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Systematic Analysis of Ovarian Cancer Empowered with Machine and Deep Learning: A Taxonomy and Future Challenges

Rabia Sajjad[1*], Muhammad Faheem Khan[2], Asif Nawaz[3*], Malik Taimur Ali[4], and Muhammad Adil[4]

[1]Department of Computer Science, University of Management & Technology, Lahore, Pakistan.
[2]Department of Computer Science, Institute of Southern Punjab, Multan, Pakistan.
[3]Electrical Engineering Division, Higher Colleges of Technology, Dubai, UAE.
[4]Department of Computer Science, Iqra National University, Peshawar, Pakistan.
[*]Corresponding Author: Rabia Sajjad. Email: rabiasajjad789@gmail.com
[*]Corresponding Author: Asif Nawaz. Email: anawaz@hct.ac.ae

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Abstract: Machine and Deep learning has witnessed an exceptional amount of admiration in recent years. ML has ability to learn data itself by predicting uncertain conditions or future and classify categories with minimum intervention of human. While in DL, computers are able to automatically, learn useful features and representation precisely from raw data. ML and DL potentially a disruptive technology in predictive healthcare analysis. A detailed understanding and evaluation of the applications and principles of radiomics, machine and deep learning is an important task to construct possible solutions that are capable of accomplish compulsory and ethical requirements, which can enhance efficiency, quality and outcomes. Machine and deep learning extensively being use in medical image analysis, medical diagnostics and medical image technology. The wide scope and sudden progress of ML and DL has remarkably change the ways of diagnosis, prediction, classification and analyzing ovarian, lungs, brain, skin and various other types of cancer. In view of multiple applications of ML and DL, in this article a review conducted on ovarian cancer. This review comprises the detailed analysis of OC (prognosis, diagnosis, classification, evaluation) by covering all the major contributions of machine and deep learning. Furthermore, a literature taxonomy of the research conferred and emerging aspects analyzed. A section of discussion also signified to elaborate the limitations and future challenges of machine and deep learning comprises with ovarian cancer.

Keywords: Ovarian cancer; Machine learning; deep learning; Medical imaging; Classification; Prediction;

1. Introduction

With the advancement of technology, medical imaging has become the most important element in the field of medical practice, as it changed the way of diagnosis, prevention and treatment of different diseases [1]. Doctors or physicians are now able to learn more about the human body with deep knowledge. All applications of computer vision based are getting more beneficial with medical imaging with respect to giving more information and better results. The most commonly used medical imaging techniques in healthcare include MRI (Magnetic-Resonance-imaging) CT (Computed-Tomography), X-ray, Ultrasound (US), and PET (Positron-Emission-tomography) [2].

Cancer is one of the leading causes of deaths all over the world. According to the World Health Organization, almost 10 million people died in 2020 due to multiple types of cancer, which includes lungs, skin, stomach, ovary, breast, prostate, colon and rectum [3].However, in accordance with the American

Cancer society, there is an estimate of 1,898,160 for new cases of cancer and 608,570 with cancer deaths in 2021[4]. Ovarian cancer is the fifth deadliest cancer type among women than any other, as per Cancer Statistics Center there is 21,410 number of women with new cases and 13,770 patients will die from OV in 2021 [5]. From 2011 to 2017 the five-year relative survival rate was 49.1% and it jumped to 52.40 % approximately during 2018 to 2020 [6].

Ovarian cancer is a type of cancer, which affects the ovaries in women. OC disease usually occurs due to abnormal spreading of cancerous cells in the ovaries. Previously in the research it w believed that OC cancer only begins in ovaries but recent studies suggest that different types of OC cancer may develop in the fallopian tubes. Ovaries are the complete reproductive system in women that are responsible for producing ova (eggs). The progesterone and estrogen hormones of females also develop by these ovaries. Each side of the uterus contains one ovary.

Ovaries consist of three different types of cells and these cells produce different kinds of tumors. These entire tumors can further classify into benign, which is not cancerous, borderline tumor that does not appear clearly to be cancerous and lastly malignant tumor, which is cancerous. The benign tumor never spreads beside the ovaries, but usually in some cases, if any part contains a benign tumor, it can remove easily. However, the malignant tumor is fatal and dangerous to spread as it affects not only the ovaries but also the other parts of the body. Three different kinds of OC are Epithelial, Germ cell and Stromal. According to [7] American cancer society approximately 85 to 90 percent of cancerous(malignant) OC cases are due to epithelial ovarian carcinomas which includes some other main types i.e. serous carcinoma about 52%, endometroid 10% clear cell 6% and mucinous 6%. The germ cell comes from the cells that produce ova in females. It is the rare type of OC, only 2% of the total OC patients diagnosed with this. However, stromal tumor is the rarest type, only 1% patients of OC have this. Usually women older than 50 suffer from stromal tumors but it also occurs in young girls, which is about 5% of the overall ratio [8]

