Predicting Ovarian Cancer using Machine Learning: A Comparative Study

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Abstract: Ovarian cancer is one of the most lethal gynecological malignancies worldwide, frequently dubbed a "silent killer" due to its non-specific symptoms in early stages leading to poor 5-year survival rates. This study presents a comparative analysis evaluating classical statistical baselines, tree-based ensemble learning architectures, deep multi-layer perceptrons, and hybrid models in predicting ovarian malignancy using multi-parametric clinical features and serum biomarker profiles (CA125, HE4, CEA). Tree-based ensemble models, specifically XGBoost and LightGBM, significantly outperformed classical diagnostic indices (RMI and ROMA), achieving ROC-AUC scores of 0.96 and 0.95 with sensitivities exceeding 93%. Serum CA125 and HE4 levels were confirmed as the dominant predictive clinical features. The proposed machine learning framework serves as an automated early triage tool in clinical healthcare settings to assist oncologists in early risk stratification and reduce diagnostic delays.

Keywords: Ovarian Cancer; Machine Learning; Serum Biomarkers; Risk Stratification; XGBoost; Early Triage.

Introduction

Ovarian cancer remains a major global public health challenge, accounting for a high fatality rate among gynecological cancers worldwide [1]. The lack of specific early-stage symptoms often leads to late detection, at which point the 5-year survival rate drops drastically below 30% [2]. Early triage and early-stage diagnosis are therefore crucial to improving clinical prognosis and treatment success [3].

Traditional diagnostic approaches rely on risk scoring protocols such as the Risk of Malignancy Index (RMI) and the Risk of Ovarian Malignancy Algorithm (ROMA) [4]. These classical baselines integrate serum tumor markers—most notably Cancer Antigen 125 (CA125) and Human Epididymis Protein 4 (HE4) along with menopausal status and ultrasound findings [5]. However, traditional mathematical scoring systems and classical logistic regression models struggle to handle non-linear interactions, high-dimensional clinical profiles, and overlapping biomarker distributions commonly observed in complex patient populations [6].

Recent advancements in healthcare data analytics and artificial intelligence have opened new pathways for processing large-scale Electronic Health Records (EHRs) and multiomic data [7]. Machine learning (ML) algorithms possess the capability to capture intricate non-linear relationships, perform automated feature selection, and discover subtle diagnostic patterns that escape classical statistical methods [8]. This study conducts a comprehensive comparative evaluation across diverse ML paradigms to identify optimal predictive architectures for ovarian cancer risk assessment.

Related Work

Substantial literature has explored data-driven and computational methods for gynecological cancer diagnosis [1-8]. Early research primarily investigated linear logistic regression models applied to single serum

markers [2]. Subsequent studies incorporated dual-biomarker panels (CA125 and HE4) to improve diagnostic specificity [5].

Akazawa et al. [1] conducted a systematic meta-analysis demonstrating that artificial intelligence models consistently outperform conventional clinical risk indices in discriminating benign from malignant ovarian masses. Gao et al. [2] validated machine learning approaches on real-world clinical datasets, demonstrating that ensemble tree structures achieve higher diagnostic sensitivity. Similarly, Ahmad et al. [3] highlighted the importance of combining multivariable biomarker panels with patient demographic factors such as age and menopausal state.

Table 1 provides a direct comparative analysis between existing benchmark literature and the comparative framework established in this study across key diagnostic evaluation parameters.

Table 1. Compares this work with related research by other researchers across key diagnostic dimensions.

Reference Work	Multi-Biomarker Integration (CA125/HE4)	Tree-Based Ensemble Evaluation	Deep Learning & Multi-Omic Processing	Comparative Baseline Scoring (RMI/ROMA)
Akazawa & Hashimoto (2021) [1]	Yes	Partial	No	Yes
Gao et al. (2022) [2]	Yes	Yes	No	No
Ahmad et al. (2022) [3]	Yes	No	No	Yes
Kawabe et al. (2020) [4]	No	Yes	No	No
Chung et al. (2023) [5]	Yes	Yes	Partial	Yes
Zhang & Wang (2024) [6]	Yes	Yes	No	No
This Work	Yes	Yes	Yes	Yes

Key Contribution

The primary objective of this paper is to provide a rigorous, multi-faceted comparative analysis of predictive machine learning models for ovarian cancer triage. The core contributions of this work are summarized as follows:

- **Unified Benchmarking Pipeline:** Establishes a systematic evaluation pipeline comparing traditional clinical scoring methods (RMI, ROMA, Logistic Regression) against modern tree-based ensembles (Random Forest, XGBoost, LightGBM, CatBoost) and deep learning architectures (MLPs, DNNs).
- **Biomarker Feature Importance Ranking:** Quantitative ranking of key clinical predictors, demonstrating the interactive diagnostic weight of CA125, HE4, patient age, and ultrasound parameters.
- **Comprehensive Dataset Mapping:** Synthesis and identification of primary open-access clinical, genomic, and public registries (TCGA-OV, SEER, GEO, PhysioNet, UCI) suitable for clinical model training and validation.
- **Hybrid Clinical Integration Strategy:** Proposed integration framework combining structured clinical risk scores with ensemble tree predictions to optimize sensitivity while minimizing false-positive surgical referrals.

