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An Innovative Approach Using Ensemble Model Improves Risk Stratification of Ovarian Cancer: A Real World Cohort with PARP Inhibitor Maintenance Treatment from China

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ABSTRACT

Ovarian cancer is the most lethal gynecologic malignancy, frequently diagnosed at advanced stages with heterogeneous treatment responses to PARP inhibitors (PARPi). We conducted a retrospective analysis of 737 ovarian cancer patients receiving PARPi maintenance therapy and developed multimodal ensemble models integrating clinical, genomic, pathological, and biochemical data via a late-fusion Cox proportional hazards approach. For primary patients (n=385), the combined clinical-pathological (CP) model achieved the best discrimination (c-index=0.71), significantly stratifying patients into high- and low-risk groups (mPFS: 53.67 vs. 25.3 months, P<0.001). For recurrent patients (n=352), the clinical-biochemical (CB) model showed the highest accuracy (c-index=0.558, P=0.054). Multimodal integration consistently outperformed single-modality models, demonstrating complementary prognostic value across data types. This real-world Chinese cohort represents the largest PARPi prognostic study in China to date.

INTRODUCTION

- Ovarian cancer is the deadliest gynecologic malignancy — often called the "silent killer"
- Ovarian cancer has poor prognosis with high recurrence after standard therapy
- PARP inhibitors improve outcomes but benefit is heterogeneous in real-world populations
- Existing models rely on single-modality data and fail to integrate multimodal clinical signals

Knowledge gap: There is a critical need for robust, multimodal ensemble models to accurately stratify patient risk and guide individualized treatment in the PARPi era.

METHODS AND MATERIALS

Study design: Single-center retrospective study, Hunan Cancer Hospital, China.
Patients: 737 of 1,694 screened patients enrolled (R0 resection, platinum-based chemo + PARPi ≥3 months); stratified into Primary and Recurrent cohorts (Figure 1).
Fusion: Final risk score was derived using a weighted late-fusion ensemble of modality-specific Cox proportional hazards models.

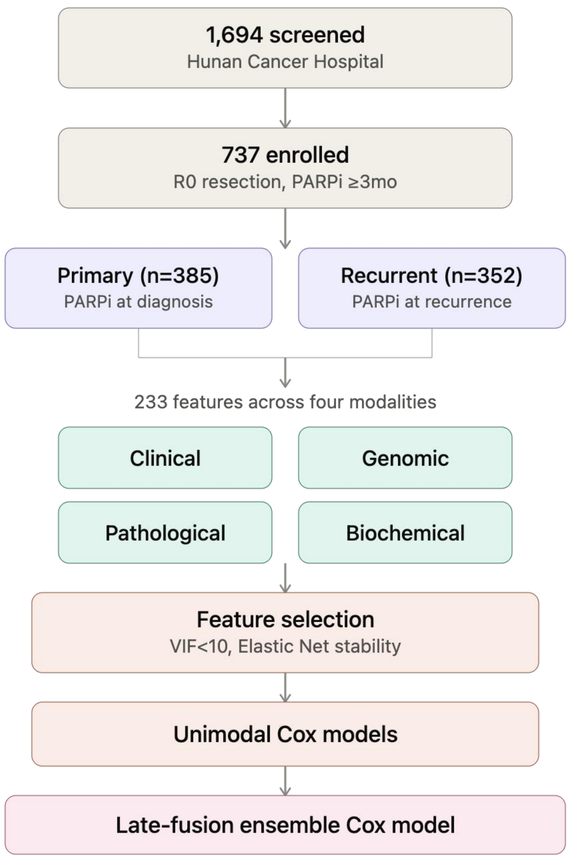

Figure 1. Study workflow from patient screening to ensemble model development.

Patient Characteristics
737 patients; mean age 56.2±8.1 years. Stage III: 75.6%; serous histology: 88.5%. Olaparib: 74.1%; niraparib: 25.9%. Median PFS: primary 52.0 months vs. recurrent 23.6 months (P<0.001).

RESULTS

Single-Modality vs. Ensemble Models

Modality	Primary	Recurrent
Genomic(G)	0.62 (P=0.042)	0.54 (P=0.344)
Clinical(C)	0.68 (P=0.002)	0.54 (P=0.045)
Pathological(P)	0.55 (P=0.248)	0.48 (P=0.902)
Biochemical(B)	0.39 (P=0.783)	0.51 (P=0.031)
CP Ensemble	**0.71 (P<0.001)**	-
CB Ensemble	-	**0.558 (P=0.054)**

Table 1. Performance comparison of single-modality and ensemble Cox proportional hazards models for PFS risk stratification. Values are c-index with log-rank P-values; all results derived from the independent test set.

