Biomarkers:
Coagulation Assays in the Prognosis of Colorectal Cancer

Can coagulation assays serve as prognostic factors in patients with colorectal cancer?

A retrospective study finds that D-dimer and INR correlate significantly with tumor markers and disease stage in patients with colorectal cancer.

Reference

Kilic L, Yildiz I, Sen FK, et al. **D-dimer and international normalized ratio (INR) are correlated with tumor markers and disease stage in colorectal cancer patients.** *Cancer Biomark.* 2015;15(4):405-411.

Overview

The aim of this study was to **evaluate the prognostic significance of coagulation tests and clarify their relationship with tumor markers and other clinical variables in colorectal cancer.**

Study Design

Retrospective cohort study.

Results

This study compared 94 patients with histologically proven colorectal cancer to healthy controls. All coagulation tests, including D-dimer, fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ration (INR), and platelet counts, were significantly different between the patient group and control group ($p < .001$ for all variables except PT). Metastatic disease correlated with elevated INR (median values 1.08 vs 1.1; $p = .03$), and stage III patients had higher D-dimer levels than stage II patients (324 IU/mL vs 589 IU/mL; $p = .03$). Comparison with tumor markers showed that high CA 19-9 (tumor marker) levels correlated with higher INR and that high CEA (tumor marker) levels correlated with elevated D-dimer. Coagulation tests did not correlate with overall survival. Analysis of factors including D-dimer, CEA, CA 19-9, state of metastasis, and age found only CEA to be an independent prognostic factor for overall survival.

Discussion

Hypercoagulation and fibrinolysis are characteristic of malignancy, with as many as 95% of metastatic patients displaying hemostatic abnormalities. Hypercoagulation not only puts patients at increased risk for thromboembolism and death but also serves as an indication of tumor activity. Coagulation pathways are activated by tumor cells or tumor-associated inflammatory cells to drive tumor stroma formation, and both fibrin remodeling and angiogenesis play a critical role in tumor growth, invasion, and metastasis.[1]

The process of tumor-related fibrin remodeling produces fibrin degradation products, including D-dimer. In previous trials of patients with colorectal cancer, plasma levels of D-dimer were associated with larger tumors, deeper wall penetration, lymph node metastases, CEA levels, and shorter survival.[2],[3] The current study confirmed 2 of these findings: that D-dimer is associated with lymph node metastases (stage III vs stage II) and CEA levels.

Although coagulation assays did not predict overall survival in the current study, they did show a statistically significant correlation with tumor markers and disease stage. The authors of the study suggest that D-dimer might be an even more reliable prognostic factor than CEA or CA 19-9 in the preoperative setting for patients with colorectal cancer.

[1] Zacharski LR, Wojtukiewicz MZ, Costantini V, Ornstein DL, Memoli VA. **Pathways of coagulation/fibrinolysis activation in malignancy.** *Semin Thromb Hemost*. 1992;18(1): 104-116.

[2] Oya M, Akiyama Y, Yanagida T, Akao S, Ishikawa H. **Plasma D-dimer level in patients with colorectal cancer: its role as a tumor marker.** *Surg Today*. 1998;28(4):373-378.

[3] Yamamoto M, Yoshinaga K, Matsuyama A, et al. **Plasma D-dimer level as a mortality predictor in patients with advanced or recurrent colorectal cancer.** *Oncology*. 2012;83(1): 10-15.