Protamine at Reduced Dose for TAVR Anticoagulation Reversal

Low Dose May Be as Effective as Standard Dose

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Disclosure of Relevant Financial Relationships

I, Mohammed Ebrahim DO NOT have any financial relationships to disclose.

Background

- TAVR is performed under systemic Anticoagulation (UFH).
  - *Post procedural major bleeding* is a significant risk (13.4%), especially in high risk groups.
- Observational studies have suggested decreased bleeding events with protamine.
  - There is limited data on optimal protamine dosing to effectively reverse heparin post-TAVR.
- Effective reversal is crucial to reduce major bleeding events.
- Protamine side effects include *profound hypotension, severe pulmonary hypertension, rebound anticoagulation at higher doses, and rarely anaphylactic* reactions.

Aims

- Typical dose: *1mg protamine per 100U heparin*.
- Protamine dosing protocols have been adopted from traditional cardiopulmonary bypass surgery protocols (a longer and higher bleeding risk procedure).
- Question: Are lower doses of protamine effective at successful heparin reversal following TAVR as compared to “standard dose”?
- *We aimed to investigate the efficacy of low dose protamine in reversing heparin (UFH) following TAVR as measured by activated coagulation time (ACT).*

Methods

- Single center *retrospective observational* study
- *508 patients* who had TAVR at Memorial Regional Hospital, Hollywood, FL.
- Inclusion:
  - *Patients >18 years old who had TAVR between January 1, 2015, and June 30, 2022.*
  - Access via trans-femoral approach
- Exclusion:
  - Patient out of the age range
  - Alternate access sites
  - Incomplete records

Methods

- Medical chart review, EPIC EMR
- ACT measurements were obtained pre- and post-administration of varying doses of protamine.
- Heparin reversal was defined as *an ACT ≤ 150 seconds*.
- Patients were categorized into tertiles of protamine-to-UFH dose (mg/100U):
  - *Low dose, < 0.67mg/100U* (median 50mg, n = 163)
  - *Intermediate 0.67- 1.0mg/100U* (median 100mg, n = 167)
  - *High dose ≥1.0mg/100U* (median 120mg, n= 178).

