

TROMBOEMBOLISMO VENOSO

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

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Introduction

Ovarian cancer (OC) 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 OC with and without VTE.

Methods

We included patients with OC consecutively enrolled in the Comprehensive Genomic Profiling (CGP) program (NCT 06020625) at Gemelli University Polyclinic Foundation IRCCS between March 2022 and December 2023. 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.

Results

Of 667 profiled patients, 413 with at least 12 months follow-up were analyzed. Most had high-grade serous OC (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, $p=0.03$) (Fig. 1a). Among patients with at least one of these mutations, VTE event rate was 67% (Fig. 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 (Fig. 1c).

Conclusion

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

Figure 1. Evaluation of the predictive role of genomic mutations in patients with ovarian cancer. a. Volcano plot of gene mutations odds ratio. b. VTE distribution among patients with at least one of mutations in FGFR2, NFE2L2 or KEAP1. c. Enrich pathway analysis. VTE: Venous Thromboembolism.

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