A Propensity Score Matching Study on Recombinant Factor VIIa Administration for Cardiac Surgical Bleeding

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BACKGROUND

- Recombinant activated factor VII (rFVIIa; NovoSeven, Novo Nordisk, Bagsvaerd, Denmark) was developed in the 1970's and used clinically in the 1980's for patients with hemophilia.[1]
- Off-label use of rFVIIa for perioperative cardiac surgical bleeding has been shown to reduce bleeding,[2-5] blood product administration[2,6,7] and the rate of reoperations.[5,7,8] However, the use of rFVIIa for cardiac surgical bleeding has been associated with increased mortality,[9] thrombosis,[10-12] stroke[8,12,13] and renal morbidity.[9,10]
- Dosing strategies of rFVIIa for cardiac surgical bleeding remain inconsistent. Older reports analyzed doses of 90 mcg/kg of rFVIIa based on recommendations for patients with hemophilia, while more recent reports have shown efficacy with lower doses ranging from as low as 12 mcg/kg[14] to 40 - 50 mcg/kg.[5,6,15-17]

PURPOSE

- To determine the effects and safety of vld-rFVIIa administration (median 13.33 mcg/kg) in patients who received vld-rFVIIa for cardiac surgical bleeding compared to matched control groups who sustained cardiac surgical bleeding and did not receive vld-rFVIIa

METHODS

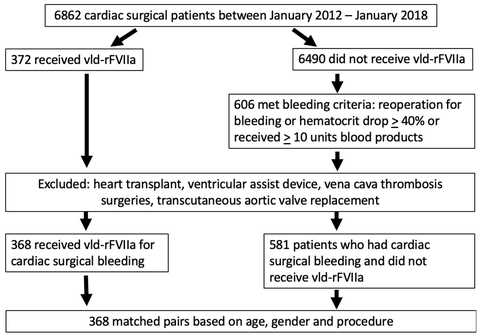
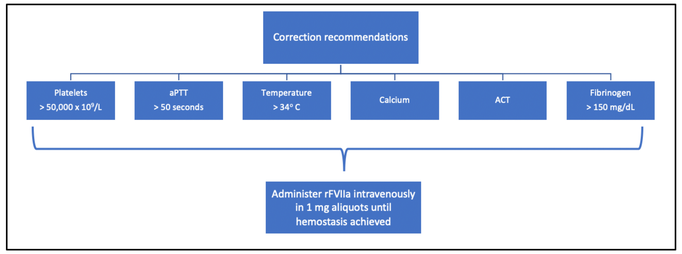


Figure 2. Inclusion Schema

METHODS (CONT.)



aPTT = activated partial thromboplastin time; ACT = activated clotting time

Figure 1. Recombinant Factor VIIa (rFVIIa) administration guideline for cardiac surgical bleeding

RESULTS

	vld-rFVIIa/Non-Factor VII pairs (n=368 matched pairs)				
Outcome	Yes/yes	Yes/no	No/yes	No/no	p-value*
30-day mortality	5	38	24	301	0.075
Postop renal risk	13	22	45	238	0.005
Reoperation for bleeding	15	54	36	263	0.058
Postop thrombosis	2	8	10	348	0.815
Postop infection	5	23	14	326	0.139

*McNemar test (exact p-values are used when the number of discordant pairs<10)

Table 2a. Outcomes for binary outcome variables.

Outcome	vld-rFVIIa	Non-Factor VII	Difference (vld-rFVIIa – non-Factor VII)	p-value*
Surgery to discharge length of stay	9.92 (9.06)	8.96 (8.02)	0.92 (11.09)	0.054
Total intraop blood products (PRBC + FFP + platelet + cryo)	4.95 (6.87)	3.1 (4.86)	1.85 (8.13)	<0.0001
Intraop PRBC	1.30 (2.28)	0.91 (1.87)	0.39 (2.89)	0.003
Intraop FFP	2.45 (3.44)	1.51 (2.77)	0.95 (4.14)	<0.0001
Intraop platelet	0.91 (1.28)	0.54 (0.86)	0.36 (1.51)	<0.0001
Intraop cryo	0.35 (1.53)	0.55 (0.86)	0.21 (1.76)	0.003
Total postop blood products (PRBC + FFP + platelet + cryo)	4.04 (8.47)	2.73 (5.93)	1.31 (10.25)	<0.0001
Postop PRBC	1.96 (4.12)	1.40 (3.32)	0.56 (5.33)	0.0008
Postop FFP	0.86 (2.97)	0.65 (3.07)	0.21 (4.30)	0.0104
Postop platelet	0.83 (1.72)	0.46 (1.46)	0.37 (1.60)	<0.0001
Postop Cryo	0.40 (1.33)	0.22 (0.94)	0.18 (1.61)	0.008
Total blood products (PRBC + FFP + platelet + cryo) for intra- and postop	9.05 (11.39)	5.83 (8.33)	3.22 (13.85)	<0.0001

Data presented as mean (STD)

*Signed rank test is used the normality assumption is violated for all outcomes.

Table 2b. Outcomes for continuous outcome variables (n = 736; 368 matched pairs).

RESULTS (CONT.)

- 736 patients were included in this study. vld-rFVIIa was administered to 368 patients with a median dose of 13.33 mcg/kg, per patient. Patients who received vld-rFVIIa were matched with 368 patients who met criteria for cardiac surgical bleeding but did not receive vld-rFVIIa therapy.
- Between matched cohorts there were no differences in age, race, Society of Thoracic Surgery morbidity or mortality risk score, preoperative INR, preoperative ejection fraction, diabetes, end-stage renal disease (ESRD) and emergent or urgent surgeries

CONCLUSIONS

- Factor 7 for cardiac surgical bleeding does not increase mortality (p=0.075) but is associated with increased blood transfusions (p<0.0001) and renal failure (p=0.005) in a matched cohort

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