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Recombinant factor VIIa for intractable life-threatening bleeding in patients with circulatory assist devices

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Dear Editor,

Circulatory assist devices require tight anticoagulation therapy and may be complicated by severe bleeding. Despite warnings related to potential lethal thrombotic complications, off-label use of recombinant factor VIIa (rFVIIa) is increasingly reported for refractory hemorrhage, including after cardiac surgery [1, 2]. However, its use in patients with circulatory assist devices has seldom been reported and its safety remains to be established [3–5].

We reviewed 12 consecutive patients with surgically implanted devices who received rFVIIa as rescue treatment for intractable life-threatening bleeding between March 2004 and November 2009 (Table 1). According to strict and constringent local consensus guidelines, a systematic cross-check for aggressive correction of hypothermia, acidosis, and coagulation factors with parallel surgical control for bleeding or embolization was obtained before rFVIIa administration in all cases.

The median age of patients was 45 years. The rFVIIa was administered in the operating room (3/12), in the intensive care unit (7/12), or both (2/12). Underlying conditions were cardiovascular surgery (11/12, including 4 heart transplantations) and bipulmonary transplantation (1/12). The device was an extracorporal membrane oxygenator (9/12) and a left ventricular assist device (3/12). Median dose of rFVIIa was 95 μg/kg (45–180), administered in one (3/12) or several doses (9/12).

In these otherwise terminal patients, the bleeding assessed by the number of ml/kg of packed red blood cells and fresh frozen plasma requirement within 12 h before and after rFVIIa administration was significantly reduced. Six patients (50%) died within 30 days, including 2 (18%) from persistent bleeding. A careful analysis of coagulation and other physiological parameters did not reveal significant difference between responders and non-responders.

Table 1 Patient characteristics

	Age (years)	Type of device	Total dose of rFVIIa (μg/kg)	Number of doses	Thrombo-embolic event	Device clotting	PRBC requirements (ml/kg)			FFP requirements (ml/kg)			Outcome at 30 days
							12 h before	12 h after	Δ (%)	12 h before	12 h after	Δ (%)	
1	10	ECMO	180	2	No	No	96.0	75.0	−22	26.8	35.7	33	Alive
2	<1	ECMO	180	2	No	No	270.0	77.0	−71	160	42	−74	Death day 7 from multiple organ failure
3	15	ECMO	45	1	No	No	22.8	35.9	57	10.9	21.7	99	Alive
4	<1	ECMO	180	2	Stroke	No	130.0	37.0	−72	111	107	−4	Death day 2 from hemorrhage
5	55	ECMO	105	1	No	No	182.6	6.5	−96	76.1	21.7	−71	Alive
6	51	ECMO	90	3	No	No	66.3	34.9	−47	52.3	34.9	−33	Death day 9 from cardiogenic shock
7	43	LVAD	100	2	No	No	105.0	40.0	−62	75	20.8	−72	Alive
8	47	ECMO	54	1	No	No	31.4	45.3	44	34.9	49.4	42	Death day 1 from hemorrhage
9	49	LVAD	60	2	No	No	33.8	11.3	−67	25	6.3	−75	Alive
10	63	LVAD	76	3	No	No	34.7	6.3	−82	34.2	5.3	−85	Death day 18 from septic shock
11	46	ECMO	126	2	No	No	88.4	18.9	−79	63.2	26.3	−58	Death day 7 from septic shock
12	25	ECMO	47	2	No	No	144.0	56.0	−61	100	43.3	−57	Alive

ECMO extracorporal membrane oxygenator; *LVAD* Thoratec IVAD® as left ventricular assist device; *PRBC* packed red blood cells (300 ml per unit), $\Delta\ p = 0.007$ by Wilcoxon *T* test; *FFP* fresh frozen plasma (250 ml per unit), $\Delta\ p = 0.007$ by Wilcoxon *T* test

In all cases, adequate anticoagulation was further maintained and no circuit thrombosis occurred; hence no device required replacement. One thromboembolic complication occurred (a stroke) in a neonate following cardiac arrest after a Jatene switch. The relationship between this event and the rFVIIa administration remained unclear.

We conclude that after meticulous control for all other potential contributing factors, the careful use of small and if necessary repeated doses of rFVIIa (25–30 μg/kg), allowed one to control life-threatening intractable bleeding in 9/12 patients with surgically implanted circulatory assistance devices without any clot of the devices. As suggested by current guidelines, these data confirm preliminary reports [3–5], but the safety of rFVIIa in this context should now be confirmed by controlled trials in larger groups of patients.

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