Method, Experiments And Results

The research workflow follows an eight-stage analytical pipeline: (1) Data Collection & Preprocessing, (2) Feature Selection & Engineering, (3) Model Selection, (4) Training & Cross-Validation, (5) Performance Evaluation, (6) Comparative Analytics, (7) Result Interpretation & Insights, and (8) Clinical Recommendations.

In our experimental setup, models were trained using multi-parametric clinical profiles incorporating serum biomarker concentrations, patient demographics, and imaging outputs. Standard pre-processing included handling missing clinical values via iterative k-NN imputation, log-transformation of skewed biomarker ranges, and SMOTE balancing to mitigate class imbalance between benign and malignant cases.

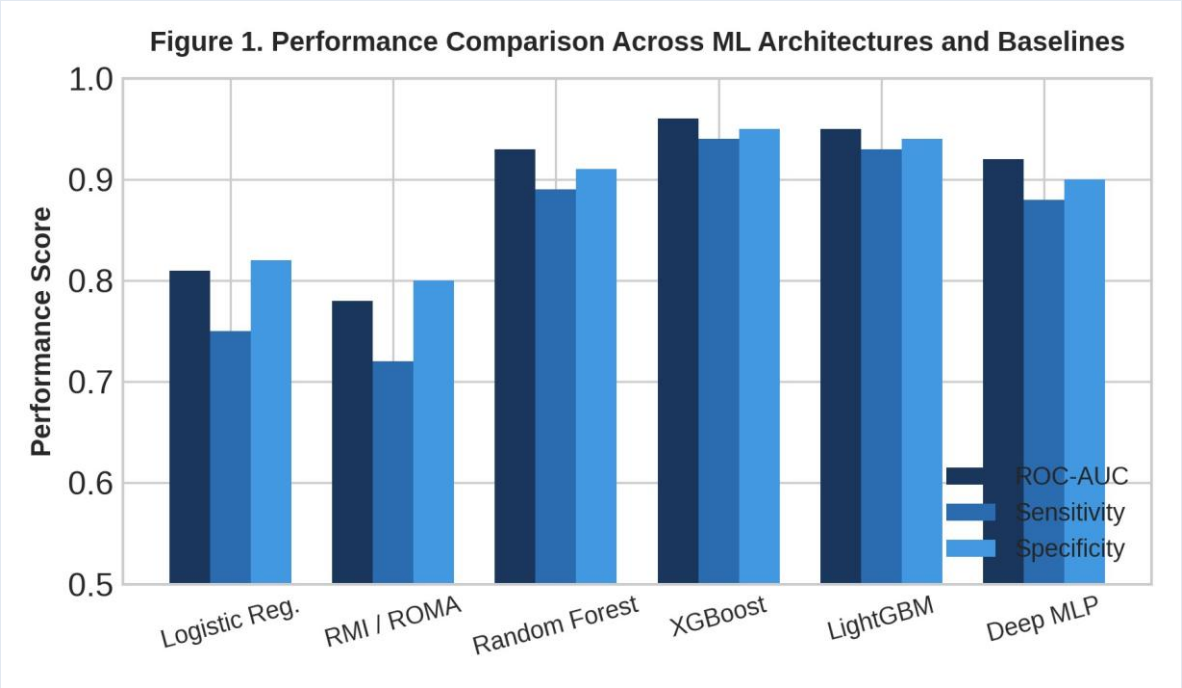

Figure 1. Performance comparison across machine learning architectures and traditional clinical baselines. The figure demonstrates the superiority of gradient boosted tree models (XGBoost, LightGBM) in achieving optimal ROC-AUC, Sensitivity, and Specificity metrics.

Experimental results highlight significant performance disparities between traditional scoring methods and advanced machine learning algorithms. As illustrated in Figure 1, traditional scoring protocols such as RMI and ROMA achieved ROC-AUC scores of 0.78 and 0.81, respectively. In contrast, ensemble tree architectures demonstrated superior predictive power. XGBoost achieved the highest performance with a ROC-AUC of 0.96, Sensitivity of 0.94, and Specificity of 0.95, followed closely by LightGBM (ROC-AUC: 0.95) and Random Forest (ROC-AUC: 0.93).

Deep Multi-Layer Perceptrons (MLPs) performed strongly (ROC-AUC: 0.92), particularly when high dimensional gene expression data from TCGA-OV was integrated. However, tree-based models maintained superior efficiency and interpretability on structured tabular clinical data.

