

## BASELINE THROMBIN GENERATION TEST DOES NOT PREDICT THROMBOTIC EVENTS IN ACUTE LEUKEMIA: A MONOCENTRIC PROSPECTIVE STUDY.

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### Background and Aims

Thromboembolic events and bleeding are frequent and clinically significant complications in patients with acute leukemia (AL), contributing to morbidity and mortality. Conventional coagulation assays (CCAs) and platelet count offer limited predictive value. Global coagulation assays such as thrombin generation assay (TGA) may provide a more comprehensive picture of the hemostatic state. This prospective monocentric study aimed to assess whether baseline TGA parameters could predict thrombotic events in patients with newly diagnosed AL.

### Methods

A total of 111 adult patients diagnosed with AL (83 AML, 15 ALL, 8 APL, 5 MPAL) were enrolled between February 2022 and September 2024. Baseline TGA was performed using the Calibrated Automated Thrombogram (CAT) system. Normal TGA parameters (lag time, ttPeak, ETP, peak) were determined based on the analysis of pooled normal plasma. CCAs (PT, PTT, fibrinogen, AT) and complete blood counts were performed too. Patients were followed for the occurrence of objectively confirmed thrombotic events. Statistical comparisons were performed using the Mann-Whitney U test and Kaplan-Meier curves.

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### Results

At diagnosis, 90.9% of patients showed increased lag time, 66.7% increased ttPeak, 63.1% increased ETP, and 52.3% increased peak (Table 1). Despite most of the cohort showing a pattern of hypercoagulability, only 8 patients (7.2%) developed thrombotic complications, all of which were associated with central venous catheter placement. No statistically significant differences were found in baseline TGA parameters between patients with and without thrombotic events (lag time  $p=0.60$ , ttPeak  $p=0.57$ , ETP  $p=0.56$ , peak  $p=0.69$ ). No differences were observed across leukemia subtypes ( $p=0.23$ ) or treatment regimens ( $p=0.62$ ).

### Conclusions

Baseline TGA parameters, despite indicating a prothrombotic profile in most AL patients, were not predictive of thrombotic events. The discrepancy between laboratory hypercoagulability and clinical thrombosis likely reflects the multifactorial nature of thrombotic risk, including factors not captured by plasma-based assays. These findings suggest that baseline TGA parameters alone do not predict thrombotic risk in AL. Future studies should consider longitudinal TGA monitoring and the integration of additional markers such as platelet function and inflammatory mediators.

Patients' Characteristics and Thrombotic Events

	Sex, M/F	Age (years), Median (Range)	Risk, Median (Range)	Bone marrow blasts (%), Median (Range)	HB (g/dl), Median (Range)	WBC* $10^9$ /mmc, Median (Range)	PLT* $10^9$ /mmc, Median (Range)	Lag time (min), Median (Range) (N.V. < 2.42 min) <sup>†</sup>	ETP (nM $\cdot$ min), Median (Range) (N.V. < 1249.63 nM $\cdot$ min) <sup>†</sup>	Peak (nM), Median (Range) (N.V. < 237.73 nM) <sup>†</sup>	ttPeak (min), Median (Range) (N.V. < 5.84 min) <sup>†</sup>	Follow up, months, Median (Range)	Thrombotic events, N (%)	Deaths, N (%)
AL (N = 111)	53/58	63.6 (18.0-86.1)	intermediate (low-high)	60 (10-100)	9.5 (4.5-14.6)	6.0 (0.4-116.7)	66.0 (3.0-361.0)	4.1 (2-11.83)	1200.44 (465.59-2412.94)	234.11 (59.18-399.51)	7 (4.17-15.5)	8.28 (0.03-32.4)	8 (7.20)	32 (28.8)
AML (N = 83)*	39/44	64.7 (19.8-88.7)	intermediate (low-high)	50 (10-90)	9.4 (4.5-14.6)	6.1 (0.4-116.7)	63.0 (3.0-361.0)	4.05 (2.17-9)	1260.59 (608.31-2412.94)	255.86 (107.99-399.51)	6.83 (4.17-12.33)	7.8 (0.03-32.4)	5 (6)	25 (30)
APL (N = 8)	3/5	56.7 (23.4-67.6)	low	56 (53-91)	11.6 (9.4-13.9)	2.4 (0.9-9.4)	64.0 (5.0-120.0)	4.83 (3.33-5.67)	1183.41 (928.11-1830.04)	174.08 (135.09-268.28)	8.5 (7-12)	15.55 (3.8-28.7)	2 (25)	0
MPAL (N = 5)	4/1	63.4 (56.6-76.4)	N.E.	82 (65-90)	9.1 (7.1-10)	72.1 (2.4-81.3)	130.0 (81.0-357.0)	4.83 (4-9.67)	982.88 (465.59-1994.06)	194.82 (59.18-214.66)	8.5 (5.33-13)	10.2 (0.13-30.0)	1 (20)	3 (60)
ALL (N = 15)	7/8	53.5 (18.0-86.1)	high (low-high)	83 (25-100)	10 (8.2-14.1)	6.4 (1.5-69.5)	66.0 (28.0-313.0)	3.67 (2-11.83)	1162.57 (853.84-2047.49)	204.08 (119.11-372.69)	6.92 (4.33-8.83)	9.33 (1.0-31.9)	0	4 (26.7)

M: Male, F: Female, HB: Hemoglobin, WBC: White Blood Cells, PLT: Platelets, N.V.: Normal Values, ETP: Endogenous Thrombin Potential, ttPeak: time to Peak, AL: Acute Leukemia, AML: Acute Myeloid Leukemia, APL: Acute Promyelocytic Leukemia, MPAL: Mixed Phenotype Acute Leukemia, ALL: Acute Lymphoblastic Leukemia, N.E.: Not Evaluable.

\*APL excluded.

<sup>†</sup>Based on pooled normal plasma.