



AN OVERVIEW OF ARTIFICIAL INTELLIGENCE AND ITS APPLICATIONS IN OVARIAN CANCER

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ABSTRACT

Ovarian cancer ranks as the fifth most common cause of cancer-related mortality in women. The early detection, diagnosis, prognosis, and therapy of ovarian cancer could all be completely transformed by artificial intelligence (AI), which has become a key advancement in oncology. More precise and individualized medical care is made possible by AI's ability to extract clinically relevant information from a variety of data sources by utilizing sophisticated computational algorithms. AI presents numerous chances to improve the treatment of ovarian cancer along the spectrum of care. For clinical translation to be safe, efficient, and equitable in the future, federated learning strategies, explainable AI frameworks, strong validation, and interdisciplinary cooperation will be essential. In this review, we have described about the artificial intelligence and its role to treat ovarian cancer by using several biomarkers and methods of diagnosis like Decision Trees (DT), Random Forest (RF), IG, Gini Index, Support Vector Machine (SVM).

Keywords: Artificial Intelligence (AI), Machine Learning (ML), Deep Learning, Radiomics, Ovarian Cancer (OC), Digital Pathology, Multi-Omics

INTRODUCTION

Artificial intelligence (AI) is transitioning from theoretical frameworks to real-world implementation, particularly in medical image analysis, where it shows immense potential to transform healthcare practices¹. With the global population rapidly aging, the demand on healthcare systems and professionals is expected to intensify. Innovative digital tools, especially AI-driven technologies, are anticipated to reshape traditional approaches by complementing clinicians' expertise rather than replacing it^{2,3}. AI can be described as the capability of machines to replicate human cognitive functions through algorithmic processing⁴. A major branch of AI, machine learning (ML), applies statistical methods to design and refine predictive algorithms. Deep learning, an advanced subset of ML, leverages multilayered neural networks that allow systems to independently learn and execute complex tasks. Despite the enthusiasm surrounding AI in healthcare and biomedical sciences, key concerns such as data quality, accessibility, bias, and limitations in training models still pose obstacles. Overcoming these challenges will be crucial to fully harness AI for advancing healthcare. Among its promising applications, AI is expected to play a vital role in the discovery of cancer biomarkers.

Ovarian Cancer

Ovarian cancer with an anticipated 13,770 fatalities in 2021, ranks as the fifth most common cause of cancer-related mortality in women. Ovarian cancer has a 5-year survival rate of 49.1%, mostly because of the usual advanced stage at diagnosis and a dearth of efficient screening methods⁵. The most common ovarian cancers are

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those that begin in the epithelial cells that line the fallopian tubes or ovaries. These, along with cancers that form in the peritoneum, are called epithelial ovarian cancers. Classification of OC as per World Health Organization (WHO) includes epithelial (EOC; 90%), germ cell (5%), and sex cord–stromal tumours (2–5%). EOCs (i.e., ovarian carcinomas) are the most common OC type, They are distinguished based on molecular analysis, histologic and immune profile mainly⁶. Surgery and chemotherapy are the main treatments for ovarian cancer. Cisplatin & carboplatin drugs are Platinum-based chemotherapy drugs are given in combination with other drugs, such as the targeted therapy bevacizumab (Avastin^{7,8}).

