Hemostatic Abnormalities and Their Correlation with the Khorana Risk Score in Patients with Lung Carcinoma: A Cross-Sectional Study from Western India

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BACKGROUND & OBJECTIVE

Lung carcinoma carries a substantially elevated risk of cancer-associated venous thromboembolism (VTE). The Khorana Risk Score (KRS) is the most widely validated clinical tool for chemotherapy-associated VTE, but does not incorporate laboratory hemostatic biomarkers. This study characterized hemostatic abnormalities in lung carcinoma and examined their relationship with KRS risk categories and actual VTE occurrence.

STUDY DESIGN & METHODS

Design: Cross-sectional observational study at a tertiary-care center in Western India, October 2020–September 2022.

Sample: 76 adults with histologically confirmed lung carcinoma; treatment-naïve or under active follow-up. Patients with pre-existing coagulation disorders, anticoagulation, pregnancy/lactation, second primary malignancy or incomplete data were excluded.

Assessment: Demographics, histology, stage, ECOG status and complete blood count. Hemostatic tests included PT, aPTT, fibrinogen, D-dimer, AT-III functional activity and anticardiolipin antibodies (ACLA IgM/IgG).

KRS: Cancer site, platelet count, hemoglobin/ESA use, leukocyte count and BMI. Categories: low 0; intermediate 1–2; high ≥3.

Statistics: JMP 16.0; t-test, Wilcoxon/Kruskal–Wallis, ANOVA, chi-square/Fisher exact tests and linear regression; p <0.05 significant.

BASELINE CHARACTERISTICS

Characteristic	Finding
Mean age	58.1 ± 12.1 years; range 29–86
Male : female	1.81 : 1 (49 : 27)
Adenocarcinoma	92.1% (70/76)
Metastatic disease	69.7% (53/76)
Smoking history	61%
ECOG ≥2	48%
Mean Hb	11.26 ± 1.51 g/dL
Mean WBC	9019.7 ± 2763.3 /mm³
Mean platelets	2.58 ± 0.99 lakh/mm³
Mean BMI	22.51 ± 1.91 kg/m²

KHORANA RISK SCORE & VTE

Mean KRS: 1.60 ± 0.88 (range 1–4). No patient had a low-risk score because lung cancer itself contributes one KRS point.

Intermediate risk (KRS 1–2): 62/76 (81.6%). High risk (KRS ≥3): 14/76 (18.4%).

VTE occurred in 2 patients (2.6%), both as pulmonary thromboembolism (PTE), and both exclusively in the high-risk KRS group: 2/14 (14.3%) versus 0/62 in the intermediate-risk group ($\chi^2 = 7.014$, p = 0.0081). Both patients with PTE died during the study period.

KEY HAEMOSTATIC FINDINGS

Parameter	Intermediate KRS	High KRS	p
PT (sec)	13.41 ± 1.17	18.39 ± 3.23	<0.0001
aPTT (sec)	32.75 ± 2.25	40.81 ± 6.77	<0.0001
Fibrinogen (mg/dL)	275.1 ± 47.9	499.3 ± 67.1	<0.0001
D-dimer (ng/mL)	0.34 ± 0.63	2.50 ± 3.94	<0.0001
AT-III activity (%)	96.42 ± 5.11	83.07 ± 1.33	<0.0001

499 mg/dL
FIBRINOGEN IN HIGH-RISK GROUP

2.50 ng/mL
D-DIMER IN HIGH-RISK GROUP

83.1%
AT-III ACTIVITY IN HIGH-RISK GROUP

THE CENTRAL FINDING

Both observed VTE events occurred in the high-risk KRS group — 14.3% of high-risk patients versus 0% in the intermediate-risk group.

n = 76
LUNG CARCINOMA PATIENTS

58.1 ± 12.1 y
MEAN AGE

2.6%
VTE / PTE

81.6%
INTERMEDIATE KRS

OVERALL HAEMOSTATIC PROFILE

Across the full cohort, mean fibrinogen was 316.4 ± 101.5 mg/dL, median D-dimer was 0.21 ng/mL, and mean AT-III activity was 93.96 ± 6.97%. The overall pattern suggested a procoagulant state even without overt thrombosis.

DOSE–RESPONSE RELATIONSHIP WITH KRS

Linear regression confirmed progressive hemostatic derangement with increasing KRS:

- PT increased significantly with KRS (PT = 11.06 + 2.04 × KRS; p <0.0001).
- aPTT, fibrinogen and D-dimer showed significant positive associations with KRS.
- AT-III activity showed a significant negative association with KRS.

Among the two VTE patients, all five hemostatic parameters were markedly deranged compared with patients without VTE.

ANTICARDIOLIPIN ANTIBODIES

ACLA IgM was positive in 6/76 (7.9%) and IgG in 9/76 (11.8%); any ACLA positivity occurred in 11/76 (14.5%). There was no statistically significant association between ACLA positivity and either VTE or KRS category. One of the two VTE patients was ACLA-IgM positive.

CLINICAL INTERPRETATION

The strong association between higher KRS and prolonged PT/aPTT, elevated fibrinogen and D-dimer, and reduced AT-III supports biological concordance between a clinical risk score and an underlying prothrombotic state. Fibrinogen and D-dimer may reflect tumour-associated inflammation, tissue-factor activity and subclinical thrombogenesis, while reduced AT-III may amplify thrombin/factor Xa activity. These findings provide biological plausibility for incorporating laboratory biomarkers into enhanced VTE prediction models.

IMPLICATIONS, LIMITATIONS & CONCLUSION

IMPLICATIONS

- Fibrinogen, D-dimer and AT-III may provide incremental information beyond KRS.
- Biomarker-informed risk assessment could help identify high-KRS patients most likely to benefit from thromboprophylaxis.
- Prospective validation is needed before routine biomarker-based escalation of prophylaxis.

LIMITATIONS

Cross-sectional design; single tertiary center; n=76 with only two VTE events; predominance of adenocarcinoma (92.1%) and metastatic disease; no systematic extended VTE follow-up; no serial hemostatic measurements or long-term survival data.

CONCLUSION

Hemostatic abnormalities were prevalent and strongly correlated with KRS. VTE occurred exclusively in high-risk patients. Fibrinogen, D-dimer and AT-III are promising candidates for enhanced risk stratification, warranting multicenter prospective validation.

SELECTED REFERENCES

1. Khorana AA, et al. Blood. 2008;111:4902–4907.
2. Lyman GH, et al. Blood Adv. 2021;5:927–974.
3. Key NS, et al. J Clin Oncol. 2020;38:496–520.
4. Falanga A, Marchetti M. Thromb Res. 2018;164:S54–S59.
5. Connors JM. N Engl J Med. 2022;386:1136–1149.
6. Buccheri G, et al. Eur Respir J. 1997;10:2183–2189.
7. Ünsal E, et al. Respir Med. 2004;98:93–98.
8. van Es N, et al. Haematologica. 2017;102:1494–1501.

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