

Background

- Nearly one third of cardiac patients experience substantial bleeding following cardiothoracic surgery.
 - Associated with ↑ length of stay, potential need for surgical re-exploration, and additional adverse outcomes including death.
- Off-label use of recombinant activated factor VII (rFVIIa) or 4-factor prothrombin complex concentrate (4PCC) are current options to treat major bleeding postoperatively.
 - Becoming more favorable to lessen need for fresh frozen plasma (FFP), given extensive risks with administration.
 - No optimal dose for either agent has been established.
 - A study that compared 4PCC to rFVIIa, utilizing doses of 25 units/kg and 45 mcg/kg respectively, showed no statistically significant differences in efficacy. Also showed no significant differences in thromboembolic events, significantly shorter hospital length of stays, and less additional administration of FFP with the 4PCC treatment group.
 - This institution currently uses rFVIIa off-label at 90 mcg/kg.
- Preferential use of 4PCC versus rFVIIa has been discussed in order to save significantly on costs of use.

Justifications

- Potential financial opportunity for cost savings by using 4PCC versus rFVIIa for post-cardiac surgery bleeding.
- Risk of thromboembolic events with rFVIIa, especially with doses > 80 mcg/kg, are the limiting factor with its administration. Given improvement in the quality of coagulation factor concentrates with 4PCC, risk of thromboembolism is thought to be diminished.
- 4PCC more easily reconstituted and thus may be able to be stored in the operating room (OR) automated medication dispensing system.
 - ↓ time to drug → ↓ time in OR → additional cost savings

Objectives

Primary Objective

- To compare the acquisition cost of rFVIIa, dosed at 90 mcg/kg, to an equivalent dose of 4PCC, determined to be 25 units/kg, for first dose factor replacement in patients with bleeding after cardiothoracic surgery over the past two years.

Secondary Objectives

- Chest tube output during the first 24 hours post-operatively
- Rates of thromboembolic events (venous and arterial thromboembolism)
- Rates of acute kidney injury
- Hospital length of stay
- Units of FFP administered

Current Practice

- Choice of treatment for post-operative bleeding after cardiothoracic surgery is at the discretion of the cardiothoracic surgeon.
- rFVIIa is used a few times a month off-label at this institution for post-operative bleeding after cardiac surgery at a dose of 90 mcg/kg.
- Mercy Hospital of Buffalo has a rFVIIa pharmacy automatic dose rounding policy (to the nearest vial size) based on patient weight.

Methods

- Retrospective chart review using electronic medical record at Mercy Hospital of Buffalo, a 360-bed tertiary care hospital in Buffalo, NY.
- Study time period: October 2017 - October 2019
- Cost of the administered dose of rFVIIa compared to the cost of a calculated equivalent dose of 4PCC.

Inclusion Criteria

- ≥ 18 years of age
- Received at least one dose of rFVIIa for bleeding after any type of cardiothoracic surgery

Exclusion Criteria

- Pregnant
- Received rFVIIa for reasons other than post-operative cardiothoracic bleeding

