

## ORIGINAL ARTICLES

# Anticoagulant-related subdural hematoma in patients with mechanical heart valves

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### Abstract

**Introduction:** There is uncertainty on the timing of surgery in patients with anticoagulant-related subdural hematoma (SDH) and also on the timing of reintroduction of anticoagulants. **Methods:** We retrospectively analyzed records of 7 patients with mechanical heart valves and anticoagulant-related SDH. **Results:** Of the 7 patients, 6 (83%) survived to discharge with good functional outcome, modified Rankin Scale 0-1. Reversal of anticoagulation (INR  $\leq$  1.4) could be achieved in 5 patients. Three patients with minimal deficit and no CT evidence of midline shifts were managed non-surgically. Three patients had surgical evacuation, 2 with acute SDH and midline shift and one patient with bilateral subacute SDH and no midline shift. The mean duration of anticoagulation withholding was 20.3 days (range 8-28). None had thrombotic events while off anticoagulation. Five patients were restarted on acenocumarol/warfarin when follow-up cranial CT showed decrease or resolution of SDH. High risk for thromboembolism was the indication for early anticoagulation in the patient with mitral position of the prosthesis and atrial fibrillation. One of the patient with subacute SDH who had post surgical residual SDH and echocardiographic evidence of valve dysfunction was initially started on unfractionated heparin followed by nadroparin calcium and subsequently on acenocumarol. There was no hematoma expansion during this period.

**Conclusions:** Patients with chronic SDH with minimal symptoms and no midline shift probably can be managed conservatively. Anticoagulant therapy can be safely withheld for 3 to 4 weeks. If early anticoagulation is required, low molecular weight heparin can be considered.

### INTRODUCTION

Mechanical heart valves are thrombogenic and require long-term anticoagulant therapy. The incidence of prosthetic valve thrombosis in patients not anticoagulated or taking anti-platelet drugs is 1.8% per patient-year. The incidence of embolism resulting in death, stroke, or peripheral ischemia requiring surgery is 4% per patient-year and this is reduced to 1.0% per-patient year with anticoagulant therapy.<sup>1</sup> However, anticoagulation is associated with a high risk of bleeding. In patients with mechanical valve on anticoagulation the incidence of hemorrhagic complications increase with international normalized ration (INR)  $>$  4.8.<sup>2</sup> The reported absolute risk of intracranial hemorrhage with anticoagulation is 0.3% to 1.0% per year and the associated mortality is about 60%.<sup>3</sup> The reported risk of subdural hematoma (SDH) with anticoagulation is 4- to 15-fold.<sup>3, 4</sup>

Recognition of anticoagulant-related SDHs is crucial because they are life threatening and amenable to therapy. However there are no clear guidelines on emergency treatment of anticoagulant-related SDH in patients with mechanical heart valve.

### METHODS

We retrospectively identified 7 patients with mechanical heart valves and anticoagulant-related SDH who were admitted to Neurological Intensive Care Unit (NICU). Medical records were reviewed and the details regarding patient characteristics, clinical features, medication details, admission prothrombin time (PT) and INR, site of hemorrhage, mode of anticoagulant reversal, treatment received, and occurrence and cause of death were obtained. Details regarding the duration of anticoagulant withholding, thromboembolic complications, and resumption

of anticoagulant treatment were also noted. Modified Rankin Scale (mRS) was the measure of functional outcome.<sup>5</sup>

Cardiac monitoring while patients were off anticoagulants included close monitoring of prosthetic heart sound, mean and peak trans-valvular pressure gradients by echocardiography. For mitral valve a mean gradient  $>5$  mmHg and for aortic valve  $>15$  were considered abnormal and suggestive of valve dysfunction. While restarting anticoagulants heparin was bridged with oral anticoagulant. We used mainly acenocumarol. Coagulation parameters studied to monitor anticoagulation included PT, INR and activated partial thromboplastin time (APTT).

Reversal of anticoagulation was achieved by injection vitamin K (10 – 20 mg) and fresh frozen plasma (FFP).

## RESULTS

During the 24 months study period, 13 patients with anticoagulant-related SDH, 7 (54%) in patients with mechanical heart valves, were admitted to NICU. The clinical characteristics of the patient series are shown in Table 1 and 2.

Of the 7 patients, 6 (83%) patients survived to discharge. Four patients had supratherapeutic anticoagulation at admission, 2 had therapeutic and 1 had subtherapeutic anticoagulation. Reversal of anticoagulation (the suggested optimal INR was 1.4<sup>6,7</sup> was achieved by injection vitamin K 10 mg and 4 to 6 units of FFP in 5 patients. However, in the patient who died (INR  $>7$ ) reversal of anticoagulation could not be achieved. In the other patient (case report) INR was 1.9 after injection vitamin K 10 mg and 3 units of fresh blood.