When OC diagnosed, the next step is to find out how far it has spread into the body. This procedure known as staging. Staging describes the condition of the Cancer in the body and helps to find out the best way for treatment. The range of OC staging is the same as per the rules. It starts from stage l to stage IV. Staging is more important as each type of cancer needs special treatment and needs to perform accurately. Staging of OC is determined by using two different systems called the International federation of Gynecology and Obstetrics (FIGO) [9] and the American Joint Committee on cancer (AJCC) [10]. These methods used three different factors to classify the cancer coded as T, N and M [11]. According to these methods, the primary tumor represented by the T symbol, this shows classification of the tumor after the results of surgery. The N shows either the cancer spread around lymph nodes in the pelvic or the aorta or lastly M represents spread of metastasis to the distant sites.

Medical imaging also plays a vital role in detection of OC. The imaging test recommended on the behalf of stage and other factors of the cancer. Usually ultrasound, PET, MRI and CT scans can have done for this purpose. These imaging tests are useful as it gives the inside pictures of the body and shows the doctors to analyze whether OC is spread to all other organs and tissues. Every image test has its own advantages and limitations.

Ultrasound is the most primary technique for OC to get to know about the existence of a tumor, and check whether it is a tumor or a fluid filled cyst [12]. MRI used for the better evaluation of the OC to determine the cancer in the pelvis. MRI is also able to separate the simple ovarian cysts from the cancerous cysts, as it is best to detect metastases of the pelvic and analyze the tumor condition [13]. The PET scan is basically used to give a kind of radioactive sugar into the body cells to check how many cells are effected with the cancer, cancer cells are more likely to take sugar as compared to normal cells-PET normally takes the images of the abnormal cells and give useful information about how much cancer has spread exactly [14]. Another medical image technique chest X-ray is also used to determine whether OC is spread to the lungs or not as some of the OC tumor causes fluid known as pleural collected near the lungs, so this fluid can be clearly seen with the help this scan [15].

The advancement of machine and deep learning in ovarian cancer inspired us to demonstrate this review. The review comprises the maximum number of recent research articles with all fields of ovarian cancer, which includes binary classification, prediction, diagnosis, identification and differentiation between the types and grading. The analysis explores the wide-ranging variety of ML and DL applications in OC. The detailed overview of all publications listed in tabular form so that readers can easily access brief knowledge. To conclude, discussion section also elaborated with open source future challenges and limitations.

2. Medical Imaging modalities with ML & DL

While medical imaging in OC helps to give the suitable results but it requires a lots of complications and keen efforts of the radiologists, pathologists and doctors to understand the problems and solve it on time. Therefore, machine and deep learning combine with medical imaging gives the desirable results for cancer related diseases. Same as [16] analysis of ultrasound images is done with the help of deep neural networks for the purpose of differentiating between ovarian benign and malignant lumps and compare them with the subjective assessment expert examiner-the DNNs contains three pertained models: Mobile-Net, VGG-16 and ResNet-50 which are implemented after transfer learning. The dataset contains 3077 number of ultrasound images of 758 patients having ovarian tumors taken from gynecological-department of karolinska-University-Hospital-Sweden. The ensemble of these models used to check the possibility of the malignancy on these images and classified the tumor as ovaryDx-1 model and ovaryDx-2 model of benign and malignant. Figure 1 represents Imaging with Machine Learning and Deep Learning.

