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Fibrinolytic therapy versus craniotomy for anticoagulant-associated intracerebral hemorrhage

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ABSTRACT

Object: Anticoagulant-associated intracerebral hemorrhages (AAICH) have a high morbidity and mortality, necessitating urgent treatment. We examined outcomes after conventional craniotomy and stereotactic fibrinolytic therapy in a series of patients with anticoagulant-associated hemorrhages.
Methods: Among 129 consecutive surgically treated patients with supratentorial intracerebral hemorrhage, 27 patients with AAICH were identified (mean age 62; range 36–79). Thirteen patients underwent craniotomy for surgical hematoma evacuation, and 14 patients hematoma puncture and catheter placement for clot lysis. The groups had comparable major prognostic factors such as hematoma volume, age, and Glasgow coma scale (GCS) score at admission.
Results: Nine patients died despite treatment (mortality = 33%). Mortality in the craniotomy group was comparable to that of the lysis group (46% versus 21%; $p = 0.13$). Good outcomes (Glasgow outcome score of 4 or 5) were seen in 3 craniotomy patients (23%) and 2 fibrinolysis patients (14%). Half the patients survived with major neurological deficits (GOS 2 or 3) ($n = 13$; 48%). One rebleed was observed two days after uneventful craniotomy and hematoma removal, while no patient who underwent fibrinolysis had rebleeding.
Conclusions: Approximately one-fifth of patients with AAICH managed surgically may have good outcomes. Mortality and favourable outcome rates are comparable between craniotomy and fibrinolytic therapy. Fibrinolytic therapy appears to be a reasonable less invasive alternative treatment modality for intracerebral hemorrhage in the anticoagulated patient.

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1. Introduction

Intracerebral bleeding is the most frequent fatal complication of patients undergoing anticoagulation for a variety of medical conditions [1–5]. Between 1988 and 1999, as the use of warfarin quadrupled, the incidence of anticoagulant-associated intracerebral hemorrhage (AAICH) increased five-fold, to 17% of all intracerebral hemorrhages (ICH) [6]. Such hemorrhages present a treatment dilemma more complex than treating ICH in the patient with intact coagulation for whom hemorrhage removal is already controversial [7]; AAICH patients risk increased blood loss during surgery, a higher rate of rebleeding, and exacerbation of underlying diseases and comorbidities due to anticoagulation reversal.

Mortality rates for AAICH can be as high as 96% at 30 days for those patients already unconscious at admission [8]. Medical options for anticoagulation reversal after ICH include fresh frozen plasma [9], prothrombin complex concentrate [10–12], vitamin K [13] or recombinant factor VII [14–16]. The use of these factors is not associated with improved outcome. For most of the factors randomized clinical trials have not been performed. Factor VII has been shown in a randomized trial to reduce the risk of cerebral hematoma expansion, but not improve outcome [17].

AAICH can be managed surgically [18,19], but few neurosurgeons relish performing a craniotomy in the coagulopathic patient, and reversal of the coagulopathy can delay surgery beyond the window for neurologic recovery. Recently two separate series of 17 and 5 AAICH patients respectively demonstrated favourable outcomes in 65% [20] and 40% [12] of patients managed surgically, suggesting that craniotomy and surgical clot removal, particularly after rapid coagulopathy reversal [12], might have a beneficial effect on outcome.

Stereotactic catheter placement and fibrinolytic lysis was first introduced for non-anticoagulant-associated ICH by Doi et al. in

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1982 [21]. Hematoma lysis via catheter injection of recombinant tissue plasminogen activator (rt-PA) or urokinase was intended as a less invasive alternative to craniotomy for clot removal [22–24]. In the few prospective, but non-randomized clinical series, mortality rates lower than those for craniotomy have been reported [23]. These studies are countered by a randomized trial showing no improvement in outcome with fibrinolysis versus craniotomy despite reduction in hematoma volume [25]. Fibrinolytic therapy has presumably not been considered for anticoagulant-related ICH because of the assumed high risk of rebleeding.

The theoretical advantage of stereotactic catheter placement in AAICHs includes avoidance of a major surgical procedure and its accompanying anesthetic considerations in a patient population that is already uniquely vulnerable to surgical risk due to their underlying comorbidities that require anticoagulation. In considering fibrinolytic therapy, the assumed higher rebleed risk of using a lytic agent has to be weighed against the reduced risk of underlying disease exacerbation. Further, with stereotactic lytic therapy, there is reduced exposure of the operative field which could place the patient at increased risk if intraoperative bleeding were to occur. While we did not see this in our series, it theoretically represents a greater risk in patients not undergoing craniotomy.

This study reports the largest retrospective series of surgically managed anticoagulant-associated hemorrhages yet published. It assesses morbidity and mortality after microsurgery and fibrinolytic therapy, and proposes the latter as a novel management strategy for the anticoagulated patient.