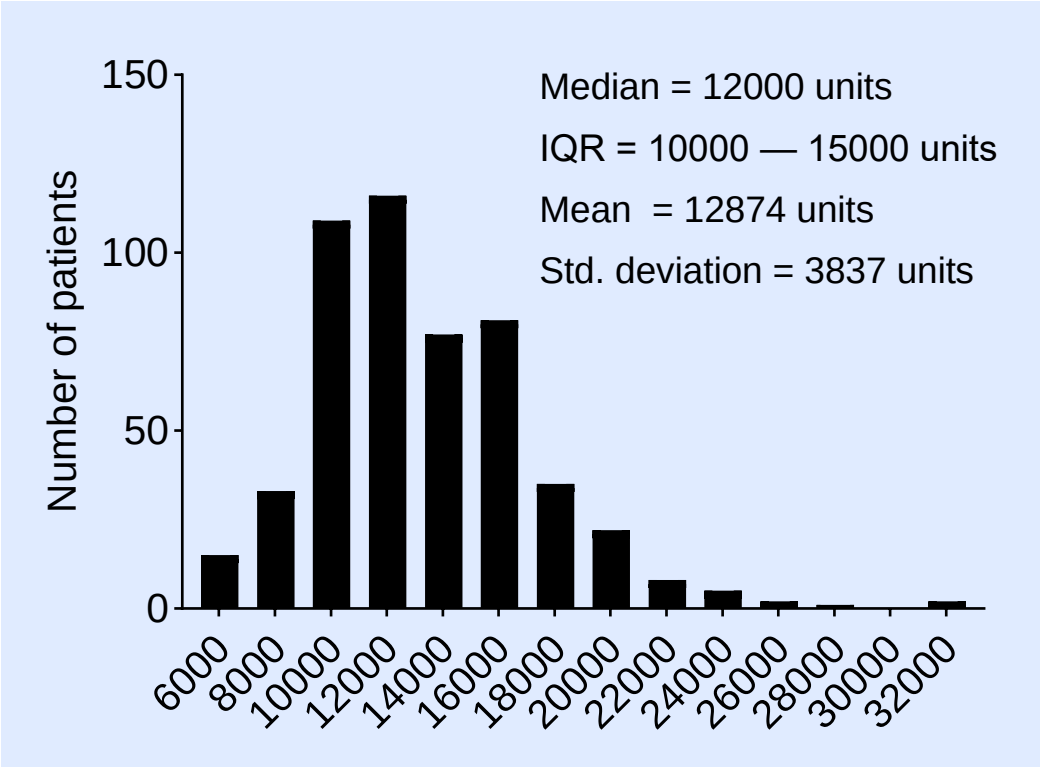
Results: Baseline Characteristics

Table 1. Clinical characteristics of study patients

Variable	Patients (*n* = 508)
Age, years	82 (75 − 87)
Male	284 (55.9)
Weight, kg	76 (64 − 91)
BMI, kg/m2	27.2 (23.5 − 31.5)
Total heparin, units	12000 (10000 − 15000)
Pre-potamine ACT, seconds	279 (257 − 307)
Total protamine, mg	100 (50 − 120)
Extra protomine	21 (4.1)
Post-protamine ACT, seconds	120 (109 − 130)
Heparin reversal	484 (95.3)

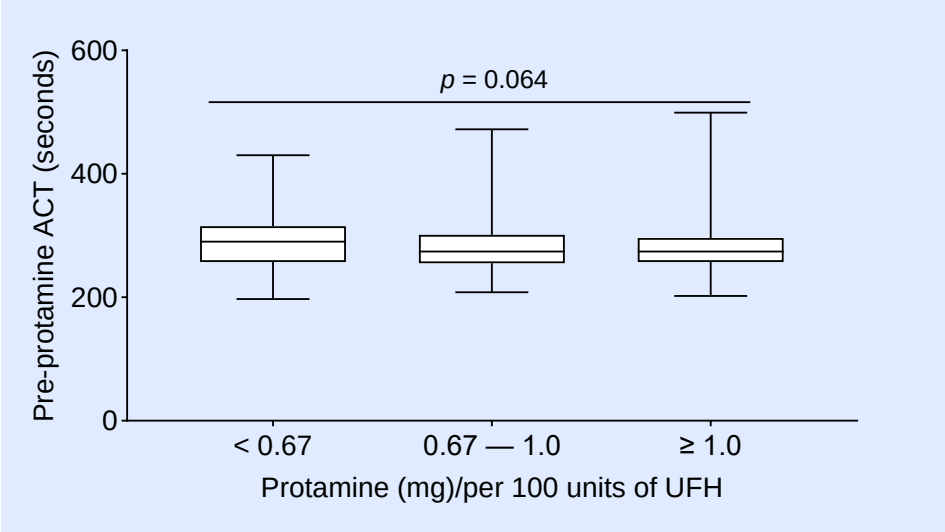
Data given as median and interquartile range (IQR) or n (%).

Results: Heparin Dosing



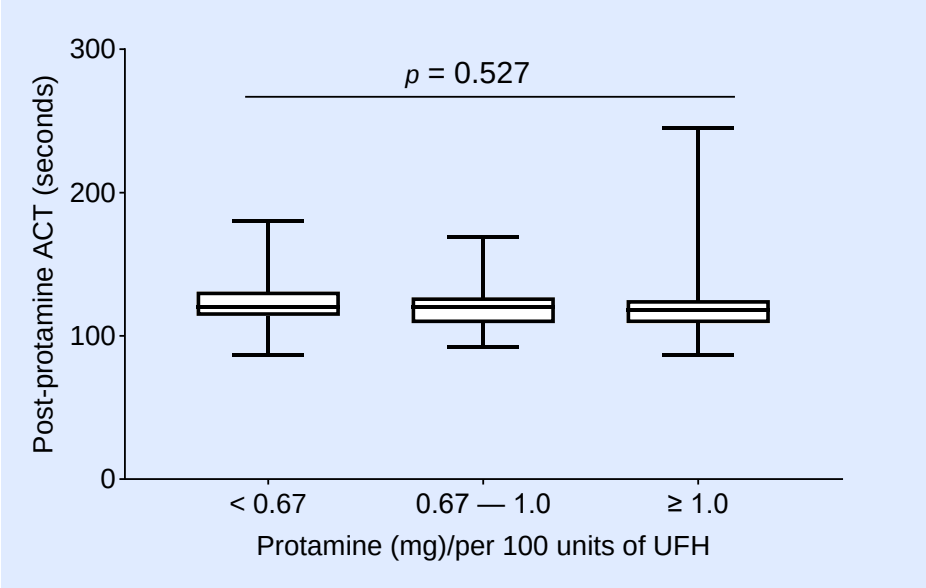
Results: ACT pre-Protamine

- ACT following heparin administration for each group:
  - *Low dose - 290 sec* (IQR, 257-315)
  - *Intermediate dose - 274 sec* (IQR, 255-301)
  - *High dose - 274 sec* (IQR, 257-296)