Three patients with chronic SDH and minimal deficits and no CT evidence of midline shifts were managed non-surgically. Three patients had surgical evacuation, 2 with acute SDH and midline shift and one with bilateral subacute SDH. This patient had surgical evacuation twice in the referral center.

The mean duration of anticoagulant withholding during hospitalization in patients who survived to discharge was 20.3 days (range 8-28). Five patients were restarted on acenocumarol or warfarin when follow-up cranial CT showed decrease or resolution of SDH. High risk for thromboembolism was the indication for early anticoagulation in the patient with mitral position of the prosthesis and atrial fibrillation. The patient with subacute SDH who had post surgical residual SDH and echocardiographic evidence of valve

dysfunction (case report) was initially started on unfractionated heparin followed by nadroparin, and subsequently on acenocumarol. There was no hematoma expansion during this period. None of the six patients had thromboembolic events when they are off anticoagulation.

Of the 7 patients, 6 survived to discharge with good function outcome, mRS 0-1. In the patient who died reversal of anticoagulation could not be achieved and his admission INR was  $>7$ . He had bilateral acute SDHs.

## Case Report

A 68 years male presented to a city private neurosurgical clinic in a district with a sudden onset severe headache and vomiting of three days duration. He had had a St Jude prosthetic mitral valve inserted 19 years earlier for rheumatic mitral stenosis and was anticoagulated with acenocumarol (target INR 3 – 3.5). He was fully alert with no neurological deficit. Ocular fundi were normal. His admission INR was 2.5. Cranial CT revealed bilateral fronto-parietal subacute SDH, right more than left (Fig 1a). Acenocumarol was stopped and anticoagulation reversal was attempted with injection vitamin K and 3 units of fresh blood. His INR was reduced to 1.9 and SDHs were evacuated. Repeat cranial CT done on the third postoperative day revealed residual right SDH (Fig 1b). He had relief of headache and was discharged with no anticoagulation. He presented to the same neurosurgeon after ten days with severe headache (17 days of initial symptom) and vomiting and no focal symptoms. Repeat cranial CT revealed large right fronto-temporo-parietal subacute SDH (Fig 1c). The INR at this admission was 1.9. Evacuation of SDH was again tried, but postoperative cranial CT revealed considerable residual hematoma (Fig 1d).

The patient was referred to our center for the decision regarding anticoagulation. Neurological examination at this admission was essentially normal. Ocular fundi were normal. He was normotensive. Prosthetic valve sounds were well heard. Trans thoracic and trans-esophageal echocardiogram revealed mechanical prosthetic valve in mitral position with normal opening and closing. Mean forward flow gradient was 8 mmHg. He was off anticoagulant for twenty-one days. After discussion with our neurosurgical team and cardiology team it was decided to defer surgery and anticoagulate him with unfractionated heparin with APTT monitoring in view of increased trans-valvular (mitral) pressure being high. Cardiac

**Table 1: Clinical characteristics of patients**

	Age, Sex	Valve Type, Location	Clinical Features	Admission PT(msec), INR	Cardiac and Echocardiographic findings	CT brain
1	36 years Male	St Jude Mitral, aortic	Headache, altered sensorium, GCS: 7, left hemiplegia	60, >7	Normal prosthetic valve sounds Normal trans-valvular pressures	Left temporal and right fronto-parietal subacute SDHs, effacement of right lateral ventricle and midline shift
2	70 years Female	St Jude Mitral	Headache, confused, GCS: 14, no motor weakness	46, 5	Normal prosthetic valve sounds Normal trans-valvular pressures	Left temporo-parietal chronic SDH, no effacement of left lateral ventricle
3	21 years Female	St Jude Aortic	Headache, drowsy, GCS: 13, no motor weakness	70, >7	Normal prosthetic valve sounds Normal trans-valvular pressures	Left parieto-temporal and right frontal chronic SDHs. No effacement of lateral ventricles
4	64 years Male	St Jude Mitral	Headache, mild confusion, GCS: 13, no motor weakness	30, 2.7	Normal prosthetic valve sounds Normal trans-valvular pressures	Bilateral fronto-parietal chronic SDHs, right > left, no effacement of lateral ventricles
5	38 years Female	St Jude Mitral	Headache, altered sensorium, GCS: 10, right hemiplegia	18.8, 1.6	Normal prosthetic valve sounds Normal trans-valvular pressures	Left fronto-parietal acute SDH, effacement of lateral ventricles and midline shift
6	68 years Male*	St Jude Mitral	Headache, drowsy, GCS: 13, mild left hemiparesis	25.1, 2.5	Normal prosthetic valve sounds Trans-valvular pressures 8 mmHg	Bilateral fronto-parietal subacute SDHs, right > left, mild effacement of right lateral ventricle
7	30 years Female	St Jude Mitral	Headache, vomiting, fully conscious, minimal pyramidal signs on right side	52.2, 4.8	Normal prosthetic valve sounds, atrial fibrillation Normal trans-valvular pressures	Left fronto-parietal acute SDH with ventricular effacement and midline shift