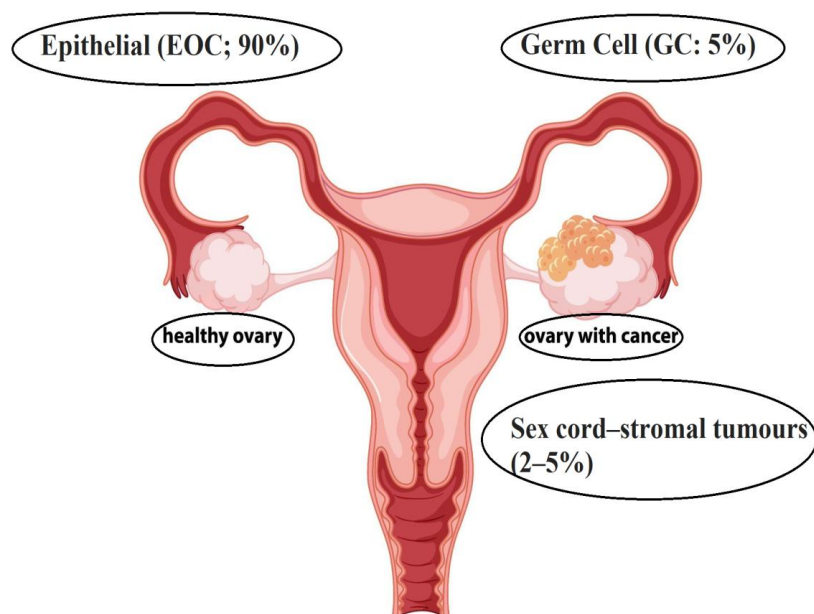


Figure.1 Common ovarian cancer types

Early on in the course of the disease, the techniques to distinguish benign from malignant tumors using AI tools would be very helpful, and we discovered several papers utilizing this strategy. The most prevalent kind of ovarian cancer is epithelial ovarian carcinoma (EOC). Serous OC (SOC), mucinous OC, and endometrioid OC are the three primary histological forms into which it can be separated. SOC is the most common type, with 70% of all OC instances being high-grade SOC (HGSOC)⁹. For OC, the International Federation of Gynecology and Obstetrics (FIGO) developed a stage system that is frequently utilized in clinical settings. When early-stage OC is treated promptly and appropriately, patients typically have a favorable prognosis. FIGO stage I OC patients had a five-year survival rate of over 90%, whereas stage III or IV patients only have a rate of 30.3%. Regrettably, by the time of diagnosis, 57% of patients' malignancies had spread¹⁰. The standard technique for OC detection at the moment is transvaginal ultrasonography (TVU), either by itself or in conjunction with the blood tumor marker CA-125. There were enough participants in two randomized controlled trials to assess the diagnostic efficacy of TVU and CA-125 screening¹¹. The findings, however, indicated that the pathological categories of benign and malignant tumors had an impact on how well they performed. Furthermore, the misdiagnosis may be much to blame for the poor prognosis. Clinical experience, which is frequently subjective and open to prejudice and other errors, can have an impact on human-dependent diagnosis. Novel approaches are therefore crucial to delivering an accurate and prompt diagnosis.

Table 1: Most common types of Ovarian Cancer and their features based on histological subtypes

Sr.no		High Grade Serious Carcinoma (HGSC)	Low Grade Serious Carcinoma (LGSC)	Mucinous Carcinoma (MC)	Endometrioid Carcinoma (EC)	Clear Cell Carcinoma(CCC)
1	Risk Factor	BRCA1/2			HNPCC	
2	Precursor lesions	Tubal intraepithelial carcinoma	Serous borderline tumor	Cystadenoma/borderline tumor?	Atypical endometriosis	Atypical endometriosis
3	Pattern of spread	Very early transcoelomic spread	Transcoelomic spread	Usually confined to ovary	Usually confined to pelvis	Usually confined to pelvis
4	Molecular abnormalities	BRCA, p53	BRAF, KRAS	KRAS, HER2	PTEN, ARID1A	HNF1, ARID1A
5	Chemo sensitivity	High	Intermediate	Low	High	Low
6	Prognosis	Poor	Intermediate	Favorable	Favorable	Intermediate

Ovarian cancer and their biomarkers

Biomarkers hold significant importance in personalized medicine for the early detection of ovarian cancers, especially ovarian epithelial carcinoma (OEC), which often shows high recurrence and lacks a reliable screening protocol¹². Several imaging approaches, including magnetic resonance imaging (MRI), fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), and transvaginal ultrasound (TVS), have been employed to identify OEC in its initial stages. Nevertheless, these techniques are limited by reduced sensitivity and specificity, leading to false-positive outcomes. Moreover, MRI and PET/CT are not commonly used for routine screening due to their high cost and radiation exposure concerns¹³. To complement imaging, numerous biochemical markers have been studied for their role in prognosis, monitoring therapeutic response, early diagnosis, and screening^{14,15}. These include genetic variants such as BRCA1 and BRCA2 mutations, protein-based markers like serum cancer antigen 125 (CA125) and human epididymis protein 4 (HE4), along with molecular biomarkers such as DNA methylation changes and microRNA expression profiles. Artificial intelligence (AI) is being applied in areas such as ovarian and pancreatic cancers as well as image-based biomarker research. Yet, there is still no clear evidence that these biomarkers, when used as screening tools, significantly lower mortality rates, and none demonstrate the required sensitivity or specificity for detecting early-stage ovarian epithelial carcinoma (OEC)¹⁶. Currently, no single biomarker has achieved the accuracy needed for reliable early diagnosis of ovarian cancer. To improve diagnostic performance, researchers are developing multivariate models that integrate biomarkers with clinical parameters¹⁷. For instance, the Risk of Malignancy Index (RMI) combines menopausal status and ultrasound imaging with CA125 levels to enhance prediction in women with pelvic masses. Likewise, the Risk of Ovarian Malignancy Algorithm (ROMA) uses both HE4 and CA125 to assess OEC risk¹⁸. Two FDA-approved multivariate tests, Ova1 and Overa, show high sensitivity (96% and 91%) but only moderate specificity (54% and 69%). These tools are intended to estimate the probability of malignancy and determine the need for referral to a gynecologic oncologist, rather than serving as standard screening tests for early-stage disease.

