhage (ICH) is an area of uncertainty. We sought to determine the practice preferences of North American neurosurgeons and thrombosis experts on optimal timing of OAC re-initiation.

**Methods:** A cross-sectional survey was disseminated to North American members of the American Association of Neurological Surgeons and the International Society for Thrombosis and Haemostasis. Demographic factors, as well as a clinical scenario with 14 modifiable clinical risk factors were included in the survey.

**Results:** 504 physicians completed our survey (response rate 34.3%). Majority of participants were affiliated with academic centres, and managed  $\leq 10$  ICH patients with MHV per year. There was wide distribution in response in optimal timing for OAC resumption following an ICH: 59% and 60% preferred to re-start OAC between 3 and 14 days following the hemorrhagic event (median of 6–7 days). Smaller hemorrhages ( $<30$  cm<sup>2</sup>). CHADS<sub>2</sub> score  $\geq 2$ , concomitant venous thromboembolism, mitral valve prosthesis, caged-ball valves and multiple valves prompted earlier OAC resumption.

**Conclusion:** Wide variation in the current practice of neurosurgeons and thrombosis specialists exist when they encounter patients with ICH and MHV, though decisions were influenced by patient- and valve-related factors. As our observed variation likely reflects the immense gap in current evidence, prospective randomized trials in this population are therefore urgently needed.

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## 1. Introduction

While oral anticoagulation is universally recommended among patients with mechanical heart valves (MHVs) [1], there is limited evidence to guide clinicians in managing patients who suffer intracerebral hemorrhage (ICH), a feared complication of anticoagulant treatment estimated to occur at 2–3% per patient-year [2]. In particular, the timing of oral anticoagulant (OAC) re-initiation following stabilization of hemorrhage is challenged by the intricate

need to balance the risks of valve thrombosis and ischemic stroke with those of recurrent bleeding. Furthermore, venous thromboembolism is relatively frequent among patients who develop anticoagulant-associated ICH, an additional factor that may influence the benefit-risk ratio of OAC resumption [3,4].

Concomitant with this uncertainty, available literature suggests wide variation in practice patterns, with case series reporting OAC re-initiation between 3 and 28 days post-ICH [5]. While the 2015 American Stroke Association guidelines recommend withholding thromboprophylaxis among AF patients who develop intracranial hemorrhage for at least 4 weeks [6], no specific guidance was provided for MHV patients. Given this uncertainty, we sought to determine the current practice of neurosurgeons and thrombosis specialists in the United States (U.S.) and Canada regarding the

\* Corresponding author at: C2 Clinic—Division of Neurosurgery, The Ottawa Hospital, 1053 Carling Avenue, Ottawa, Ontario, Canada.  
E-mail address: [falkherayf@toh.ca](mailto:falkherayf@toh.ca) (F. AlKherayf).

**Table 1**  
Demographic Characteristics of Survey Respondents.

|  |                       | Neurosurgeons (%<br>n = 428) | Thrombosis Experts (%<br>n = 75) |
|--|-----------------------|------------------------------|----------------------------------|
| Thrombosis Subspecialties              | Hematology            |                              | 81                               |
|  | Internal Medicine     |                              | 19                               |
| Country of Practice                    | United States         | 89                           | 52                               |
|  | Canada                | 11                           | 48                               |
|  | Other                 | 0                            | 0                                |
| Years of Practice                      | 0–5                   | 30                           | 8                                |
|  | 6–10                  | 13                           | 13                               |
|  | 11–15                 | 16                           | 20                               |
|  | 16–20                 | 12                           | 13                               |
|  | 21–25                 | 12                           | 12                               |
|  | >25                   | 17                           | 33                               |
| Practice Setting                       | University            | 44                           | 76                               |
|  | University-Affiliated | 19                           | 17                               |
|  | Community/Private     | 37                           | 7                                |
| Average ICH Patients with MHV per year | 0–5                   | 44.2                         | 86.7                             |
|  | 6–10                  | 32.5                         | 12                               |
|  | 11–15                 | 12.6                         | 1.3                              |
|  | >15                   | 10.7                         | 0                                |

time to restart OAC in adult patients with MHV who present with anticoagulant-associated ICH.

## 2. Methods

### 2.1. Study population

We surveyed North American members of the American Association of Neurological Surgeons (AANS) and International Society of Thrombosis and Haemostasis (ISTH) in 2015. Active members of the AANS include neurosurgeons practising general neurosurgery or with specialized interests in neurosurgical subspecialties related to ICH, while ISTH members include clinicians (hematologists, stroke neurologists and cardiologists) with an interest in thrombotic diseases.

### 2.2. Survey

An online, cross-sectional survey (Appendix A in Supplementary material) was constructed on the SurveyMonkey platform using Dillman's principles of self-administered survey design [7,8]. The questionnaire began with 6 questions on the respondents' background, type of practice and exposure to anticoagulant-associated ICH in patients with MHV. This was followed by a clinical scenario involving ICH, qualified by 14 risk factors that may change a clinician's decision on OAC resumption. For each risk factor, respondents were asked when they would restart OAC from the time of hemorrhagic diagnosis. All answers were multiple choice with single response. Finally, respondents were asked whether they would be interested in enrolling patients into a randomized controlled trial or in a cohort study that aimed to address these clinical questions.

All data were initially collected and stored online via the SurveyMonkey tool, and only the survey administrator had access to the results. Reminder e-mails were sent to respondents who had completed ≤50% of the survey.

### 2.3. Data analysis

The outcome of interest was timing of OAC resumption, and we considered participant characteristics and demographics (speciality, country of practice, years in practice, type of practice and ICH cases managed per year) as covariates. For descriptive analysis, uni-

variate analysis was used to calculate variable characteristics at baseline, which were then stratified by covariates.

In addition, we performed bivariate analysis to examine the relationship of participant characteristics and demographics in response to the clinical scenarios.  $\chi^2$  test, Fisher's Exact test (for cell size ≤5) and student's *t*-test were used in bivariate analysis. P-value of 0.05 was considered statistically significant. STATA 11, SPSS, R2.15.1 and Microsoft Excel were used for the analysis.

### 2.4. Ethics

The survey was approved by the Ottawa Hospital Research Ethics Board (OHREB).

## 3. Results

A total of 1469 potential participants were identified, consisting of 1267 neurosurgeons and 202 thrombosis experts. 504 physicians (428 neurosurgeons and 75 thrombosis experts) completed our survey, for a response rate of 34.3%. Majority of participants were affiliated with academic centres, and managed ≤ 10 ICH patients with MHV per year. Details of participant characteristics are listed in Table 1.

In the case of ICH with no modifiable risk factors, there was wide distribution in response in optimal timing for OAC resumption (Fig. 1), though no specialty-specific difference was observed (*p* = 0.33 by  $\chi^2$  test). Among neurosurgeons and thrombosis experts, 59% and 60% preferred to re-start OAC between 4 and 14 days following the ICH diagnosis, with a median of 6–7 days. 16% of respondents intended to wait >21 days prior to re-initiation of thromboprophylaxis.

### 3.1. Impact of hemorrhage-related factors

When presented with scenario of hematoma size <30 cm<sup>2</sup>, respondents elected for earlier OAC re-start compared to hematomas >30 cm<sup>2</sup> (*p* < 0.001), especially among thrombosis experts (median restart time category 6–7 days vs. 8–14 days). For cases requiring surgical interventions, respondents opted to restart patients on anticoagulation with a median time of 6–7 days post-bleed; this did not differ from response to ICH with no risk factors, and there was no difference between neurosurgeons and thrombosis experts.

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