PT: Partial thromboplastin time; INR: International normalized ratio; SDH: Subdural hematoma; GCS: Glasgow Coma Scale

\* GCS score and the PT and INR values were the findings at his first admission in a district clinic and the echocardiogram findings were from the studies in our center

**Table 2: Treatment, hospital course, and outcome**

	Reversal of anticoagulation	PT(msec), INR after reversal	No of days of anticoagulation withholding	Hospital course	Outcome
1	Vitamin K: 20mg FFP: 6 units	50, 4.4	At admission	Surgery could not be done because optimal coagulation parameters could not be achieved	Death
2	Vitamin K: 10mg FFP: 6 units	13.0, 1.1	24	Managed non-surgically after reversal of anticoagulation with close clinical and cardiac monitoring. With the reduction in SDH volume acenocumarol was restarted	mRS 0
3	Vitamin K: 10mg FFP: 6 units	12.1, 1.0	22	Managed non-surgically after reversal of anticoagulation with close clinical and cardiac monitoring. With the reduction in SDH volume acenocumarol was restarted	mRS 0
4	Vitamin K: 10mg FFP: 4 units	13.7, 1.1	18	Managed conservatively after reversal of anticoagulation with close clinical and cardiac monitoring. With the reduction in SDH volume acenocumarol was restarted	mRS 0
5	Vitamin K: 10mg FFP: 4 units	12.5, 1.0	28	Optimal coagulation parameters could be achieved, in view of clinical deterioration and CT midline shift she had SDH evacuation and subsequent anticoagulation with acenocumarol	mRS 1
6*	At the referral hospital he was given vitamin K 10 mg and 3 units of fresh blood	13, 1.2	22	Without achieving optimal coagulation he was operated at the referral hospital twice. Subsequently he was put on heparin followed by nadroparin and acenocumarol	mRS 0
7	Vitamin K: 10mg FFP: 6 units	16.5, 1.4	8	Optimal coagulation parameters could be achieved. In view of midline shift she had SDH evacuation. Atrial fibrillation, and mitral position which increase thromboembolic risk she was started early on warfarin	mRS 0

FFP: Fresh frozen plasma; PT: Partial thromboplastin time; INR: International normalized ratio; SDH: Subdural hematoma; mRS: Modified Rankin Scale



Figure 1a: CT brain scan on admission showing bilateral fronto-parietal subacute SDH, right more than left.

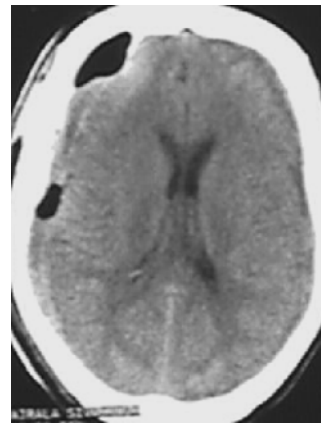


Figure 1b: CT scan on the 3<sup>rd</sup> postoperative day showing residual right SDH.

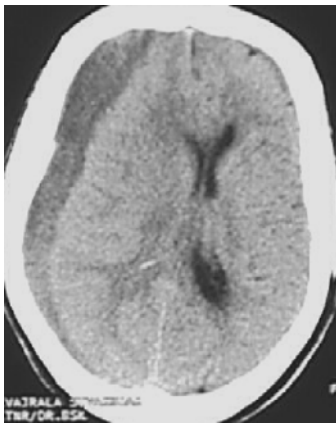


Figure 1c: CT brain scan 10 days after discharge from Hospital showing large right fronto-temporo-parietal subacute SDH.

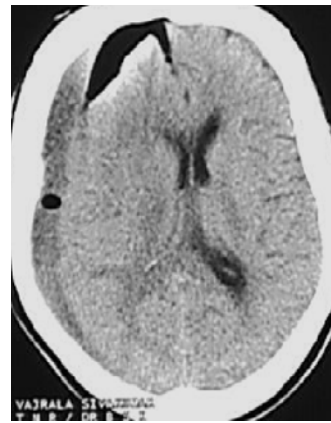


Figure 1d: CT brain scan after surgical evacuation showing considerable residual hematoma.