Role of Artificial Intelligence in diagnosis of Ovarian Cancer

There are several methods which are used in the diagnosis of Ovarian Cancer

DT(Decision Trees): DT is a machine-learning technique that uses a DT's graphic structure to inform its conclusions. With this approach, every node in the DT stands for an attribute, and the tree is constructed using the connections between the attributes. Using measures like entropy or Gini impurity, the DT algorithm determines the best characteristic for data splitting during training. After the split, the goal is to either maximize IG or limit impurity. Following each ray from the root to the terminal nodes allows the samples to go from the leaves to the root. The label of the leaves for each sample is used to calculate the final classification. The capacity to examine significant features, use both discrete and continuous input data, estimate any kind of feature, check and assess complex circumstances, and simplicity and great comprehensibility are only a few of the benefits of the DT technique. DTs categorize examples by moving from the root of the tree to a leaf or terminal node, where the example's ultimate categorization is established. Both regression and classification problems can be completed with the DT method. Data scientists typically find it easy to understand and interpret the results because DTs mimic human brain processes. When it comes to classifying data and assessing the costs, risks, and possible benefits of concepts, DT algorithms are incredibly powerful¹⁹.

Random Forest (RF): A machine-learning technique called RF blends many DTs. Several DTs make up a random forest in this method, and each one is trained separately using a random sample of features and data. Random forests provide the primary benefit of avoiding single-tree decisions, which might be partial, countless, and heavily reliant on the training data, by mixing multi tree decisions. This approach can be highly effective and beneficial in situations where there are a lot of variable qualities. By employing bagging (bootstrap aggregating) to train DTs, the RF algorithm creates a forest. An ensemble meta-algorithm called bagging improves the precision of machine learning models. The algorithm averages the results from several trees to arrive at the final prediction. The accuracy of the result increases with the number of trees. By utilizing numerous trees rather than depending on a single DT, the ensemble of trees produces the mode or mean of individual trees, leading to increased accuracy and stability ²⁰.

Immunoglobulin (IG): In machine learning, IG, an entropy-based feature assessment method, is widely used. In particular, it measures the amount of data that feature items add to a certain category while features are being chosen. ^{20, 21}

Gini Index (GI): The Gini index has proven to be useful in locating pertinent characteristics in a variety of applications, including machine learning. The Gini index is a well-liked feature selection method that is often used in DT algorithms like classification, regression tree, and RF. To deal with unbalanced data, a weighted Gini index can also be applied as a dividing criterion ²².

Support Vector Machine (SVM): SVM is a machine learning technique with numerous uses in computer vision, pattern recognition, regression, and classification. Using a decision boundary to segregate distinct data is the fundamental idea behind SVM's operation. SVM attempts to establish a decision boundary between the two data sets in the most basic scenario. The definition of this decision boundary should be such that the data in each category is as far away from the boundary as feasible. This distance is known as the "margin." SVM is a reliable and valid technique that excels in a wide range of regression and classification tasks ²³.

