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Postoperative Anticoagulation in Patients with Mechanical Heart Valves Following Surgical Treatment of Subdural Hematomas

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Abstract

Background—Thromboembolic events and anticoagulation-associated bleeding events represent frequent complications following cardiac mechanical valve replacement. Management guidelines regarding the timing for resuming anticoagulation therapy following a surgically treated subdural hematoma (SDH) in patients with mechanical valves remains to be determined.

Objective—To determine optimal anticoagulation management in patients with mechanical heart valves following treatment of SDH.

Anubhav G. Amin and Julie Ng contributed equally to this study.

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Methods—Outcomes were retrospectively reviewed for 12 patients on anticoagulation therapy for thromboembolic prophylaxis for mechanical cardiac valves who underwent surgical intervention for a SDH at the Johns Hopkins Hospital between 1995 and 2010.

Results—The mean age at admission was 71 years. All patients had St. Jude's mechanical heart valves and were receiving anticoagulation therapy. All patients had their anticoagulation reversed with vitamin K and fresh frozen plasma and underwent surgical evacuation. Anticoagulation was withheld for a mean of 14 days upon admission and a mean of 9 days postoperatively. The average length of stay was 19 days. No deaths or thromboembolic events occurred during the hospitalization. Average follow-up time was 50 months, during which two patients had a recurrent SDH. No other associated morbidities occurred during follow-up.

Conclusion—Interruptions in anticoagulation therapy for up to 3 weeks pose minimal thromboembolic risk in patients with mechanical heart valves. Close follow-up after discharge is highly recommended, as recurrent hemorrhages can occur several weeks after the resumption of anticoagulation.

Keywords

Anticoagulation; Hemorrhage; Mechanical heart valve; Subdural hematoma; Thromboembolism

Introduction

Anticoagulation therapy is recommended for all patients following mechanical heart valve replacement [1]. Current guidelines recommend a target international normalized ratio (INR) between 2.0 and 4.5, depending on the thrombogenicity of the valve, the site of replacement, and the presence of associated risk factors [2]. Thromboembolic and bleeding events associated with chronic anticoagulation therapy represent the most frequent complications of mechanical valves; intracranial hemorrhages (ICHs) have been estimated to contribute to 90 % of deaths from warfarin-associated bleeding [3].

A survey of 435 patients aged 55 or older admitted to the neurology, neurosurgery or internal medicine services with primary supratentorial ICH at the Massachusetts General Hospital between 1994 and 2001 showed that approximately a quarter of those patients were on therapeutic levels of warfarin therapy at the time of admissions, which represented an average of one patient per month [4]. The annual incidence of anticoagulation-associated ICH has increased from 0.8 cases/100,000 persons per year in 1988 to 4.4/100,000 persons per year in 1999 and remains a significant source of morbidity and mortality [5]. Although the epidemiology of warfarin-related ICH has not been well studied in a population-based setting, the use of antithrombotic agents have been reported to account for approximately 15 % of ICH cases, and is associated with a mortality rate of 40–60 %, which has remained stable over time despite improvements in medical management [6].

Despite a progressive increase in the incidence of anticoagulation-associated ICHs, unified criteria for management remain undefined. Among unclear issues in management, the timing for resuming anticoagulation following a surgically treated subdural hematoma (SDH) in patients with mechanical heart valves remains to be determined. A review of the literature

within the past decade looking at the appropriate length of time to withhold anticoagulation after an intracerebral hemorrhage to prevent a re-bleed revealed a paucity of studies available to guide clinical decision-making with respect to balancing the risks of recurrent hemorrhage versus the risk of thromboembolism [7, 8].

In the present study we retrospectively analyzed a single center series of patients with mechanical heart valves who underwent surgical treatment of SDHs to evaluate the risk of thromboembolic complications following cessation of anticoagulation treatment, the risk of recurrent SDHs following re-initiation of anticoagulation treatment, and a review of the published literature.

Methods

Patients

After obtaining approval from the institutional review board (IRB) for our study, a retrospective review of electronic medical records at the Johns Hopkins Hospital (JHH) between 1995 and 2010 was performed and 12 patients on anticoagulation therapy for thromboembolic prophylaxis of mechanical cardiac valves who were hospitalized with a SDH requiring surgical intervention were identified. Medical records were reviewed and patient demographics, anticoagulation status (INR) on admission, treatment(s) received, number of days after admission with a subtherapeutic INR (INR < 2.5), number of days after surgery with a subtherapeutic INR (INR < 2.5), and postoperative morbidity and mortality were analyzed. The occurrence of clinically significant thromboembolic events (i.e., transient ischemic attack or stroke) and recurrent SDH requiring further intervention were used to evaluate the safety of withholding anticoagulation therapy in this patient population. The decision to restart anticoagulation postoperatively was made at the discretion of the treating physician as there is no hospital policy in place at our institution for this clinical situation since there is insufficient clinical data to guide decision-making. All patients obtained a head CT on postoperative day 1 to confirm evacuation of hematoma without evidence of reaccumulation. Anticoagulation therapy was standardized based on INR.

