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# Development of a predictive model for nafamostat mesylate dosing in hemodialysis

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**Objectives :** Nafamostat mesylate, an anticoagulant with a short half-life, is useful in hemodialysis for patients with a high risk of bleeding. Research on the appropriate dosage of nafamostat has been insufficient. This study aims to develop a dosage prediction model using data from patients adequately anticoagulated with nafamostat.
**Methods :** We retrospectively analyzed medical records from 12 centers affiliated with Yeolin Medical Foundation over an 8-month period. We evaluated coagulation records from dialysis membranes and vein chambers and cases demonstrating adequate coagulation were included. Candidate predictor variables were evaluated using bootstrapping and stepwise regression to determine feature importance. Several predictive models were developed, and the best model was selected based on RMSE and adjusted $R^2$ metrics.
**Results :** Data from 88 patients and 308 cases were analyzed, with an average nafamostat dose of 21.90 ± 6.82 mg/hr. The top five important features were oral anticoagulant use, dry body weight, age, hemoglobin, and cancer history. The Stepwise 70% model using 12 variables showed the best prediction with an RMSE of 4.11 (95% CI: 4.06, 4.15) and an adjusted $R^2$ of 0.49. In the multivariate linear regression results using the optimal model, variables such as oral anticoagulant use [coeff. -14.20, 95% CI (-18.28, -10.12), P value <0.001] and age [-0.13, 95% CI (-0.19, -0.08), <0.001] were associated with a decrease in nafamostat dosage. Conversely, variables such as dry body weight [0.15, 95% CI (0.09, 0.22),<0.001] and hemoglobin[1.13, 95% CI (0.51, 1.76), <0.001] were associated with an increase in nafamostat dosage.
**Conclusions :** The nafamostat dosage prediction formula derived from the Stepwise 70% model enables individualized dosage calculations. However, further studies for model improvement and external validation are required due to the retrospective nature of this study. Body weight, age, oral anticoagulant, and hemoglobin should be considered when determining the dose of Nafamostat.

figure2.jpg


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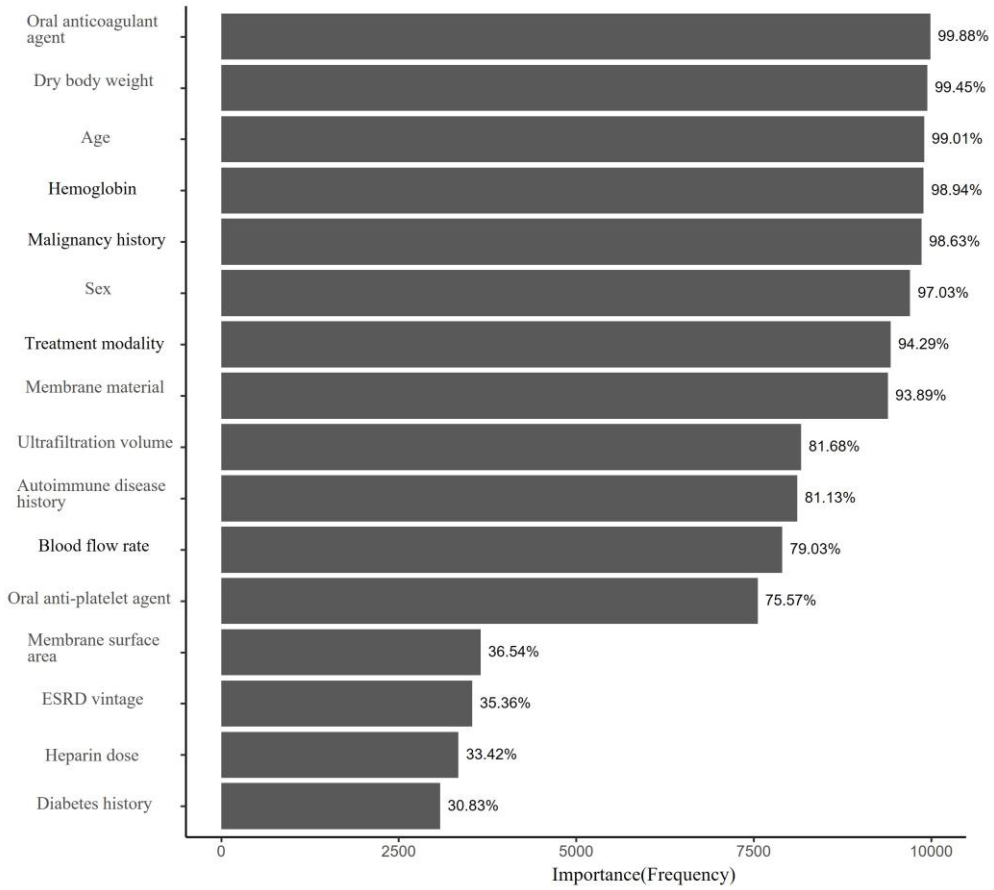
Oral anticoagulant agent
Dry body weight
Age
Hemoglobin
Malignancy history
Sex
Treatment modality
Membrane material
Ultrafiltration volume
Autoimmune disease history
Blood flow rate
Oral anti-platelet agent
Membrane surface area
ESRD vintage
Heparin dose
Diabetes history
99.88%
99.45%
99.01%
98.94%
98.63%
97.03%
94.29%
93.89%
81.68%
81.13%
79.03%
75.57%
36.54%
35.36%
33.42%
30.83%
0
2500
5000
7500
10000
Importance(Frequency)

