Anticoagulation after Spontaneous Intraparenchymal Hemorrhage in Patients with Mechanical Heart Valves and Concomitant Atrial Fibrillation

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Abstract

Aim Patients with mechanical heart valves and coexisting atrial fibrillation (AFib-MHV) who suffer an intraparenchymal hemorrhage (IPH, defined as bleeding solely within the brain parenchyma and/or ventricle) are at a high risk of thromboembolism without anticoagulation. Data are lacking regarding the safety of early re-initiation of anticoagulation in these patients.

Patients and Methods We performed a descriptive, single-institution retrospective analysis of patients with AFib-MHV who suffered a non-traumatic, supratentorial IPH between July 2013 and June 2017. We analyzed the patients and IPH characteristics, anticoagulation and antiplatelet use, the occurrence of thrombotic and hemorrhage complications, and discharge disposition. We described the timing of initiation of anticoagulation and outcomes after IPH while in-patient.

Results Six patients with AFib-MHV suffered a spontaneous IPH. Four were initiated on anticoagulation prior to discharge, of whom two were initiated within 3 days post-hemorrhage. These patients suffered no bleeding complications and were discharged home with a modified Rankin Scale of 1.

Conclusion Patients with AFib-MHV who suffer a spontaneous IPH are a rare population to study. Further studies to guide the management of restarting anticoagulation in this select population are warranted.

Keywords
- anticoagulation
- intracerebral hemorrhage
- mechanical heart valve
- atrial fibrillation

Introduction

Patients with mechanical heart valves and coexisting atrial fibrillation (AFib-MHV) who suffer an intraparenchymal hemorrhage (IPH, defined as bleeding solely within the brain parenchyma and/or ventricle) are at a considerably high risk of thromboembolism when off their anticoagulation.[1-3] There are no studies determining when it is safe to restart anticoagulation after IPH for this select population.[1,4,5] Neurologists, cardiologists, and intensivists must weigh the risk of re-bleeding against the high risk of thromboembolism, and due to the lack of data, decisions must be made with little evidence, only that extrapolated from studies of patients with atrial fibrillation or mechanical heart valves (MHV) alone.

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The European Society of Cardiology (ESC) and American Heart Association/American Stroke Association (AHA/ASA) emphasize the need for earlier anticoagulation for patients with MHV due to their higher risk of embolism than patients with atrial fibrillation or other indications for anticoagulation, but there are no clear guidelines as to when it is most safe.[1-3,6] At best, the ESC states it "may be safe" to start systemic heparin 3 days after IPH and switch to a vitamin K antagonist (VKA) at 7 days.[1-3,6]

Patients with AFib-MHV have a higher risk of thromboembolic events compared with patients with high-risk atrial fibrillation (CHA_2DS_2-VAS_c >2)[7] and those with MHV with sinus rhythm.[8] The emphasis of early anticoagulation for patients with MHV is extrapolated to those with AFib-MHV but without better evidence of risk factors associated with good outcomes, the worry of IPH expansion after reinitiating anticoagulation will strongly persist.

To address the gap in the literature, we performed a retrospective analysis of patients admitted to our institution with non-traumatic supratentorial IPH in patients with AFib-MHV and compared those who were started on anticoagulation while in-patient with those who were not. We characterized the patients and their IPH and evaluated outcomes in terms of thromboembolic events, bleeding rates, and disposition. We hypothesized that anticoagulation within a few days post-IPH would be tolerated in select patients of this high-risk group.

Patients and Methods

We performed a single-institution retrospective analysis of patients with non-traumatic, supratentorial IPH. This study was approved by the Duke University Institutional Review Board. Adult patients ≥ 18 years old who were admitted to any Duke University Hospital for non-traumatic, supratentorial IPH between July 1, 2013, and June 20, 2017, were retrospectively identified from the DENDRITe database (DukE Neurocritical Care Patient Data ReposITory) and the Get With The Guidelines Stroke Database. Based on past medical history, we identified patients who had the following indications for anticoagulation prior to their hospitalization: atrial fibrillation or MHV. For this type of study, formal consent was not required.

The following data were extracted from the Duke electronic health record: patient's medical history; admission laboratory values; systolic blood pressure at the time of presentation to the hospital; IPH characteristics (including etiology, location—deep, hemispheric, lobar, multiple); intracerebral hemorrhage (ICH) score[9]; if applicable, type of neurosurgical intervention performed; code status; and if applicable, type, timing, and dose of anticoagulation or antiplatelet agent reinitiated. By chart review, we determined the occurrence of thromboembolic complications, defined as ischemic stroke, transient ischemic attack, myocardial infarction, valvular thrombus, or peripheral arterial embolism, and the occurrence of bleeding complications, defined as hematoma expansion >33% or >6 mL,[10] any major extracranial hemorrhage, or any overt, actionable sign of hemorrhage

Table 1 Patients with mechanical heart valve and concomitant atrial fibrillation initiated on anticoagulation prior to discharge

