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ANTICOAGULANT PRIMARY PROPHYLAXIS

KHORANA RISK SCORE AND GENOMIC PROFILING FOR PREDICTION OF VENOUS THROMBOEMBOLISM IN OVARIAN CANCER

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Introduction. Ovarian cancer carries a high thromboembolic risk, with VTE incidence up to 13.3%. We conducted a retrospective cohort study to assess Khorana Risk Score (KRS) performance and explore mutational differences between patients with ovarian cancer with and without VTE.

Aims. To assess the predictive value of the KRS for VTE in ovarian cancer and to investigate differences in somatic mutational profiles between patients who developed VTE and those who did not, with the goal of identifying potential molecular determinants associated with thromboembolic risk.

Methods. We included patients with ovarian cancer consecutively enrolled in the Comprehensive Genomic Profiling (CGP) program (NCT 06020625) at Gemelli University Polyclinic Foundation IRCCS between March 2022 and December 2023, profiled using TruSight Oncology 500. Informed consent was obtained prior to CGP. VTE events within 12 months from chemotherapy start were recorded. KRS was calculated at the time of genomic profiling, before chemotherapy initiation. KRS was dichotomized as low (1) or intermediate-high (≥2) risk. Somatic mutations with a variant allele frequency ≥0.05, classified as oncogenic or likely oncogenic according to OncoKB, were included in the analysis. Differences between cohorts were assessed using Fisher's test.

Results. Of 667 profiled patients, 413 with at least 12 months follow-up were analyzed. Most had high-grade serous ovarian cancer (84%) and advanced-stage disease (86%). VTE occurred in 20% (n=84) of patients. Age, histology, and stage showed no significant differences between those with and without VTE. KRS showed a sensitivity of 87% and a specificity of 17% (72% accuracy), with no significant association with VTE (p=0.54). In patients with VTE, we observed a significantly higher proportion of mutations in FGFR2 (OR 11.7, p=0.03), NFE2L2 (OR 11.7, p=0.03), and KEAP1 (OR 5.3, p=0.03) (Figure 1a). Among patients with at least one of these mutations, VTE event rate was 67% (Figure 1b). In these patients, significant enrichment was observed in pathways related to cellular response to oxidative stress and chemical stress, as well as fluid shear and atherosclerosis, driven by NFE2L2 and KEAP1 (Figure 1c).

Conclusions. Our study showed a limited predictive role of KRS in ovarian cancer. Our mutational findings suggest a potential role for KEAP1 and NFE2L2 in VTE development, warranting further investigation through multiomic approach.

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