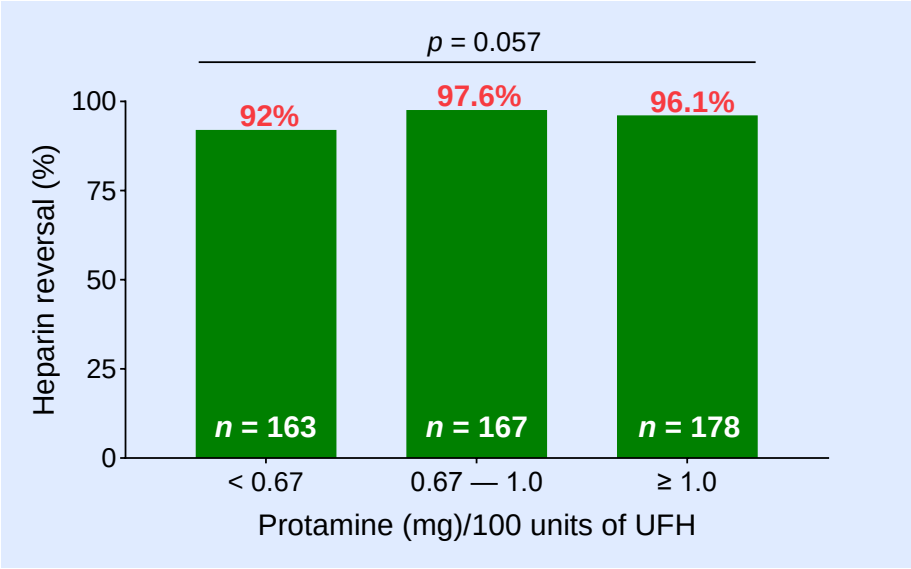
Results: ACT post-Protamine

- ACT after protamine, (p=0.527):
  - *Low dose – 120 sec* (IQR, 114-131)
  - *Intermediate dose - 120 sec* (IQR, 109-127)
  - *High Dose – 118 sec* (IQR, 109-125)



Results

- Corresponding heparin reversal rates:
  - *Low dose: 92%*
  - *Intermediate dose: 97.6%*
  - *High dose: 96.1%*
    - (p = 0.057)



Conclusion

- Multivariate analysis showed comparable rates of heparin reversal with *intermediate (OR 2.42, CI 0.82-7.14, p=0.111)* and *high dose (OR 1.96, CI, 0.75 - 5.13, p=0.171)* compared with low dose protamine.
- This retrospective analysis suggests that *low dose protamine may be as effective as higher doses* in achieving heparin reversal following TAVR.

CENTRAL ILLUSTRATION:
Efficacy of Low-Dose Protamine in Heparin Reversal following TAVR

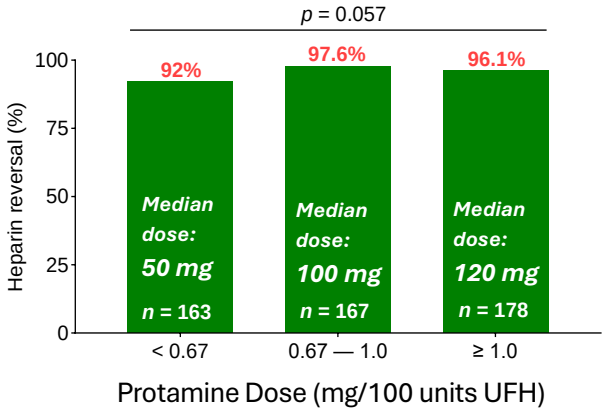
Transcatheter aortic valve replacement (TAVR)

Protamine administration for heparin reversal (*n* = 508)

Tertiles of protamine dose (mg/100 units of UFH)

Low	Internediate	High
(< 0.67)	(0.67 — 1.0)	(≥ 1.0)

Outcome of Heparin Reversal (ACT <150 Sec)



Key Learning Objectives

1. Protamine is effective for the reversal of UFH. There is evidence that this *reduced major bleeding events*.
2. *Low dose protamine appears to be as effective* as intermediate or high dose at reversing heparin post-TAVR.
3. Lower protamine dose may mitigate or reduce potential adverse effects.
4. Further studies investigating the down stream effects and side effect rate from reduced protamine would be useful.