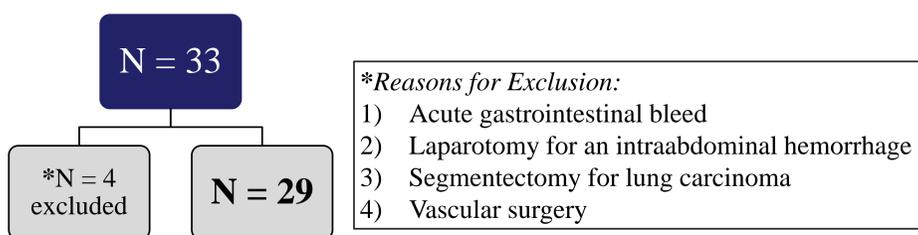


Table I. Baseline Characteristics

Characteristic	rFVIIa (n = 29)
Age, years (average)	65
Sex, percentage male	69
Weight, kg (average)	85.8
Baseline serum creatinine, mg/dL (average)	1.0
History of hemophilia (%)	0
History of ischemic stroke (%)	4 (n = 1)
History of VTE (%)	7 (n = 2)
History of anticoagulation use in the previous 48 hours, (%)	21 (n = 6)
Baseline hemoglobin, g/dL (average)	13.5
Baseline hematocrit, g/dL (average)	40
Average cumulative dose	7,134 mcg (83 mcg/kg)
Type of surgery	
Coronary artery bypass graft (CABG) (%)	14% (n = 4)
Valve replacement (%)	28% (n = 8)
Aortic dissection (%)	48% (n = 14)
Valve replacement + CABG (%)	10% (n = 3)

Results

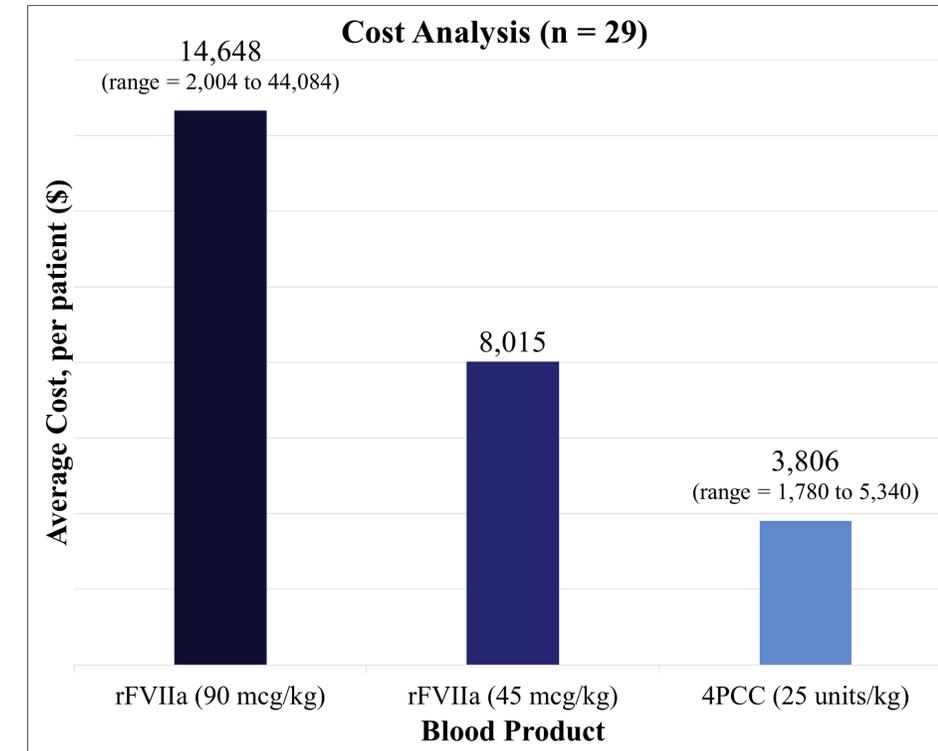


Table II. Efficacy and Safety of rFVIIa

Secondary Objectives	rFVIIa
Average chest tube output during the first 24 hours post-operatively (mL)	1629 (n = 25)
Rate of thromboembolic events (%)	11 (n = 3/28)
Rates of acute kidney injury	50 (n = 14/28)
Hospital length of stay, days (average)	10.2 (n = 25)
Units of FFP administered (average)	6 (n = 28)

Conclusion

- Based on the results, off-label use of 4PCC to treat major bleeding following cardiothoracic surgery offers significant cost savings in comparison to rFVIIa. Projected annual savings is \$157,223.
- The results of this study's secondary outcomes are similar to those reported in the 2018 retrospective chart review assessing the efficacy of rFVIIa, at a dose of 45 mcg/kg, in comparison to 4PCC.
- With lack of data regarding off-label use of 4PCC and rFVIIa in treating postoperative bleeding, more studies needed to confidently conclude that both are equally efficacious with minimal additive negative outcomes.

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