

GRADING DYNAMIC FIBRINOLYSIS RESISTANCE IN SEPSIS

A simple bedside tool that associates with disease severity and ICU outcomes

THE PROBLEM

Sepsis is associated with fibrinolysis resistance → thrombotic microvascular obstruction, organ failure and death.



THE SOLUTION

A point-of-care grading system using tPA-enhanced viscoelastic testing (tPA-VET) adjusted for fibrin clot strength.

Metric: TPA-LT / FIB_{A10} (sec/mm)



THE IMPACT

- ✓ Rapid bedside assessment
- ✓ Risk stratification
- ✓ Monitors changes over time
- ✓ Identifies patients at highest risk
- ✓ Supports clinical trial enrichment



FIBRINOLYSIS RESISTANCE GRADING SYSTEM

GRADE 1 – LOW RESISTANCE

TPA-LT/FIB_{A10} < 13 sec/mm

Normal fibrinolytic capacity



Preserved TPA-LT ↔ FIB_{A10} correlation ($r = 0.85$) — like non-septic controls



Similar to non-septic controls

CLINICAL PROFILE

- Lower disease severity (APACHE III, SOFA)
- Lower organ support requirements
- Lowest mortality (15% at 28 days)



MAINTAINED FIBRINOLYSIS
34% of septic patients

GRADE 2 – MODERATE RESISTANCE

TPA-LT/FIB_{A10} 13 – <26 sec/mm

Moderately decreased fibrinolytic capacity



Partial loss of TPA-LT ↔ FIB_{A10} correlation ($r = 0.41$)



Intermediate fibrinolysis marker changes

CLINICAL PROFILE

- Intermediate disease severity
- Increased organ support needs
- Intermediate mortality (24% at 28 days)



MODERATELY RESISTANT
Trend toward inhibitory profile

GRADE 3 – HIGH RESISTANCE

TPA-LT/FIB_{A10} ≥ 26 sec/mm

Severely decreased / absent fibrinolytic capacity



Loss of TPA-LT ↔ FIB_{A10} correlation ($r = 0.15$, ns)



Strongest inhibitory fibrinolysis profile

CLINICAL PROFILE

- Highest disease severity (APACHE III, SOFA)
 - Highest organ support requirements
 - Highest mortality (42% at 28 days)
- 3.9-fold ↑ hazard for death vs Grade 1 ($p < 0.001$)



SEVERELY RESISTANT
Highest risk

FIBRINOLYSIS MARKER PROFILE (NESTED SUBSTUDY, n=40 PATIENTS)

PAI-1 ACTIVITY



Lowest in Grade 1
Highest in Grade 3

PLASMINOGEN



Highest in Grade 1
Lowest in Grade 3

PAI-1/TPA RATIO



Progressively increases 1 → 3

α2AP/PLASMINOGEN RATIO



Progressively increases 1 → 3

DYNAMIC CHANGES OVER TIME: WHY IT MATTERS



- ✓ Patients moved between grades over time
- ✓ Improvement to a lower grade was associated with lower risk of death
- ✓ Grade 3 had the lowest probability of discharge alive and the highest probability of ICU death

CLINICAL SIGNIFICANCE FOR MEDICAL STAFF



RISK STRATIFICATION

Identify high-risk patients (Grade 3) early and monitor for deterioration.



GUIDE MANAGEMENT

Tailor intensity of monitoring, organ support and anticoagulant strategies based on fibrinolysis status.



MONITOR RESPONSE

Track dynamic changes in fibrinolysis resistance to assess response to treatment over time.



CLINICAL TRIALS ENRICHMENT

Enables targeted enrollment of patients most likely to benefit from fibrinolytic therapies.



BETTER OUTCOMES

Early identification and appropriate intervention may reduce organ failure and improve survival.



KEY TAKEAWAY: A simple, bedside grading system using TPA-LT/FIB_{A10} identifies three distinct fibrinolysis resistance endotypes in sepsis that associate with disease severity, organ failure and 28-day outcomes.

MEASURE. GRADE. MONITOR. ACT.