Patient	Age	Sex	GCS on admission	Location of hemorrhage	INR on admission	ICH volume (mL)	ICH score	Atrial fibrillation rate control	Mechanical valve type	CHA_2DS_2	HASBLED	Anticoagulation start date (days post-bleeding)	Anticoagulation restarted	LOS (days)	DC mRS	DC Dispo
1	45	F	15	Frontal lobe	4	6.6	0	Yes	Mitral	1	1	1	VKA[a]	18	1	Home
2	44	M	15	Frontal lobe	3.4	3	0	No	Aortic	1	3	2	VKA	2	1	Home
3	80	F	14	Basal ganglia	2.4	10	1	Yes	Mitral	1	4	13	VKA	12	2	SNF
4	72	M	15	Parietal lobe	4.8	6.6	1	No	Aortic and Mitral	6	5	18	VKA[a]	26	1	Home

Abbreviations: Afib, atrial fibrillation; DC, discharge; Dispo, disposition; F, female; GCS, Glasgow coma scale; ICH, intracerebral hemorrhage; INR, international normalized ratio; LOS, length of stay; M, male; mRS, modified Rankin Scale; SNF, skilled nursing facility; VKA, vitamin K antagonist.
[a]VKA started with a heparin.

(i.e., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that met at least one of the following criteria: (1) requiring nonsurgical, medical intervention by a healthcare professional, (2) leading to the increased level of care, or (3) prompting evaluation, according to Bleeding Academic Research Consortium Type 2 or greater.[11] We also reviewed the patient's chart for the modified Rankin Scale (mRS) at discharge[12]; discharge disposition; and date of death, if applicable. Hematoma volume was calculated based on the ABC/2 method.[13] The following were calculated based on extracted data whenever applicable: for patients with atrial fibrillation, and CHA_2DS_2-VASc and HAS-BLED scores[7,14] and for patients with a thromboembolic or hemorrhagic complication, time from IPH to complication and time from anticoagulation (if started) until complication.

Results

Non-traumatic supratentorial IPH was identified in 395 patients admitted to the Duke Health System during the study period, of whom 6 patients were identified to have Afib-MHV and were analyzed.

All patients suffered an IPH in the setting of anticoagulation and received reversal agents to correct their coagulopathy. All patients were managed medically according to the ASA/AHA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage,[2] which included treatment of coagulopathy and thrombocytopenia and acute lowering of blood pressure to < 140 mm Hg until stable intracranial imaging. One patient underwent hematoma evacuation out of concern for abscess as the etiology of the hemorrhage (►**Table 1**, Patient 1). The final pathology report revealed only blood products. One patient underwent placement of an extra-ventricular drain (►**Table 2**, Patient 2).

Four patients were initiated on anticoagulation prior to discharge (median 8.5 days post-IPH, range 1–18), and two of these patients were initiated on anticoagulation within 3 days post-IPH (►**Table 1**). Patients started on early anticoagulation had small hematoma volumes (<10 mL, mL), were relatively young (<50 years old), and tolerated anticoagulation without any hemorrhagic complications. There were no thromboembolic complications in these patients.

Two patients were not initiated on anticoagulation and died during their admission (►**Table 2**). These patients were older (>60 years) with large hematoma volumes (>30 mL). One died of multiorgan failure; the other was made comfort care.

Discussion

This is a descriptive study evaluating solely patients with AFib-MHV who suffered non-traumatic, supratentorial IPH and were reinitiated on anticoagulation while in-patient. As far as we know, this is the first study specific to this population to date. Four patients were started on therapeutic anticoagulation prior to hospital discharge, and two within 3 days after IPH. The etiology of IPH for all was predominantly due to therapeutic anticoagulation and all patients' coagulopathies were adequately reversed. Patients initiated on early anticoagulation were younger (<50 years old) and had smaller hematoma volumes (<10 mL). No patients suffered hemorrhagic complications of initiating anticoagulation. There was no institutional protocol to guide decision-making for whom and when to restart anticoagulation.

This study is unique from prior studies regarding atrial fibrillation and MHV because of its focus on patients with only concomitant Afib-MHV, who should be uniquely studied because of their different risk factors of both thromboembolic and bleeding complications off anticoagulation compared with patients with sole atrial fibrillation or MHV.[8] Kuramatsu et al's study,[8] the largest analysis of patients with MHVs who suffered vitamin-K antagonist associated IPH, revealed a statistically significant higher risk of bleeding complications and a non-statistically significant but higher risk of thromboembolic complications off anticoagulation for those with MHV-afib (n = 21) compared with those with sinus rhythm (n = 50).[8] There was no difference in bleeding complications when both groups were therapeutically anticoagulated.[8] The authors recommended waiting until day 14 to re-initiate anticoagulation for patients with MHV, except for patients with MHV-afib, who had a higher risk of thromboembolic complications. For these patients, anticoagulation 6 days post-bleeding seemed reasonable.[8]

Our patient population was also unique from prior studies because of its focus on patients who suffered only spontaneous, supratentorial IPH. A systematic review by Chandra et al. that has influenced guidelines determined that initiating heparin infusion within 3 days and oral anticoagulation within 7 days after intracerebral hemorrhage can be safe for patients with prosthetic heart valves[2,6]; however, their data were extrapolated from studies of patients with various indications for anticoagulation and various types of intracerebral hemorrhage, not just IPH.[2,6] Given its incomparable rate of re-bleeding and different pathophysiology than traumatic

