

Supplementary Materials

Table S1. NRF phenotype and BDNF quartile gradient.

| Item | Category | n/N (%) or value |
|------------------------------|-----------------------|------------------|
| Primary endpoint | Any angiographic NRF | 114/700 (16.3) |
| Final TIMI flow in NRF cases | TIMI 0-1 | 14/114 (12.3) |
| Final TIMI flow in NRF cases | TIMI 2 | 59/114 (51.8) |
| Final TIMI flow in NRF cases | TIMI 3 with MBG 0-1 | 41/114 (36.0) |
| BDNF quartile 1 | ≤ 310 pg/mL | 12/175 (6.9) |
| BDNF quartile 2 | 311-407 pg/mL | 19/175 (10.9) |
| BDNF quartile 3 | 408-532 pg/mL | 30/175 (17.1) |
| BDNF quartile 4 | > 532 pg/mL | 53/175 (30.3) |
| Trend test | Across BDNF quartiles | $p < 0.001$ |

Table S2. Spearman correlation between serum total BDNF and selected parameters.

| Variable | Spearman r | p value |
|--------------------------|-------------------|----------------|
| Age | 0.08 | 0.041 |
| eGFR | -0.20 | <0.001 |
| WBC | 0.20 | <0.001 |
| NLR | 0.23 | <0.001 |
| hs-CRP | 0.32 | <0.001 |
| Peak hs-cTnI | 0.27 | <0.001 |
| NT-proBNP | 0.25 | <0.001 |
| Platelet count | 0.17 | <0.001 |
| MPV | 0.21 | <0.001 |
| PDW | 0.18 | <0.001 |
| LVEF | -0.35 | <0.001 |
| Baseline TIMI flow grade | -0.30 | <0.001 |
| SYNTAX score | 0.19 | <0.001 |
| Lesion length | 0.16 | <0.001 |
| High thrombus burden | 0.24 | <0.001 |

Table S3. Univariable logistic regression for angiographic NRF.

| Variable | Unit/category | OR | 95% CI | p value |
|-----------------------------|--------------------------------------|------|-----------|---------|
| BDNF | per 100 pg/mL increase | 1.78 | 1.54-2.06 | <0.001 |
| Age | per 10-year increase | 1.35 | 1.11-1.63 | 0.002 |
| Male sex | yes vs. no | 0.92 | 0.59-1.43 | 0.724 |
| Diabetes mellitus | yes vs. no | 1.74 | 1.16-2.60 | 0.007 |
| Hypertension | yes vs. no | 1.30 | 0.87-1.94 | 0.205 |
| BMI | per 1 kg/m ² | 1.03 | 0.98-1.08 | 0.238 |
| Symptom-to-angiography time | per 6 h increase | 1.16 | 1.08-1.25 | <0.001 |
| eGFR | per 10 mL/min decrease | 1.43 | 1.24-1.65 | <0.001 |
| hs-CRP | per ln-unit increase | 1.74 | 1.41-2.14 | <0.001 |
| WBC | per 1 x10 ³ /uL increase | 1.17 | 1.09-1.26 | <0.001 |
| NLR | per ln-unit increase | 1.66 | 1.32-2.08 | <0.001 |
| Hemoglobin | per 1 g/dL decrease | 1.26 | 1.10-1.45 | 0.001 |
| Platelet count | per 50 x10 ³ /uL increase | 1.23 | 1.08-1.40 | 0.002 |
| MPV | per 1 fL increase | 1.45 | 1.18-1.78 | <0.001 |
| LVEF | per 5% decrease | 1.61 | 1.39-1.87 | <0.001 |
| Peak hs-cTnI | per ln-unit increase | 1.35 | 1.16-1.58 | <0.001 |
| Baseline TIMI 0-1 | yes vs. no | 3.14 | 2.04-4.83 | <0.001 |
| High thrombus burden | yes vs. no | 3.62 | 2.28-5.75 | <0.001 |
| SYNTAX score | per 5-point increase | 1.47 | 1.27-1.71 | <0.001 |
| Lesion length | per 5-mm increase | 1.45 | 1.28-1.65 | <0.001 |
| Multivessel disease | yes vs. no | 1.43 | 0.96-2.13 | 0.080 |