Finding 1: Clinical dominance but multimodal gain (Table 1)
- CP model: best performance, P<0.001
- CB model: better in recurrence subgroup, P=0.054

Finding 2: Single-modality instability (Figure 3)
- low cross-modality correlation, supporting ensemble modeling
- inconsistent predictive performance

Finding 3: Ensemble benefit (Figure 2)
- KM separation improved
- better mPFS separation

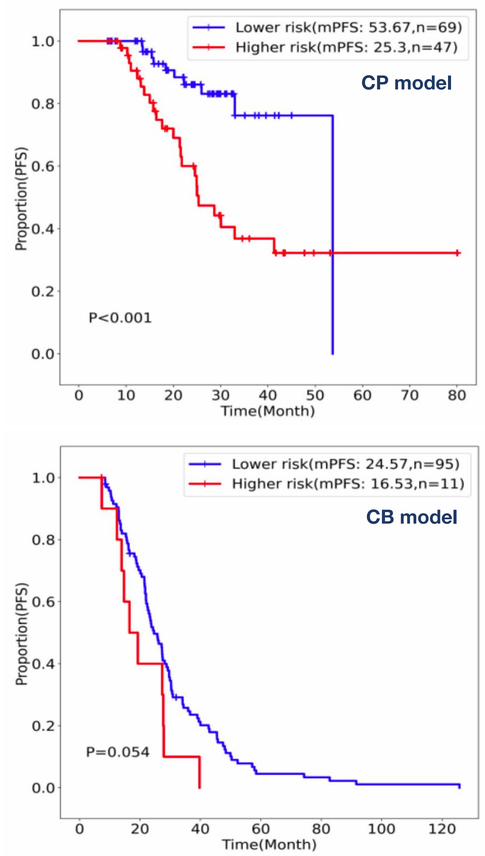

Figure 2. Kaplan-Meier PFS curves for the CP and CB ensemble models in the independent test set. Top: CP model stratification of primary ovarian cancer patients into lower- and higher-risk groups Bottom: CB model stratification of recurrent ovarian cancer patients.

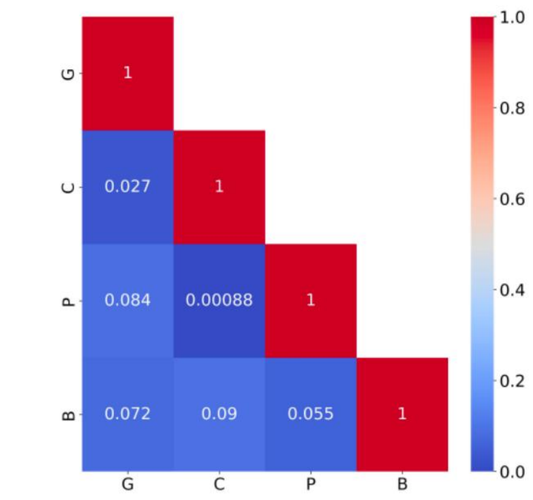

Figure 3. Modality independence justification figure: Kendall rank correlation coefficients of risk score rankings across genomic, clinical, pathological, and biochemical models in the primary cohort test set. Low correlations indicate that each modality captures distinct, complementary prognostic information.

DISCUSSION

- Largest real-world Chinese cohort of PARPi-treated OC patients to date (n=737).
- Multimodal integration improves prognostic stratification in real-world PARPi-treated patients
- The improvement likely reflects complementary predictive signals captured across heterogeneous data modalities.
- Single-modality models are insufficient for generalization.
- Ensemble approach may support future clinical decision support systems. Low cross-modal Kendall correlations confirm each modality captures independent prognostic signals. (Figure 3)
- Routine clinical data source supports future deployment after multi-center validation.

CONCLUSIONS

- Multimodal ensemble Cox model improves risk stratification in PARP-treated ovarian cancer.
- Clinical features remain dominant but benefit from multimodal integration.
- Single-modality models show limited robustness.
- The framework supports individualized prognostic assessment in real-world practice.

CONTACT

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