Figure 1e: CT brain scan at 27<sup>th</sup> day of first symptom showing considerable resolution of the SDH.



Figure 1f: CT brain scan at 49<sup>th</sup> day showing near resolution of SDH.





Figure 1g: CT brain scan at follow up showing resolution of SDH.

status was evaluated on every third day clinically by cardiologist and echocardiographic examination was done on every fifth day. He was given unfractionated heparin for 12 days and was discharged on nadroparin calcium 0.6 ml twice a day subcutaneously. Cranial CT done before discharge on the twenty-seventh day of the first symptom revealed considerable resolution of the SDH (Fig 1e). At every follow-up visit he had cardiac evaluation and echocardiographic examination. Cranial CT done on the forty-ninth day revealed near resolution of SDH (Fig 1f). He was started on acenocumarol (target INR 3–3.5). During the follow-up he did not have any cardioembolic events or recurrence of intracranial hemorrhage (Fig 1g).

He was not on any anticoagulation initially for 21 days, later on unfractionated heparin for 12 days and low molecular heparin for 16 days before he was put on acenocumarol (target INR 3–3.5).

## DISCUSSION

The exact incidence of anticoagulant-related SDH is uncertain. Before the advent of CT, of the anticoagulant-related intracranial hemorrhages, SDH was usually considered more common than intracranial hemorrhage.<sup>8,9</sup> In recent studies ICHs constitute about 70%, while SDHs compose the bulk of the remainder.<sup>3,8,10-12</sup> Approximately 20% are bilateral. SDH accounted for 50% of anticoagulant-related intracranial hemorrhages in patients with mechanical heart valves.<sup>12</sup> Intensity of anticoagulation<sup>4,10</sup> and advanced age<sup>10</sup> were the risk factors. The reported mortality of anticoagulant-related SDH in recent series is between 13% and 20%.<sup>8,10</sup>

In patients with anticoagulant-related SDH surgical evacuation is usually undertaken. Surgical evacuation of chronic SDH is associated with good outcome.<sup>12,13</sup> However it is unclear whether small SDH causing minimal symptoms can be safely managed non-surgically, with reversal of anticoagulation.<sup>8</sup> In our series three patients with chronic SDH with minimal symptoms and no midline shift were managed conservatively with good functional outcome. However, in patients with acute SDH the outcome may not be always good.<sup>13</sup> Failure to achieve reversal of anticoagulation preoperatively may be associated with poor outcome.<sup>13</sup> Similar was the outcome in one of our patients in whom optimal coagulation parameters could not be achieved. Current guidelines for reversal of oral anticoagulant-related anticoagulation are use of vitamin K, FFP, or factor concentrates.<sup>6,8,14-16</sup> The correction may take 9 hours with standard FFP and with factor IX complex in conjuncture with FFP it may take 2.93 hours.<sup>6</sup> Recombinant-activated factor VII (rFVIIa) was used to rapidly reverse excessive warfarin induced anticoagulation.<sup>17</sup> It appears rFVIIa may be the best candidate to date for reversal of coagulopathy in intracranial hemorrhage.<sup>21</sup> The suggested optimal coagulation parameter at which neurosurgical procedures can be performed is an INR of at least 1.4 or less.<sup>6,7</sup>

Reintroduction of anticoagulation should be based on the balance between a patient's thromboembolic risk and their bleeding risk. When the risk is equal for both, use of intravenous unfractionated heparin may be considered.<sup>15</sup> However, the use of intravenous unfractionated heparin is associated with both altered platelet function and with thrombocytosis. Low molecular heparins (LMWH) are an attractive alternative because of their pharmacokinetic and pharmacodynamic properties.<sup>18</sup> Anticoagulation with enoxaparin after mechanical heart valve replacement has been found to provide adequate biological anticoagulation, and compares favorable with unfractionated heparin anticoagulation.<sup>19</sup> Enoxaparin has been found to be effective and relatively safe substitute anticoagulant for patients with mechanical heart valves who must withhold oral anticoagulant.<sup>20</sup> In the patient with subacute SDH (case report) no hematoma expansion was noted during the period of treatment with unfractionated heparin and nadroparin calcium. Discontinuation of oral anticoagulant therapy for about 2 to 3 weeks has comparatively a low probability of embolic events in patients with mechanical heart valve.<sup>21, 22</sup>

Even though our series is too small to make any definite conclusions, there is a suggestion that patients with chronic SDH with minimal symptoms and no midline shifts may be managed non-surgically. In patients who need early anticoagulation, LMWH can safely be used.

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