Table S4. Calibration and internal validation of the final BDNF-enriched Model 4.

| Validation method | Statistic | Value |
|---------------------------|--------------------------------------|---------------|
| Apparent performance | AUC | 0.866 |
| Apparent performance | Brier score | 0.085 |
| Apparent performance | Calibration intercept | -0.02 |
| Apparent performance | Calibration slope | 0.97 |
| Hosmer-Lemeshow test | chi-square (df=8), p | 6.28, p=0.620 |
| Bootstrap, 1000 resamples | Mean optimism | 0.014 |
| Bootstrap, 1000 resamples | Optimism-corrected AUC | 0.852 |
| Bootstrap, 1000 resamples | Optimism-corrected calibration slope | 0.92 |
| Bootstrap, 1000 resamples | Optimism-corrected Brier score | 0.090 |
| 10-fold cross-validation | Mean AUC | 0.845 |
| 10-fold cross-validation | AUC range across folds | 0.809-0.876 |
| 10-fold cross-validation | Mean calibration slope | 0.90 |
| 10-fold cross-validation | Mean Brier score | 0.092 |
| Shrinkage estimate | Uniform shrinkage factor | 0.92 |

Table S5. Incremental value of adding BDNF to clinical and clinical-angiographic models.

| Comparison | Delta AUC | p value | Continuous NRI (95% CI) | p value | IDI (95% CI) | p value |
|---|------------------|----------------|------------------------------------|----------------|---------------------|----------------|
| Model 4 with BDNF vs Model 4 without BDNF | +0.032 | 0.005 | 0.238 (0.096-0.380) | 0.001 | 0.049 (0.025-0.073) | <0.001 |
| BDNF + clinical model vs clinical model alone | +0.087 | <0.001 | 0.326 (0.178-0.474) | <0.001 | 0.066 (0.038-0.094) | <0.001 |

Table S6. Sensitivity and robustness analyses for BDNF as a predictor of NRF.

| Analysis | BDNF effect estimate | 95% CI | p value | Comment |
|---|-----------------------------|---------------|----------------|--|
| BDNF per 100 pg/mL in Model 4 | OR 1.31 | 1.07-1.60 | 0.009 | Primary analysis |
| BDNF log-transformed | OR 1.82 | 1.20-2.75 | 0.004 | Consistent after skewness adjustment |
| BDNF highest quartile vs lower three quartiles | OR 2.01 | 1.14-3.54 | 0.016 | Threshold-like gradient |
| Replacing hs-CRP with NLR | OR 1.32 | 1.08-1.61 | 0.007 | Stable alternative inflammatory adjustment |
| Adding MPV to the final model | OR 1.29 | 1.05-1.59 | 0.016 | Not fully explained by platelet indices |
| Excluding patients with rescue GP IIb/IIIa use | OR 1.28 | 1.03-1.59 | 0.026 | Not driven by bailout pharmacology |
| Excluding baseline TIMI 0-1 culprit lesions | OR 1.27 | 1.00-1.61 | 0.049 | Persists in non-occlusive baseline flow |
| Using final TIMI <3 only as endpoint | OR 1.36 | 1.06-1.74 | 0.015 | Robust with stricter endpoint |
| Replacing SYNTAX score with multivessel disease | OR 1.33 | 1.09-1.63 | 0.005 | Stable alternative anatomic adjustment |
| Complete-case analysis only | OR 1.30 | 1.06-1.60 | 0.012 | Similar to primary analysis |

Table S7. Multicollinearity diagnostics and missing-data summary for the final model.