figure2.jpg

Table 3. Linear Regression Results (with Train data set)

| | univariable | | mutivariable[stepwise 70% model] | |
|---|---|---|---|---|
| value | Coefficient (95% CI) | P-value | Coefficient (95% CI) | P-value |
| Oral anticoagulant agent | -12.02 (-17.00, -7.03) | <0.001 | -14.20 (-18.28, -10.12) | <0.001 |
| Dry body weight, kg | 0.11 (0.05, 0.18) | <0.001 | 0.15 (0.09, 0.22) | <0.001 |
| Age, yr | -0.20 (-0.25, -0.14) | <0.001 | -0.13 (-0.19, -0.08) | <0.001 |
| Hemoglobin, g/dL | 0.99 (0.27, 1.71) | 0.008 | 1.13 (0.51, 1.76) | <0.001 |
| Malignancy history : None | ref | | ref | |
| Cured for more than 5 years | -3.46 (-8.92, 2.00) | 0.214 | -3.20 (-7.44, 1.05) | 0.139 |
| Under 5 years or in treatment | -5.25 (-8.89, -1.60) | 0.005 | -3.92 (-6.91, -0.94) | 0.010 |
| Hemotologic malignancy | 5.57 (1.08, 10.06) | 0.015 | 7.72 (3.45, 12.00) | <0.001 |
| Sex : Male | ref | | ref | |
| Sex : Female | -2.38 (-4.14, -0.63) | 0.008 | -3.17 (-4.89, -1.45) | <0.001 |
| Treatment modality : HD | ref | | ref | |
| Treatment modality : pre-dilution HDF | 2.47 (-1.03, 5.97) | 0.165 | 4.47 (1.65, 7.28) | 0.002 |
| Treatment modality : Post-dilution HDF | 2.83 (0.87, 4.79) | 0.005 | 2.56 (0.71, 4.41) | 0.007 |
| Membrane material : polysurfone | ref | | ref | |
| Membrane material : cellulose triacetate | -0.63 (-5.51, 4.26) | 0.801 | -6.23 (-10.20, -2.27) | 0.002 |
| Ultrafiltration volume, L | -0.78 (-1.60, 0.04) | 0.061 | -1.11 (-1.95, -0.27) | 0.010 |
| Autoimmune disease : None | ref | | ref | |
| Lupus nephritis | 3.48 (-0.89, 7.85) | 0.118 | 4.22 (0.91, 7.52) | 0.013 |
| TMA | 3.12 (-10.44, 16.69) | 0.650 | 3.74 (-6.37, 13.85) | 0.467 |
| Blood flow rate, ml/min | 0.01 (-0.01, 0.03) | 0.241 | -0.03 (-0.05, -0.01) | 0.018 |
| Anti-platelet agent | 3.41 (1.67, 5.16) | <0.001 | 1.69 (0.13, 3.26) | 0.034 |
| Membrane surface area, $m^2$ | 1.97 (-0.66, 4.60) | 0.142 | | |
| ESRD vintage, year | -0.18 (-0.29, -0.07) | <0.001 | | |
| Heparin dose, $IU/10^3$ | 1.95 (1.12, 2.78) | <0.001 | | |
| Diabetes history | 0.42 (-1.35, 2.19) | 0.641 | | |