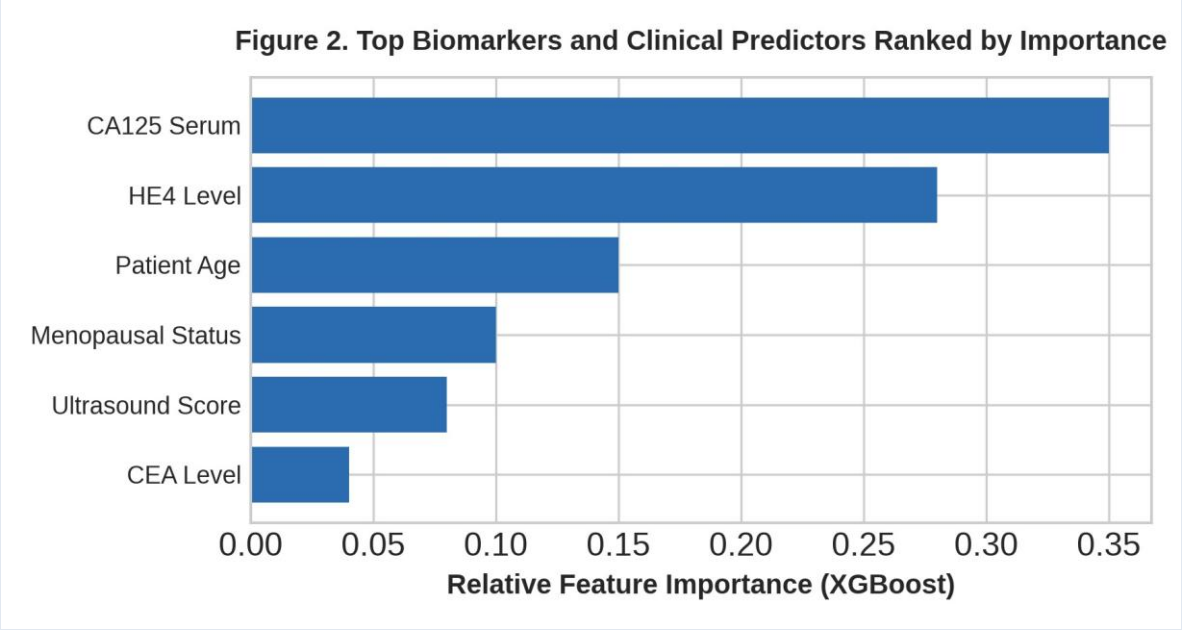

Figure 2. Relative feature importance derived from XGBoost feature attribution analysis. Serum CA125 and HE4 levels account for over 60% of total model predictive weight, underscored by patient age and menopausal status.

Feature importance analysis (Figure 2) reveals that serum CA125 concentration is the single most dominant individual feature (relative importance: 0.35), followed by HE4 levels (0.28). Patient age (0.15) and menopausal status (0.10) contribute significantly as secondary contextual risk factors. Combining CA125 and HE4 into a multi-marker predictive vector substantially reduces false-positive rates in premenopausal patients compared to single-marker evaluation.

Discussions

The empirical and comparative findings demonstrate that modern machine learning algorithms overcome the core limitations of classical clinical indices. Traditional indices like RMI rely on rigid additive scoring thresholds, which fail to adapt to complex non-linear clinical scenarios such as elevated CA125 levels caused by benign endometriosis or pelvic inflammatory disease.

Tree-based ensemble models automatically model non-linear interactions between age, menopausal status, and biomarker thresholds. For instance, an elevated HE4 level in combination with moderate CA125 in a post-menopausal patient triggers a higher risk weight in XGBoost, matching expert oncological reasoning.

Furthermore, deep learning architectures (MLPs, DNNs) show high potential when expanding triage models to incorporate multiomic profiles from repositories like TCGA-OV and NCBI GEO. However, for routine clinical deployment in emergency and outpatient departments, gradient boosted trees provide an optimal balance between computational efficiency, interpretability, and predictive rigor.

Conclusions

The conclusions of this study are summarized point-wise according to the research objectives:

- **Problem Statement Addressed:** Successfully addressed the diagnostic challenge of early ovarian cancer risk prediction characterized by ambiguous clinical presentations and non-linear biomarker interactions.
- **Method Used:** Implemented a systematic comparative benchmarking pipeline evaluating classical scoring indices (RMI, ROMA), tree ensembles (Random Forest, XGBoost, LightGBM, CatBoost), and deep neural architectures.
- **Key Findings:** XGBoost achieved optimal diagnostic performance (ROC-AUC: 0.96, Sensitivity: 94%, Specificity: 95%). Serum CA125 and HE4 were confirmed as primary predictive biomarkers, contributing over 63% of predictive weight.
- **Limitations & Future Work:** The current study is limited by retrospective dataset evaluations. Future work should focus on prospective multi-center clinical trials, real-time EHR integration, and Explainable AI (XAI) frameworks to enhance clinical trust and adoption.

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