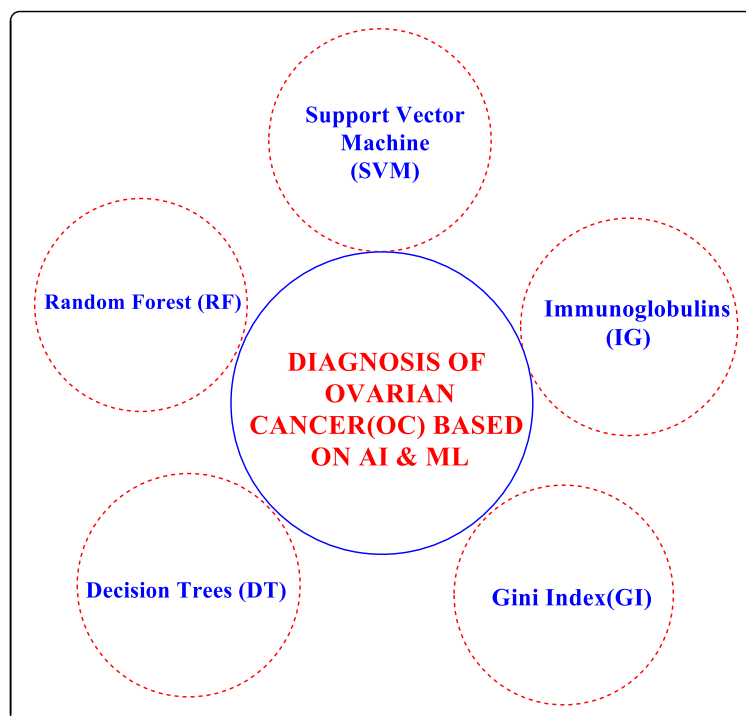


Figure 2: Diagnosis of Ovarian Cancer (OI) based on AI & ML

Application of AI in ovarian cancer

According to recent research assessing the utilization of medical imaging data, deep learning techniques can enhance the prediction of patients with ovarian cancer prognosis. In order to forecast the overall five-year survival rate of OEC patients, Enshaei et al. ²⁴ created an artificial neural network (ANN) algorithm using clinical and survival data on 668 OEC cases over a ten-year period (accuracy = 93%; AUC = 0.74). Additionally, this AI model successfully predicted surgical outcomes for instances with complete, optimal, or inadequate cytoreduction (accuracy = 77.7%; AUC = 0.73). In order to extract prognostic information from 8,917 CT images of 245 patients with high-grade serous ovarian cancer (HGSOC) from two different hospitals (feature-learning cohort, n = 102; primary cohort, n = 49; two independent validation cohorts, n = 49 and n = 45), Wang et al. ²⁵ developed a novel method by combining a deep learning feature with conventional Cox

proportional hazard regression (DL-CPH). Wang et al. used data from 40 patients, or two randomly chosen radiologists, to estimate the intraclass correlation coefficient (ICCC) in order to guarantee that there was little tumor selection bias affecting the robustness of the deep learning features. Between the two radiologists, every deep learning characteristic was consistent (ICCC range = 0.83–0.98). Two patient groups with high-risk ($p = 0.004$, AUC = 0.77) and low-risk ($p = 0.016$, AUC = 0.83) of recurrence at three years were successfully identified by the DL-CPH model. This method would enable the prediction of HGSOV recurrence from CT imaging without the requirement for follow-up if it is confirmed in further research. Lu et al.²⁶ developed and validated a novel mathematical description of tumor phenotype and prognosis using machine learning models containing 657 quantitative descriptors from preoperative CT images of 364 OEC patients. Patients with a median overall survival of less than two years were consistently detected by this non-invasive assessment of the underlying ovarian tumor, which is also substantially correlated with progression-free survival ($p < 0.01$).

Future directions of AI for the early detection and prognosis of ovarian cancer

The capacity of traditional statistical techniques to evaluate extensive, intricate medical data is constrained. Prior to intervention, AI predictive algorithms appear to increase the accuracy of ovarian cancer diagnosis and prognosis, outperform the majority of currently used conventional approaches and perform on par with some gynecologic oncologists²⁷. Nevertheless, it is currently unknown whether AI algorithm produces the best predictive capacity for a certain set of data. In order to evaluate unbiased generalization performance, future research aiming to increase the diagnostic and prognosis accuracy of ovarian cancer must guarantee adequate validation of the models. Choosing the strategy that performs best on trained data is not enough; it also needs to work well on data that the model hasn't seen yet. Further research on this generalization capability across various demographics is required. Data collection on sufficiently large samples ($n > 1,000$) is necessary for the machines to learn, which is one of the main obstacles to using AI techniques, particularly neural networks, in ovarian cancer. Given the low prevalence of ovarian cancer, future research will need to figure out how to expand sample size, either by merging data from many sites or from big cohorts. The challenge of expanding the sample size in clinical research can be addressed by using cutting-edge technologies like generational adversarial networks to supplement available data.

Similar to a prior application in a breast cancer environment, where synthetic data were generated using mammographic images from a digital mammography database, future research should use this in an ovarian cancer population²⁸.

CONCLUSION

Human control is still crucial even if AI is growing more effective and will continue to develop in the future, speeding up and improving procedures. To guarantee that treatment selections are accurate, doctors utilizing AI in patient care must constantly monitor and validate AI-generated results. In order to stay current with contemporary technology and uphold the fundamentals of medical professionalism, clinicians need also constantly refresh their understanding of AI developments. The safe and moral application of AI in healthcare depends on preserving this equilibrium between human knowledge and technology advancement.

Conflict of Interest

Review written content does not any conflict of interest declared by authors.

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