2. Materials and methods

129 patients with spontaneous supratentorial ICH underwent surgery during a period of 6 years at a single medical center in Aachen, Germany. Twenty-seven of these patients had been anticoagulated. In general, the decision for or against surgery, regardless of coagulation status, was guided by the following inclusion and exclusion criteria: Surgery was performed if the patient presented with impaired consciousness and/or if the clot volume exceeded 30 ml in basal ganglia hematomas and 50 ml in lobar hematomas. Surgery was not performed if the patient presented with the signs of impending brain death. The neurosurgeons on call decided whether patients would receive craniotomy for surgical clot removal or fibrinolytic therapy on a case-by-case basis according to personal surgical preference. Some surgeons generally preferred to perform open craniotomy versus stereotactic clot lysis and vice versa. In consequence, the management of non-anticoagulated ICH and AAICH was similar during the study period.

Of the 27 patients with AAICH, 13 patients underwent craniotomy for clot removal, followed by a CT scan 4 h later. For the remaining 14 patients, burr hole trephination, careful hematoma aspiration and catheter placement into the hematoma core was performed. Correct positioning of the catheter was augmented by stereotaxy or CT-guidance in 8 of the 14 patients. Urokinase (5000 IE) or rt-PA (2–10 mg depending on hematoma size [23]) was injected via the catheter. The dose of the rt-PA was calculated by measuring the maximum diameter of the hematoma in centimeters

Table 1

Demographic data of 13 patients with anticoagulant-related intracerebral hemorrhage and craniotomy for clot removal (GCS: Glasgow coma scale score—severe coma GCS < 8, moderate coma GCS 9–12, mild coma GCS > 13; GOS: Glasgow outcome scale score, 1—death, 2—persistent vegetative state, 3—severe disability, 4—moderate disability, 5—good recovery). Preop Q = preoperative Quick percentage (as a percentage of normal; normal range is between 70% and 130%), Preop PTT = partial thromboplastin time (s). Nl = Normal and unk = unknown.

No.	Age (years)/sex	GCS	Anticoagulation, underlying disease	Hematoma site	Hematoma volume (ml)	Preop Q, PTT	GOS
1	63/M	12	Warfarin/artificial valve	Temporooccipital rt	94	40, >150	3
2	36/F	6	Heparin/malaria	Frontoparietal rt	23	nl, nl	1
3	67/M	11	Warfarin/sinus thrombosis	Frontal lt	50	98, unk	4
4	55/M	15	tPA/pulmonary embolism	Frontal lt	87	nl, nl	3
5	63/M	4	Heparin/myocardial infarction	Occipital lt	49	63, 150	1
6	64/M	7	Warfarin/artificial valve	Temporoparietal lt	63	55, 33	1
7	68/F	10	Warfarin/artificial valve	Thalamus rt	41	69, 35	3
8	69/M	13	Heparin/stroke	Parietooccipital lt	97	unk, unk	5
9	63/M	13	Warfarin/sinus thrombosis	Parietooccipital lt	56	nl, nl	4
10	65/F	4	Heparin/myocardial infarction	Frontal rt	104	33, unk	1
11	62/M	3	Warfarin/peripheral arterial disease	Basal ganglia rt	86	nl, nl	1
12	57/M	7	Urokinase/myocardial infarction	Basal ganglia rt	40	nl, nl	1
13	68/M	14	Warfarin/not known	Frontal rt	78	nl, nl	3
Mean 61.4		9.2			72		2.4 ± 1.4

Table 2

Demographic data of 14 patients with anticoagulant-related intracerebral hemorrhage undergoing hematoma puncture and subsequent fibrinolytic therapy (GCS: Glasgow coma scale score—severe coma GCS < 8, moderate coma GCS 9–12, mild coma GCS > 13; GOS: Glasgow outcome scale score, 1—death, 2—persistent vegetative state, 3—severe disability, 4—moderate disability, 5—good recovery). Preop Q = preoperative Quick percentage (as a percentage of normal; normal range is between 70% and 130%), Preop PTT = partial thromboplastin time (s). Nl = Normal and unk = unknown.

No.	Age (years)/sex	GCS	Anticoagulation, underlying disease	Hematoma site	Hematoma volume (ml)	Preop Q, PTT	GOS
1	56/M	13	Heparin/heart transplantation	Occipital rt	44	nl, nl	3
2	74/M	14	Warfarin/coronary bypass	Temporal rt	41	50, 36	3
3	60/F	6	Urokinase/pulmonary embolism	Temporooccipital rt	105	nl, nl	4
4	79/M	12	Warfarin/unknown	Temporooccipital rt	68	52, 31	1
5	57/M	15	Heparin/vertebral artery stenosis	Occipital rt	67	nl, nl	4
6	73/F	11	Warfarin/artrial fibrillation	Temporal rt	58	59, 33	3
7	62/F	14	Warfarin n/prosthetic valve	Parietooccipital lt	68	50, 44	3
8	48/M	6	Heparin/stroke	Temporooccipital lt	132	unk, unk	2
9	63/M	14	Warfarin/myocardial infarction	Frontal lt	47	nl, nl	3
10	61/M	6	Heparin/unknown	Temporal rt	46	unk, unk	3
11	66/F	3	Warfarin/prosthetic valve	Temporooccipital lt	75	7, 70	1
12	61/M	4	Heparin/stroke	Temporooccipital lt	103	nl, nl	1
13	76/F	6	Warfarin/pulmonary embolism	Basal ganglia rt	72	16, 54	3
14	56/F	12	Warfarin/arterial septal defect	Temporoparietal rt	89	13, 55	3
Mean 63.7		9.7			69		2.6 ± 1.0