Table 2 Patients with a mechanical heart valve and concomitant atrial fibrillation not initiated on anticoagulation

Patient	Age	Sex	GCS on admission	Location of hemorrhage	INR on admission	ICH volume (mL)	ICH score	Atrial fibrillation rate control agent	Mechanical valve type	CHA_2DS_2	HASBLED	Why no anticoagulation	Time from IPH until death (days)
1	84	M	10	Temporal	4.2	32	3	No	Mitral	7	2	Critical illness	10
2	85	M	5T	Frontal	5	60	5	Yes	Aortic	7	5	Comfort care within 48 h	2

Abbreviations: GCS, Glasgow coma scale; ICH, intracerebral hemorrhage; INR, international normalized ratio; IPH, intraparenchymal hemorrhage; mL, milliliters.

hemorrhages or subarachnoid hemorrhages, patients with IPH should not be concomitantly studied with other types of intracerebral hemorrhage when determining the safe timing of re-initiating anticoagulation post-bleeding.

For the time being, patients with Afib-MHV can only be anticoagulated with VKAs. There is currently no approval for the newer, direct oral anticoagulants for these indications. VKA-associated IPH can be reversed by several agents. Uncorrected coagulopathy in vitamin K antagonist-associated IPH is associated with worse outcomes, namely increased frequency of hematoma enlargement and rate of in-hospital mortality.[15] In light of this, the impact of the Kuramatsu et al's study is dampened by the fact that international normalized ratio (INR) reversal was achieved in only 25% of all patients.[8,15] Kuramatsu et al's conclusion to wait 6 days based on the hemorrhagic risk profile was likely skewed, given the known association between inadequate correction of coagulopathy and increased bleeding complication rate.

We acknowledge that a sample of two patients initiated on early anticoagulation is the main limitation of this study, in addition to its retrospective design. Given the small sample size and a sparse number of adverse events, we could not evaluate significant risk factors for those who tolerated early anticoagulation or risk of thromboembolic events if anticoagulation was delayed. Moreover, as a retrospective study, there was no systematic method of identifying thromboembolic and bleeding complications. A complication would have only been identified if the primary provider was concerned enough to order a diagnostic study.

This study highlights the rarity of this population. Prior studies emphasize the fact that the population is understudied, and there is a need for more robust data for this population of patients whose thromboembolic risk off anticoagulation is greater than those with sole MHV or Afib. A prospective or larger retrospective study is needed to inform the management and guidelines of this select population who face no option to stay off anticoagulation. Our study did show tolerance of early anticoagulation (within 3 days) in young patients with small hematoma volumes and coagulopathy-associated etiology of their IPH, which was corrected. Age, hematoma volume, and correction of coagulopathy are suggested risks factors to explore in future studies. Uncontrolled hypertension, poor neurological status, and the presence of cerebral amyloid angiopathy are also other known risk factors for recurrent IPH and worse outcomes. Although these were not a concern in our patient group, these could also be explored as additional risk factors.[2,16-19] Long-term risk of re-hemorrhage should also be studied.

Conclusion

Patients with MHV and coexistent atrial fibrillation who suffer spontaneous IPH are a rare population to study, and further research regarding risk factors for early anticoagulation in these patients is warranted to best inform the management of these patients with a high risk of thromboembolism off anticoagulation. We report two patients who tolerated early anticoagulation (within 3 days) after suffering a spontaneous IPH attributed to anticoagulation. We note that their small hematoma size, young age, adequate reversal of coagulopathy, and no comorbid hypertension or amyloid angiopathy may have been favorable risk factors for early anticoagulation.

Conflict of Interest

M.W.L. reports personal fees from Zinfandel Pharmaceutics, outside the submitted work. C.B.S. has received a speaker's honorarium from UCB and Eisai, and consulting fees from Marinus and Minnetronix, outside the submitted work. The other authors report no conflict of interest.

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Case Report

Endovascular Coiling in a Patient with Chronic Kidney Disease—A Challenge for Anesthesiologist

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Abstract

A 41-year-old male patient, a known case of autosomal dominant polycystic kidney disease (ADPCKD), presented to our institute with right middle cerebral artery aneurysm for which balloon-assisted endovascular coiling was planned. The major comorbidities were hypertension and end-stage renal disease (ESRD) on hemodialysis, twice weekly. Endovascular coiling was performed under general anesthesia, and special precautions were taken with regard to monitoring, fluid management, use of heparin, and contrast agent. The intraoperative and postoperative course was uneventful, and the patient was discharged after 7 days. In this report, various perioperative challenges of patients with chronic renal failure during coiling are discussed along with the measures to prevent the occurrence of contrast-induced nephropathy.

Keywords
- autosomal dominant polycystic kidney disease
- contrast induced nephropathy
- end-stage renal disease
- endovascular coiling
- iso-osmolar contrast medium

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