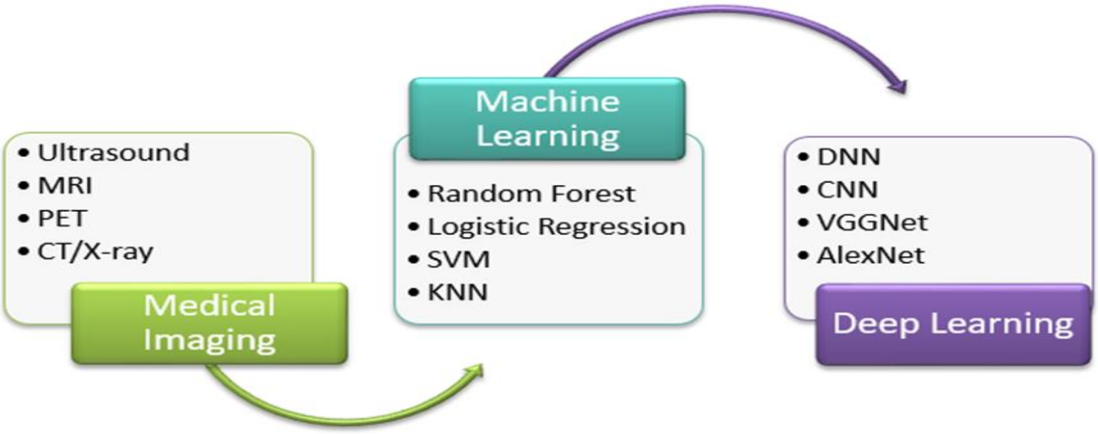

Figure 1. Medical Imaging with ML & DL

Morphological study of the ovarian cancer tissues is also difficult for the pathologists to separate the cancerous and non-cancerous cells. So, the hyperspectral imaging facilitates to differentiate the cancer stages at cellular level. In order to check the correlation between the malignancy and hyperspectral imaging SVM applied on nuclei of ovarian cancer [17]. The researchers in [18] developed novel single and multi-parameter assessment models of machine learning which based on MRI to discriminate Borderline epithelial ovarian cancer tumor from the malignant epithelial ovarian cancer tumor. The research done with the help of Retrospective study that includes the dataset from eight different clinical centers between the years of 2010 to 2018. The 501 of the total dataset consists of 336 of MEOT patients and 165 BEOT patients, in which MEOT contains 64 clear cell, 211 for serous,29 for endometroid and 32 for mucinous of the total where BEOT includes 6 endometroid, 89 serous, 4 seromucinous and 66 mucinous. The cohort study divided into three sub-cohorts of training, internal and external validation. The 250 numbers of data taken for training while 92 and 159 for internal and external validation respectively. The two ML models built by using four sequences of MRI, which were (ADC) apparent diffusion coefficient, (FS) fat saturation, (T2W1) T2 weighted imaging and (DWT) diffusion weighted. The early diagnosis also done for both tumors. The proposed model was capable of differentiating the both tumors with AUCs of 0.909 for BEOT and 0.902 for MEOT than the radiologist performances. Figure 2 represents taxonomy of ovarian cancer.

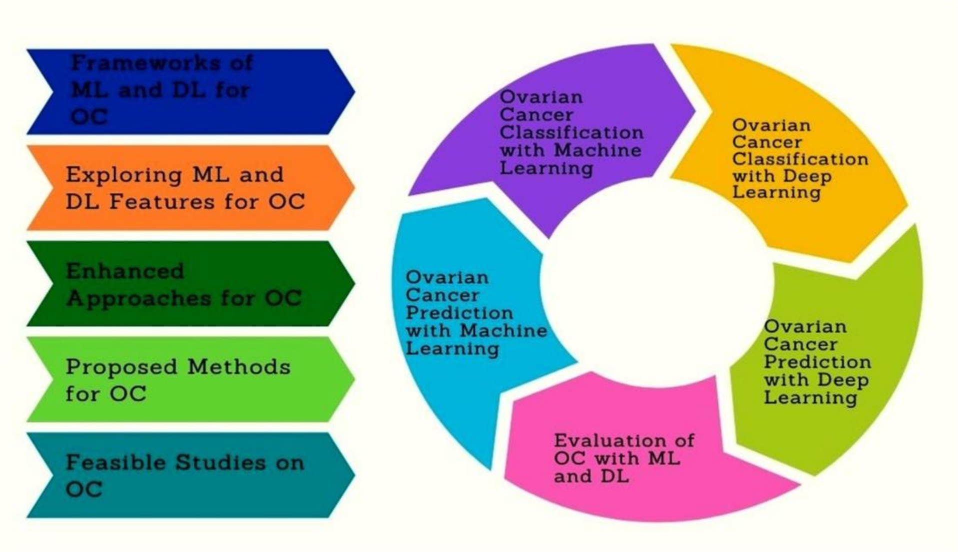

Figure 2. A Taxonomy of Ovarian Cancer Using ML & DL

2.1. Classification of Ovarian Cancer with Machine Learning

The state-of-the-art research methods have been discovered using machine learning techniques for ovarian cancer classification, the below table 1, shows the overview of the recent study with their proposed methods/tools and libraries along with the data source.