| Variable | Tolerance | VIF | Missing, n (%) |
|-----------------------------|-----------|------|----------------|
| BDNF | 0.80 | 1.25 | 0 (0.0) |
| Age | 0.84 | 1.19 | 0 (0.0) |
| Diabetes mellitus | 0.87 | 1.15 | 0 (0.0) |
| eGFR | 0.76 | 1.32 | 2 (0.3) |
| hs-CRP | 0.70 | 1.43 | 18 (2.6) |
| WBC | 0.72 | 1.39 | 0 (0.0) |
| Hemoglobin | 0.88 | 1.14 | 0 (0.0) |
| Platelet count | 0.84 | 1.19 | 0 (0.0) |
| LVEF | 0.74 | 1.35 | 9 (1.3) |
| Peak hs-cTnI | 0.78 | 1.28 | 5 (0.7) |
| Symptom-to-angiography time | 0.82 | 1.22 | 4 (0.6) |
| Baseline TIMI 0-1 | 0.79 | 1.27 | 0 (0.0) |
| High thrombus burden | 0.77 | 1.30 | 0 (0.0) |
| SYNTAX score | 0.68 | 1.47 | 0 (0.0) |
| Lesion length | 0.70 | 1.43 | 0 (0.0) |

Table S8. Exploratory comparison of BDNF with simple laboratory-marker models.

| Model | AUC (95% CI) | Delta AUC | p value | Sensitivity (%) | Specificity (%) |
|--------------------------------------|---------------------|-----------|---------|-----------------|-----------------|
| hs-CRP + platelet count | 0.732 (0.681-0.783) | Reference | - | 66.7 | 69.8 |
| hs-CRP + platelet count + BDNF | 0.812 (0.770-0.854) | +0.080 | <0.001 | 73.7 | 77.0 |
| hs-CRP + platelet count + MPV | 0.754 (0.704-0.803) | Reference | - | 68.4 | 70.6 |
| hs-CRP + platelet count + MPV + BDNF | 0.819 (0.778-0.860) | +0.065 | <0.001 | 74.6 | 77.8 |
| BDNF alone | 0.787 (0.742-0.833) | - | - | 70.2 | 74.1 |

AUC: area under the curve; BDNF: brain-derived neurotrophic factor; hs-CRP: high-sensitivity C-reactive protein; MPV: mean platelet volume. These analyses were exploratory and were performed to evaluate whether the BDNF signal duplicated simple inflammatory and platelet-related laboratory information.