Statistical Analysis

The results are presented as mean $\pm$ standard deviation (SD). All statistical analyses were performed using Stata 11.0 (College Station, TX).

Results

Patients

In the 16-year study period, 12 patients underwent surgical treatment for evacuation of a SDH that developed while on anticoagulation therapy for mechanical heart valves. Demographic information and clinical characteristics of the study population are presented in Table 1. All the 12 patients had St. Jude's mechanical heart valves. Eleven patients had aortic valve replacements and one patient had a mitral valve replacement. Individual patient characteristics, anticoagulation status during hospital course, and outcomes are presented in Table 2.

Admissions Characteristics

Presumed precipitating events resulting in an admission for a SDH included trauma in five patients, supratherapeutic INR levels (>4) in two patients, and prior surgery in two patients. The remaining three patients in the study population had no identifiable precipitating event. At the time of admission, 11 patients were anticoagulated with warfarin and one patient with enoxaparin. Four patients were concomitantly using aspirin for antiplatelet therapy. The majority ($n = 9$) of patients had a presenting INR below the target goal of 2.5, with a median of 2.0. All patients had their anticoagulation reversed with vitamin K and fresh frozen plasma before surgical evacuation.

Hospital Course and Outcomes

Nine patients underwent surgical evacuation within 24 h of admission. Three patients were initially treated conservatively with anticoagulation reversal alone, but eventually required surgical intervention. The anticoagulation status of the study population is summarized in Table 2. The mean number of days after admission with subtherapeutic INR was 14 ± 7.8 days (range 5–32 days). Postoperatively, anticoagulation was withheld for a mean of 9 ± 8.7 days (range 3–32). Anticoagulation therapy was withheld postoperatively for less than 7 days in six patients, between 7 and 14 days in four patients, and for longer than 2 weeks in two patients. Antiplatelet therapy (aspirin) was also withheld in parallel with anticoagulation therapy. The average length of stay (LOS) was 19 days. No deaths or clinically evident thromboembolic events occurred during hospitalization. After discharge, the average follow-up time was 50 months, during which two patients had a recurrent SDH. In these two patients, the average time to hemorrhage recurrence from the time of resumed anticoagulation was 19 days. For one patient (case #2, Table 2), imaging revealed that hemorrhage recurred in the original location in addition to a distinct non-communicating location in the setting of supratherapeutic INR. After repeat subdural evacuation, the patient underwent surgical replacement of the mechanical valve with a bioprosthetic valve so that anticoagulation could be withheld permanently. For the second patient (case #5, Table 2), blood re-accumulated in the original location after resuming anticoagulation therapy. Following a repeat subdural evacuation, the patient did not require any further interventions. The two patients who experienced a recurrent SDH both suffered from hypertension; however, they did not display any other obvious clinical characteristics that would predicate an increased risk for hemorrhage recurrence. No other associated morbidities occurred during the follow-up period.

Discussion

In the present study, we analyzed the impact of anticoagulation management on the risk of thromboembolic events and incidence of recurrent SDH in a series of patients with mechanical heart valves who underwent surgical evacuation of a SDH at the Johns Hopkins Hospital. The majority of patients were anticoagulated with warfarin and presented with a subtherapeutic INR (<2.5). Anticoagulation was withheld for an average of 9 days after surgery, during which no deaths or thromboembolic events occurred.

Following mechanical heart valve placement, patients require lifelong anticoagulation therapy with a target INR between 2.0 and 4.5 to prevent thromboembolic complications [2]. The incidence of CNS hemorrhage in anticoagulated patients with cardiac valves, however, is approximately 0.5 %/year [9, 10]. Furthermore, the results of a retrospective case-controlled study performed by Jeffree et al. [11] demonstrated that warfarin use was associated with an increased risk of ICH, despite appropriate INR monitoring and anticoagulation within the therapeutic window. Thus, neurosurgeons are often faced with the difficult task of determining the appropriate duration of withholding anticoagulation when a patient presents with anticoagulation-associated CNS hemorrhage without sufficient evidence-based recommendations to effectively balance the risk of further hemorrhage with the risk of thromboembolism.

In one retrospective study evaluating the safety and duration of withholding warfarin in 28 hospitalized prosthetic valve patients with major hemorrhage, Ananthasubramaniam et al. [10] concluded that warfarin can be safely withheld for up to 2–3 weeks with a low risk of thromboembolism. Most patients in this study, however, presented with gastrointestinal bleeds, and only three patients had CNS hemorrhages. Thus, the applicability of the study's conclusions to CNS hemorrhages is limited.

