

CONGENITAL AND ACQUIRED RISK FACTORS

IMPACT OF INHERITED THROMBOPHILIA ON CANCER-ASSOCIATED THROMBOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction. Cancer-associated thrombosis (CAT) is a frequent and clinically relevant complication in patients with malignancy. While inherited thrombophilia is a well-established risk factor for venous thromboembolism in the general population, its contribution to CAT remains uncertain, and routine thrombophilia testing is not recommended in current guidelines.

Aim. To evaluate the association between inherited thrombophilia, specifically factor V Leiden and the prothrombin G20210A mutation, and the risk of CAT.

Materials and Methods. We conducted a systematic review and meta-analysis in accordance with PRISMA 2020 guidelines. Observational studies enrolling adult cancer patients with and without VTE were included. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using random-effects Mantel-Haenszel models. Heterogeneity was assessed using the I² statistic. Risk of bias was evaluated using the Newcastle-Ottawa Scale, and certainty of evidence was assessed with the GRADE approach.

Results. Eight studies evaluating factor V Leiden and six studies evaluating the prothrombin G20210A mutation met

the inclusion criteria. As shown in Figure 1, factor V Leiden was significantly associated with an increased risk of cancer-associated thrombosis (pooled OR 2.75, 95% CI 1.34-5.64; p = 0.006), with moderate heterogeneity (I² = 64%) (A). The prothrombin G20210A mutation was also associated with CAT (pooled OR 2.17, 95% CI 1.06-4.45; p = 0.03), with no observed heterogeneity (I² = 0%) (B). Sensitivity analysis excluding studies primarily focused on catheter-related thrombosis confirmed the robustness of the association between factor V Leiden and CAT (pooled OR 2.52, 95% CI 1.17-5.45; p = 0.02; I² = 67%) (Figure 1, C). Severe inherited thrombophilia could not be quantitatively analyzed because it was reported in only one eligible study. According to GRADE, the certainty of evidence was rated as moderate for factor V Leiden and low for the prothrombin G20210A mutation.

Conclusions. Inherited thrombophilia, particularly factor V Leiden, is associated with an increased risk of CAT. These findings support a role for genetic predisposition as a risk modifier in CAT and may contribute to refined, individualized risk stratification strategies in selected cancer populations. □□

Figure 1. Forest plots of the association between inherited thrombophilia and cancer-associated thrombosis: factor V Leiden (A), prothrombin G20210A mutation (B), and sensitivity analysis for factor V Leiden excluding catheter-related thrombosis studies (C). Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using random-effects models.

