EP308/#1547 THE IMPACT OF LYMPH NODE DISSECTION ON SURVIVAL IN PATIENTS WITH STAGE I OVARIAN ENDOMETRIOID CARCINOMA

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Introduction Compared with other pathological types, the prognosis of ovarian endometrioid carcinoma (OEC) is better. The treatment of OEC follows the general principles of epithelial ovarian cancer treatment, with comprehensive staging surgery and tumor reduction surgery. However, patients underwent lymphadenectomy may affect their quality of life. This study investigated the value of lymph node dissection in improving the prognosis of early stage OEC patients and sought the optimal number of lymph node resections.

Methods We collected and organized the clinical and pathological materials of 2717 postoperative patients with stage I OEC in the SEER database from 2004 to 2018. Uni- and multi- Cox regression models were used to screen for the independent risk factors and divide patients into subgroups. Kaplan-Meier was used for survival analysis in subgroups to explore the relationship between lymph node dissection and survival in stage I OEC patients. We used Cox regression combined with restricted cubic spline (RCS) function to analyze the optimal number of lymph node dissections (LNN).

Results Age, marital status, tumor size, histological grade, and lymphadenectomy are independent risk factors affecting the overall survival (OS) of stage I OEC patients. Patients who underwent lymphadenectomy had an improved OS compared to those who did not. Cox regression analysis and restrictive cubic spline function analysis suggests that when LNN is 21, patients receive the best survival benefit.

Conclusion/Implications Lymphectomy can improve the prognosis of stage I OEC patients, and we recommend 21 LNNs as the entry point for evaluating the stratification of prognosis in stage I OEC patients.

EP309/#597 HISTONE LACTYLATION INDUCES CISPLATIN RESISTANCE IN OVARIAN CANCER VIA IMPROVING HOMOLOGOUS RECOMBINATION REPAIR

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Introduction Ovarian cancer is a fatal tumor in the female, majorly associated with chemotherapy resistance. Lactylation, a novel post-translational modification, is proven to be involved in multiple biological processes. This study aims to unravel the role of histone lactylation in the development of chemoresistance in ovarian cancer.

Methods We utilized GSEA to investigate alterations in glycolysis in cisplatin sensitive/resistant patients. Differential expression of H3K9la was demonstrated using WB and IHC. Cell viability or apoptosis were measured using CCK8 or apoptosis kit, respectively. Then ChiP-seq and ChiP-qPCR were performed to identify downstream targets of H3K9la. GCN5, the potential regulator of H3K9la, was validated using protein-protein interactions and cell experiments. And IP-mass spectrometry was used to identify lactylation sites for non-histone. Lastly, we established ovarian cancer PDX models to validate the therapeutic effects of GCN5.

Results Cisplatin-resistant ovarian cancer is characterized by increased glycolysis and H3K9la expression. Inhibiting glycolysis decreased H3K9la levels and made ovarian cancer cells more sensitive to cisplatin. RAD50 were targets of H3K9la, which facilitated HR repair and conferred cisplatin resistance. Our study also found that lactylation of RAD50 enhanced HR repair. Additionally, GCN5 was identified as an upregulator of H3K9la. When combined with cisplatin, CPTH2 was effective in repressing tumor growth and burden of PDX models.

Conclusion/Implications Our study demonstrates the crucial importance of histone lactylation in regulating cisplatin response of ovarian cancer. Additionally, we identified novel potential therapy targets to overcome chemotherapy resistance, improving prognosis for patients.

EP310/#537 SPATIAL HETEROGENEITY OF THE ACTIONABLE GENOMIC ALTERATIONS IN OVARIAN CLEAR CELL CARCINOMA

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Introduction Spatial heterogeneity in malignant tumors (heterogenous distribution of genetically diverse tumor subpopulations across different sites) is associated with resistance to treatment. The current study aimed to identify the spatial heterogeneity of the actionable genomic alterations (AGAs) in ovarian clear cell carcinoma (OCCC).

Methods Advanced OCCCs with four or more metastatic lesions resected at primary debulking surgery were included. Genomic DNA extracted from the formalin-fixed paraffin-embedded blocks of multiple cancerous lesions was analyzed by targeted deep sequencing with the custom panel including 84 OCCC-related genes. The genomic profiles of multiple cancerous lesions were compared to identify the spatial heterogeneity of the AGAs in individual cases.

Results Fifty cancerous lesions obtained from eight OCCCs were analyzed, and seventy-six potentially pathogenic variants (sixteen types of AGAs in six genes) were identified in five of eight OCCCs. Fifteen of sixteen AGAs in six genes, including ARID1A, PIK3CA, CTNNB1, TP53, PIK3R1, and KRAS, were shared across the primary and all metastatic lesions. However, in one case, the AGA of PIK3CA was only detected in the omental dissemination in which KRAS mutations were shown in all cancerous lesions.

Conclusion/Implications One AGA in PIK3CA showed spatial heterogeneity in advanced OCCC, suggesting that therapeutic strategies considering the spatial heterogeneity of the AGAs may be required in OCCC.