Delayed surgery in patients with acute type A aortic dissection who are receiving novel oral anticoagulants

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Video clip is available online.

Use of novel oral anticoagulants (NOACs) is increasing, but without a means of rapid and efficacious reversal, this can represent a disaster should urgent and invasive surgical care be required. Here we describe our overall management,

Normal coagulation per TEM test 60 hours postpresentation after receiving 1000 IU PCC.

Central Message

In managing acute type A ascending aortic dissection in patients receiving NOACs, risk of rupture weighs against risk of intractable bleeding. Delaying surgery should be considered in selected cases.

See Editorial Commentary page e5.

FIGURE 1. In patient 1, 60 hours after presentation and after receiving 1000 IU of prothrombin complex concentrate, thromboelastometry testing showed normal coagulation.

TABLE 1. Coagulation parameters on thromboelastometry testing

	18 h after onset	Incision	Closure
Patient 1			
60 h			
INTEM			
CT (s)		140	167
CFT (s)		91	172 ↑
α (degrees)		73	71
MA (mm)		60	48
EXTEM			
CT (s)		97 ↑	12 ↓
CFT (s)		97	91
α (degrees)		74	73
MA (mm)		61	61
FIBTEM			
CT (s)		75	97
CFT (s)		2312	—
α (degrees)		71	58
MA (mm)		20	16
HEPTEM			
CT (s)		159	225
CFT (s)		89	200
α (degrees)		73	64
MA (mm)		58	40
Patient 2			
40 h			
INTEM			
CT (s)	170	180	1923 ↑
CFT (s)	103	81	—
α (degrees)	71	75	—
MA (mm)	59	62	—
EXTEM			
CT (s)	71	73	92 ↑
CFT (s)	105	92	114
α (degrees)	70	72	71
MA (mm)	61	63	59
FIBTEM			
CT (s)	64	65	95
CFT (s)	—	1477	—
α (degrees)	73	76	73
MA (mm)	17	20	20
HEPTEM			
CT (s)	164	168	186
CFT (s)	97	82	94
α (degrees)	71	76	75
MA (mm)	60	61	60

INTEM, Intrinsic rotational thromboelastometry; EXTEM, extrinsic rotational thromboelastometry; FIBTEM, fibrinogen rotational thromboelastometry; HEPTEM, heparin rotational thromboelastometry; CT, clotting time; CFT, clot formation time; α , α -angle; MA, maximum amplitude.

including delayed surgery, of 2 patients who each presented with acute Stanford type A aortic dissection while receiving NOACs (rivaroxaban and dabigatran).

CLINICAL SUMMARIES

Patient 1

An 87-year-old woman came to a primary care hospital with retrosternal pain and syncope. She was being treated

KEY POINTS FROM

Delayed Surgery in Patients with Acute Type A Aortic Dissection on Novel Anticoagulants

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VIDEO 1. Key points on delayed operative repair and computed tomographic scan findings for patients 1 and 2. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)31778-6/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)31778-6/fulltext).

with rivaroxaban at 15 mg daily for paroxysmal atrial fibrillation, and her last dose had been at noon the same day. Angioscan showed an acute Stanford type A aortic dissection sparing the supra-aortic vessels and coronary arteries and only minimal hemopericardium. These findings are presented in Video 1. She was transferred to our facility with a nitroprusside sodium drip. At arrival, she was in hemodynamically stable condition and showed no signs of malperfusion. Labetalol was initiated to achieve a systolic blood pressure of at most 100 mm Hg. She received 1000 IU of human prothrombin complex that same day. A control angioscan 24 h later showed no progression. Twice-daily anti-activated factor X assays calibrated for rivaroxaban were performed until negligible levels (10 U/mL) were reached 40 h after the last dose. Around 60 hours after initial presentation, the patient underwent an ascending aortic replacement with a hypothermic circulatory arrest of 15 minutes and a cardiopulmonary bypass time of 132 minutes. Preoperative thromboelastometry showed no deficit (Figure 1 and Table 1), but thrombocytopenia was corrected with 5 units of platelets. Perioperative blood loss was 1000 mL. Chest tube output was minimal. There were no postoperative complications, and the patient was discharged on postoperative day 6.

Patient 2

A 67-year-old man with known hypertension, hypothyroidism, dyslipidemia, and treatment with dabigatran at 150 mg twice daily for chronic atrial fibrillation (last dose that morning) presented with acute type A aortic dissection. There was no aortic insufficiency, no hemopericardium, and no signs of malperfusion. Hemodynamics were stable. Nitroprusside, labetalol, and clonidine were initiated to achieve a systolic blood pressure of at most 100 mm Hg. The decision was taken with the family to delay the procedure and closely monitor the patient to minimize the risk of massive bleeding, weighing against the risk of rupture. The patient immediately received 5 g of idarucizumab. Forty hours later, the results of preoperative thromboelastometry (Table 1) were normal, and he underwent an ascending aorta and total arch replacement with a frozen elephant trunk

TABLE 2. Review of published cases of acute type A aortic dissection in patients receiving novel oral anticoagulants