Evidence specifically addressing anticoagulation management in patients with intracranial hemorrhages is limited to only a few case reports and small case series [12, 13]. Kawamata et al. [12] showed that in 20 patients with prosthetic valves with CNS hemorrhage, it was possible to resume warfarin therapy in nine patients within 3 days of surgery without any incidence of recurrent bleeding. However, one patient had a recurrent hemorrhage despite withholding anticoagulation therapy, and another patient had a thromboembolic event even after resuming anticoagulation therapy. The outcomes of these two patients emphasize the complexities of anticoagulation therapy in such patients and make it difficult to extrapolate the study's results to guidelines for management. More recently, Phan et al. [13] retrospectively evaluated the management of anticoagulation in 52 patients with prosthetic cardiac valves who presented with intracranial hemorrhage. The patients presented with ICHs that included cerebellar, brainstem, lobar, basal ganglia, subarachnoid, subdural and primary intra-ventricular hemorrhage, and anticoagulation was withheld in all patients. In this study, 28 patients (54 %) had resumed anticoagulation therapy by day 30 without recurrence of intracranial hemorrhages. However, it is difficult to make conclusions on the safety of withholding anticoagulation from this study since 22 (40 %) of the patients in the series had died by day 30, and it is unclear which patients underwent surgical intervention.

Currently, a standard of care that defines the appropriate length of withholding anticoagulation therapy after surgical evacuation of anticoagulation-associated SDH has not been proposed. In one case series, Wijdicks et al. [14] surgically evacuated 15 of 20 SDHs in patients with prosthetic valves after reversal of anticoagulation therapy. No thromboembolic complications or recurrence of ICH was observed during hospitalization, and the authors suggest that anticoagulation therapy can be discontinued for up to 1–2 weeks with minimal risk of thromboembolism.

The present study evaluates the incidence of thromboembolic complications and recurrent hemorrhages after reversal of anticoagulation therapy in prosthetic heart valve patients presenting with a SDH that required surgical evacuation. While a previous study [14] showed no recurrence of bleeding after resuming anticoagulation therapy, our data shows that two patients suffered from recurrent hemorrhage after resuming anticoagulation therapy for an average of 19 days postoperatively. However, the results of this study support small reports by other groups demonstrating that interruption in anticoagulation therapy for several weeks does not lead to a higher risk of thromboembolic complications.

Conclusion

The results of this study suggest that brief interruptions in anticoagulation therapy for as long as 3 weeks pose minimal thromboembolic risk in patients with mechanical heart valves. Furthermore, close follow-up after discharge is highly recommended, as recurrent hemorrhages can occur several weeks after the resumption of anticoagulation.

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Table 1

Demographics and pre-admission clinical characteristics of study population

Demographics	
Mean age at valve replacement (range)	64 (50–71) ^a
Age at hemorrhage (range)	71 (46–78)
Years to hemorrhage from replacement	9 ± 7
Sex, Female (%)	3 (25)
Clinical characteristics	
	<i>n</i> (%)
Diabetes,	6 (50)
Hypertension	6 (50)
Atrial fibrillation	4 (33)
Coronary artery disease	5 (42)
History of myocardial infarction	3 (25)
Obesity	2 (17)
Pulmonary disease (ex: COPD)	2 (17)
Prosthetic valve characteristics	
	<i>n</i> (%)
Location of valve	
Aortic	11 (92)
Mitral	1 (8)
Type of mechanical valve	
St. Jude's	12 (100)

^aMean age at valve replacement was not available for three patients

Table 2

Patient characteristics, anticoagulation status during hospital course, and outcomes

Case no.	Sex	Age	Admission INR	Precipitating factor	Anticoagulation therapy	Antiplatelet therapy	Days anticoagulation withheld	Days anticoagulation	Subdural recurrence withheld postoperatively
1	M	60	3.2	Trauma	Warfarin	None	22	20	No
2	M	76	1.7	Prior surgery	Warfarin	Aspirin	5	3	Yes
3	M	76	1.9	Trauma	Warfarin	None	9	8	No
4	F	78	2.2	None identified	Warfarin	Aspirin	8	5	No
5	M	73	9.8	Supratherapeutic INR	Warfarin	None	18	7	Yes
6	M	77	1.9	Trauma	Warfarin	None	21	3	No
7	M	75	2	Trauma	Warfarin	Aspirin	16	4	No
8	M	72	1.4	Prior surgery	Warfarin	None	12	4	No
9	M	46	1	None identified	Enoxaparin	None	8	8	No
10	F	73	1.8	Trauma	Warfarin	None	32	32	No
11	F	67	5	Supratherapeutic INR	Warfarin	None	10	3	No
12	M	74	2	None identified	Warfarin	Aspirin	10	9	No