Supplementary Figures

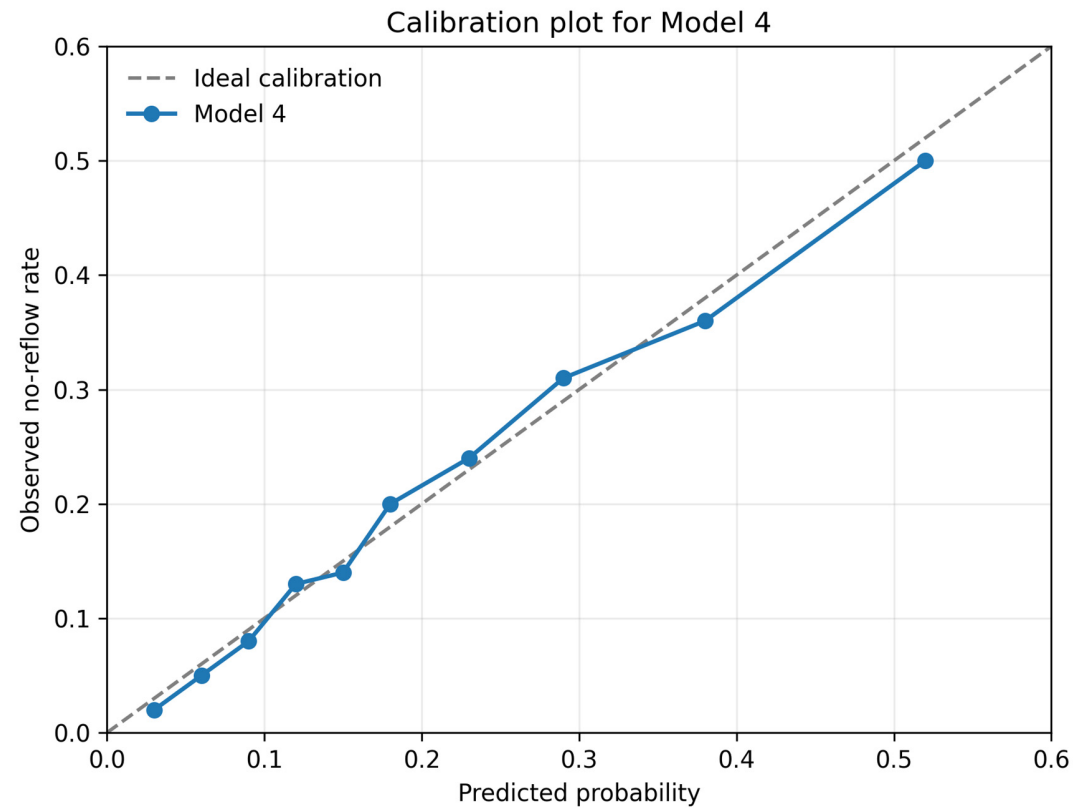


Figure S1. Calibration plot for Model 4. Points represent observed NRF rates across deciles of predicted probability.

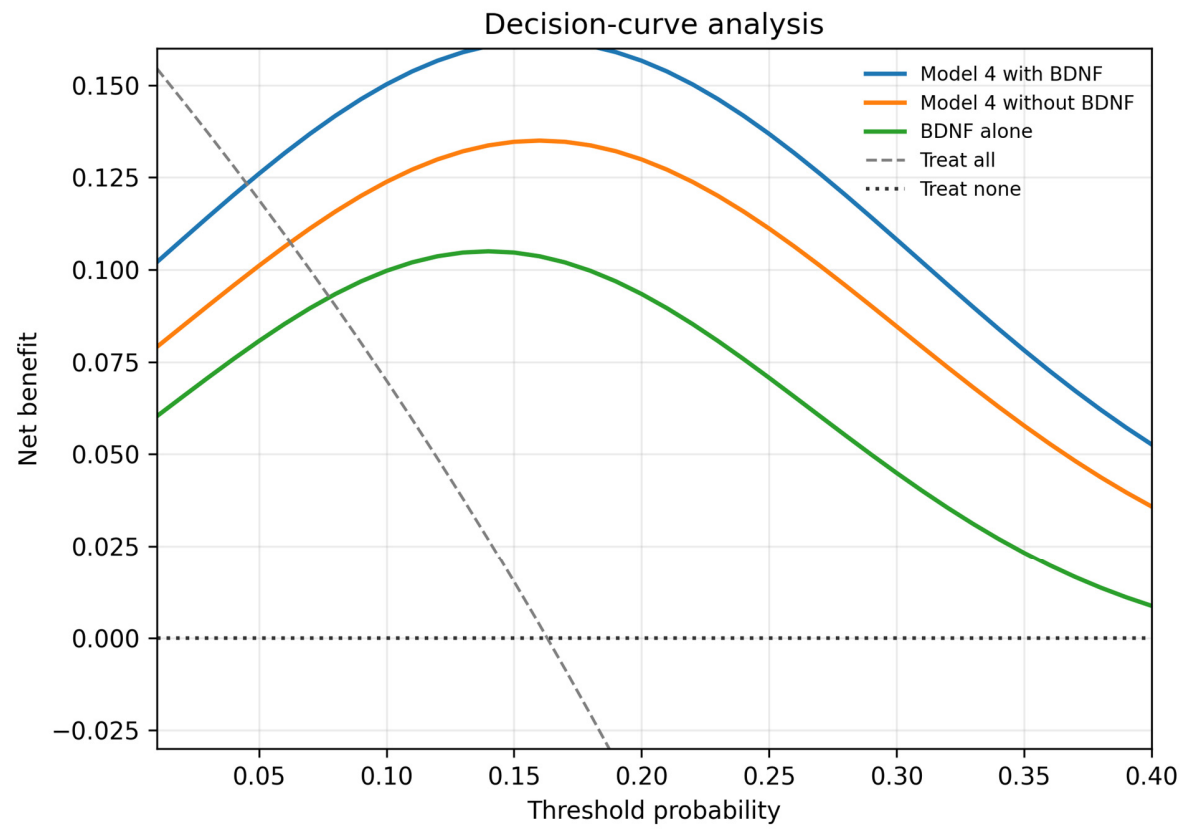


Figure S2. Decision-curve analysis comparing Model 4 with BDNF, Model 4 without BDNF, BDNF alone, treat-all, and treat-none strategies.