Comparison of a non-weight-based vs weight-based dose titration protocol for intravenous unfractionated heparin

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Background

- Unfractionated heparin (UFH) for the treatment of acute coronary syndrome, valve surgery, and venous thromboembolism is dosed according to weight and partial thromboplastin time (PTT) with low target (PTT 50-70s) and standard target (PTT 60-90s) protocols.
- The UFH protocols at St. Paul's Hospital (SPH) changed in May 2019 with implementation of Cerner electronic medical record.
- Previous protocol: Weight-based initial dose and subsequent dose adjustments.
- Current protocol: Weight-based initial dose only

Objectives

- **Primary objective:** To compare the effectiveness of a non-weight-based vs weight-based dose titration protocol for IV UFH
- **Secondary objective:** To assess the effectiveness of the non-weight-based low-target protocol compared to weight-based low-target protocol for IV UFH

Methods

- **Design:** Retrospective, observational, before-and-after study
- **Inclusion:** SPH cardiology and cardiac surgery wards, Jan 2015–Aug 2016 (weight-based) and Jan-Oct 2020 (non-weight-based), Age >18, on IV UFH for any indication; convenience sample
- **Exclusion:** Did not follow UFH protocol, antiphospholipid antibody syndrome, acute liver failure (ALT 3xULN), contraindications to heparin
- **Primary outcomes:** (1) Number of dosage adjustments required to reach therapeutic PTT. (2) % of patients within therapeutic PTT 24h after initiation
- **Secondary outcome:** For low target protocol: Proportion of patients therapeutic after the 1st PTT measurement (at 6h)
- **Statistics:** Descriptive statistics
  - Continuous variables: Parametric and non-parametric data analyses by two-sample t-test and Wilcoxon rank sum test, respectively.
  - Categorical variables: p-values tested by chi-squared tests
  - Multivariate analyses included age, sex, and weight
  - Comparisons of outcomes based on Poisson regression models for count data, logistic regression models for binary data, and multinomial logistic regression models for ordinal data

Results

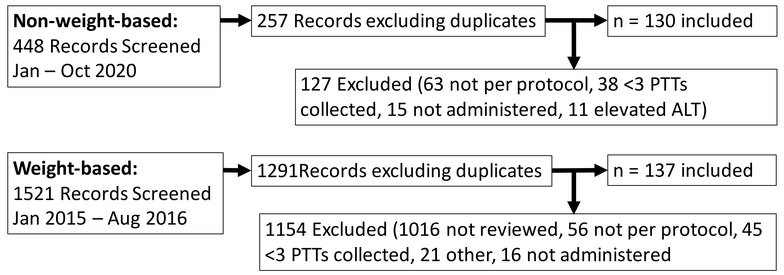

Figure 1: Flow Diagram

Table 1: Baseline Characteristics

	Total (n= 267)	Non-weight-based (n = 130)	Weight based (n = 137)	p-value
Age				
Mean ± SD	65.6 ± 14.0	66.2 ± 13.4	65.1 ± 14.5	0.531
Sex: n (%)				
F	82 (30.7)	40 (30.8)	42 (30.7)	0.984
Weight (kg)				
Mean ± SD	82.8±20.5	82.6 ± 21.6	83.0 ± 19.5	0.874
Indication: n (%)				
UA + NSTE-ACS	75 (28.1)	29 (22.3)	46 (33.6)	
STE-ACS	31 (11.6)	28 (21.5)	3 (2.2)	
Atrial Fibrillation	109 (40.8)	49 (37.7)	60 (43.8)	
Heart Valve	19 (7.1)	13 (10.0)	6 (4.4)	
Other	33 (12.4)	11 (8.5)	22 (16.1)	
Protocol: n (%)				
Low target	158 (59.2)	66 (50.8)	92 (67.2)	
Standard target	109 (40.8)	64 (49.2)	45 (32.8)	

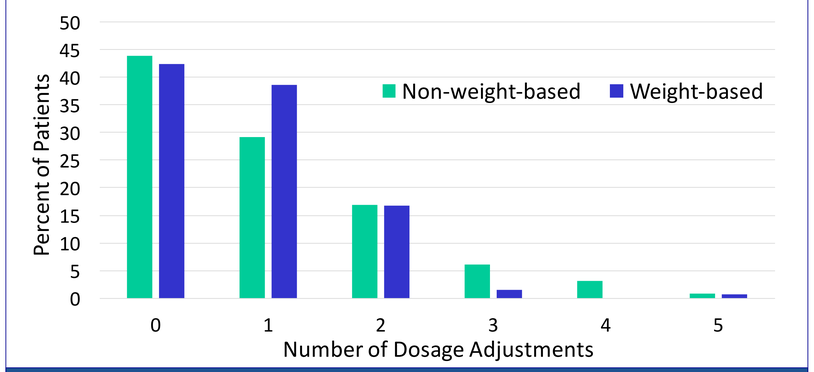

Figure 2: Total number of adjustments needed to reach therapeutic PTT

Table 2: Summary of Outcomes

	Non-weight-based (n = 130)	Weight-based (n = 137)	p-value
Primary Outcome 1: Total number of adjustments to reach 1st therapeutic PTT: median (Q1, Q3)	1 (0 , 2)	1 (0 , 1)	0.483
Primary Outcome 2: Patients therapeutic at 24h: n (%)			
Yes	125 (96.1)	136 (99.3)	0.086
Secondary Outcome 1: Among Low target patients, therapeutic at 1st PTT: n (%)	n = 66	n = 92	
Yes	25 (37.9)	41 (44.6)	0.033
No	41 (62.1)	51 (55.4)	
Above 70s	16 (24.2)	33 (35.9)	
Below 50s	25 (37.9)	18 (19.5)	

Table 3: Multivariate Analyses (Non-weight-based vs weight-based)

		p-value
Primary Outcome 1: Total number of adjustments to reach 1st therapeutic PTT	RR 1.23 (0.95, 1.58)	0.119
Primary Outcome 2: Patients therapeutic at 24h Modelling unfeasible with most patients meeting outcome	OR 0.18 (0.02, 1.60)	0.124
Secondary Outcome 1: Among Low target patients, therapeutic at 1st PTT		
Above vs In Target	OR 0.73 (0.33, 1.62)	0.439
Below vs In Target	OR 2.23 (1.00, 4.99)	0.051
Above vs Below	OR 0.33 (0.14, 0.78)	0.012

Discussion

- Our study is the first to compare a UFH protocol using only weight-based initial dosing to a fully weight-based protocol.
- Both protocols resulted in high proportion of therapeutic PTTs at 24h (>96%), with median number of dose adjustments to 1st therapeutic PTT of 1 in both groups and similar to previous studies.
- The results suggest only weight-based initial dosing may be important for achieving therapeutic PTT. Weight-based dose adjustments did not impact protocol effectiveness in our study.
- Our data suggest lower initial dosing in the non-weight-based low target protocol resulted in more subtherapeutic measurements at 1st PTT
- Limitations of the study: non-randomized study design, change from paper to electronic order entry and charting

Conclusion

- This study suggests the current UFH protocol using only weight-based initial dosing is effective at achieving therapeutic PTT by 24h and similar to the previous fully weight-based protocol