Report	NOAC	Interventions		Survived
		Preoperative	Perioperative/postoperative	
Current report				
Patient 1	Rivaroxaban	PCC, ~60 h delay	Plt	Yes
Patient 2	Dabigatran	Praxbind, ~40 h delay	—	Yes
Crapelli et al, ² 2016*	Dabigatran	—	UF, PCC, rVIIa, Plt, FFP, Fg, PRBC	No
Dumps et al, ³ 2016	Apixaban	—	UF, PCC, Plt, FFP Fg, PRBC	No
Henderson et al, ⁴ 2016	Dabigatran	Idarucizumab	—	No
Marchetti et al, ⁷ 2016	Dabigatran	HD, FEIBA	—	Yes
Béné et al, ¹ 2015†	Rivaroxaban	PCC	—	No
Ashikhmina et al, ⁸ 2014	Dabigatran	—	UF, PCC, FEIBA, ACA	Yes
Williamson et al, ⁶ 2014	Rivaroxaban	—	PCC, FEIBA, Plt, FFP, Cryo, PRBC	Yes
Stein et al, ⁵ 2014	Dabigatran	—	HD, PCC, rFVIIa, FVIII/vWF, FXIII, Plt, FFP, Fg, PRBC	No
Mastrobuoni et al, ⁹ 2012*	Dabigatran	—	PCC, rFVIIa, FFP, Cryo	Yes

NOAC, Novel oral anticoagulants; PCC, prothrombin complex concentrate; Plt, platelets; UF, ultrafiltration; rVIIa, recombinant factor VIIa; FFP, fresh-frozen plasma; Fg, fibrinogen; PRBC, packed red blood cells; HD, hemodialysis; FEIBA, factor VIII inhibitor bypassing activity; ACA, aminocaproic acid; Cryo, cryoprecipitate; rFVIIa, recombinant activated factor VII; FVIII/vWF, factor VIII/von Willebrand factor; FXIII, factor XIII. *Intramural hematoma. †Patient died awaiting surgery.

procedure with 28-mm Dacron polyester fabric grafts and a Gore TAG 31 × 15 mm graft (W. L. Gore & Associates; Flagstaff, Ariz). Arrest time was 14 minutes, and cardiopulmonary bypass time was 108 minutes. Blood loss was 390 mL. Chest tube outputs were 180 mL in the first 8 hours and 290 mL in the first day. Notably, the patient received no blood products or coagulation factors. The postoperative course was uneventful, and the patient was discharged on postoperative day 7.

DISCUSSION

Prevalence of use of NOACs, such as rivaroxaban and dabigatran, is increasing because they present many

advantages relative vitamin K antagonists; however, rapid reversal still poses concern. Acute Stanford type A aortic dissection carries a mortality risk of 1% per hour for the first hours when treated medically. We describe 2 cases successfully managed by delaying surgery between 40 and 60 hours. Both patients were fortunate to have stable hemodynamics, no malperfusion, and no rupture. This allowed them to receive adequate surgery with minimal amounts of blood products and coagulation factors.

There is little existing literature on aortic dissection in patients treated with NOACs (Table 2). One report describes a patient receiving rivaroxaban who died before surgery.¹ Another 4 reports describe the patient surviving at the price

TABLE 3. Mode of action, pharmacokinetic data, and monitoring for common novel oral anticoagulants

	Dabigatran	Apixaban	Rivaroxaban
Mode of action	Direct inhibition of thrombin	Direct inhibition of FXa	Direct inhibition of FXa
T _{max} (h)	1	3-4	2-4
Elimination			
Mode	Renal	Renal	Renal
Unchanged	80%	27%	36%
Elimination half-life (h)	12-17	12	11-13
Best monitoring	Ecarin-based assays in therapeutic range; TT to rule out residual levels	Calibrated anti-FXa, does not rule out residual levels	Calibrated anti-FXa, does not rule out residual levels
Commonly available monitoring	APTT sensitive in therapeutic range, insensitive to rule out residual levels; INR/PT insensitive	INR/PT and APTT insensitive	INR/PT sensitive in therapeutic range, insensitive to rule out residual levels; APTT insensitive.
Hemodialysis	50% in 4 h	Not effective	Not effective

FXa, Activated factor X; T_{max}, time to maximal effect; TT, thrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; PT, prothrombin time.

of significant transfusions, whereas 4 others describe the patient dying from intractable coagulopathy despite receiving massive amounts of blood products, coagulation factors, and, in 1 case, idarucizumab.²⁻⁹

There is no consensus regarding the optimal management of these patients. The persistent risk of rupture must be weighed against the risk of intractable bleeding and multiple transfusions. If the patient is in hemodynamically and clinically stable condition, with no signs of malperfusion, we suggest that it is reasonable to wait under intensive surveillance until coagulopathy has resolved. The timing of last NOAC dose is important in evaluating the bleeding risk. Coagulation status must be assessed frequently during the waiting interval. Calibrated anti-activated factor X assays are most sensitive to exclude therapeutic levels of apixaban or rivaroxaban, but they remain insensitive in the subtherapeutic range. In addition, these tests are not widely available. Thrombin time is most sensitive to exclude residual dabigatran levels. Prothrombin time, international normalized ration, and activated partial thromboplastin time are insensitive in this range for all three compounds¹⁰ (Table 3). If the patient has been treated with dabigatran and is in hemodynamically stable condition, continuous hemodialysis may be used to decrease serum concentration, although a rebound effect may be seen because of compartment redistribution. The most appropriate period of delay and the acceptable level of residual anticoagulation remain

unknown. This paradigm should be confirmed in further studies.

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