Table 1. Overview of recent study with their purposed methods and data sources

Sr.	Year	Methods	Purposed approaches/Techniques	Tools/Libraries/ Software's /Modules	Data Sources	Analysis
1	2021	k-nearest neighbor	SHG-imaging, TPOT	Python 3.6.5, Scikit-learn library	Cancer Hospital of Fujian Medical University, China	ROCCs=1.00, 0.99,0.98,0.97
2	2021	SVM,KNN	SVM, KNN Comparison	KNN with Grid Search method, SVM with Radial basis function kernel	AI-Islam Bandung hospital, Malaysia	KNN=94.11% SVM=92.30%
3	2020	Logistic-Regression	Ridge-logistic regression, ANOVA-F-Value	Scikit-learn 24 python package	Public Dataset: (https://seer.cancer.gov/)	AUC=0.621
4	2020	DNN	Transfer-learning on VGG-16, MobileNet, ResNet-15	Not mentioned	Gynecological-Department of karolinska-University-Hospital-Sweden	AUC-ovaryDx-1 = 0.950, AUC-ovaryDx-1 = 0.958

5	2019	SVM	Hyperspectral camera with SVM	Linear and Gaussian	Kitasato-university Japan	ACC= 95%
6	2020	Mann-Whitney-u-test	SP-ML,MP-ML	R-software-V.3.5.1	Institution review board-China	AUCs-BEOT=0.909, AUCs-MEOT=0.902
7	2020	LSVM, KNN, LR	KNN,LSVM,LR, DT, LDA comparison	Multiresolution-segmentation	The University of Oklahoma-health-sciences-Center , USA	ACC=91.0%, AUC= 0.910
8	2020	RF,SVM,KNN	Non-negative-matrix-factorization	Bioconductor-V3.10, R- V3.6.2, kernlab-V0.9-29	European-nucleotide-archive, UK	SVM=0.98%, RF=0.93%, KNN=1%
9	2020	Boosted-logistic regression	Whole-exome sequencing	Whole exome libraries, NOVASeq-6000	The Cancer-genome Atlas, Gynecologic-oncology-tissue bank	AUC=0.982
10	2019	Random Forest-Bagging method	Microarray data with RF and bagging	Not mentioned	UCI- machine learning-repository.	Bagging=100%, Random forest=98%
11	2019	Logistic-regression	Bayesian-Logistic-regression	R-studio-Version-1.1.453	RS-Al-Islam Bandung	ACC= 77.33%
12	2021	RF, KNN, XG-boosted	Transvaginal-ultrasonography and CA-125 with ML	Scikit learn, KNN-imputer, Standard Scaler python, library	PLOC-National cancer-institute, USA	XGB=99.50%, RF=99%, KNN=93.82%
13	2021	Ensemble-Algorithm	FIGO with ensemble algorithm	SEER, dendrogram, C-index	SEER, National cancer institute	EACCD=0.739%, FIGO=0.731%
14	2020	KNN, RF, Logistic Regression	Comparison with Logistic regression	Not mentioned	Leeds teaching hospital trust, Leeds UK	ACC=66%
15	2020	SVM	Radiomics with ensemble SVM	Trace4- Radiomics plate from	International-cancer institute of Milan	ACC=89%
16	2021	DCNN	AleXnet-model	Python, Tensor Flow and Keras	National cancer institute’s genomic	ACC=83.93%

					data-commons-data portal	
17	2021	Deep machine learning	MeTylnet and IlluminaEpic	Lasso-statistical learning regression	University of lowa.	ACC=95%
18	2021	Deep machine learning	Alternative-Splicing-Analysis	Deep-learning-augmented-RnA-sequencing S/W suite	Not-mentioned	ACC=91%
19	2020	DCNN	Deep hybrid learner	Smote, ImageJ with Java 1.8.0, ROOT	Tata-Medical Center, Kolkata	AUC=0.99%
20	2020	DNN	VGG -16	Fine-tuning	Not-mentioned	ACC=92.11%
21	2020	DCNN	Cost Sensitive-RF classifier	WEKA, GooglENet-model, Local-binary-pattern	The peking-uninon medical college and university, China	ACC=99.15%
22	2020	DNN	Multilayer-Feedforward deep neural network	Keras library SGD optimizer, Grid search, Rectifier linear unit activation function	Asan-medical center, Seoul-national-University and Hospital, Korea	AUC=0.718
23	2018	DL network	Cox-proportional-hazard, CT	Python lifeline package, R-software V3.0.1, Keras V2.1.5	West-china-second- university hospital of Sichuan-University	AUC=0.865
24	2019	ANN	15-neurons with ANN and Taguchi-method	MatLab tool, Math work	National cancer institute PBSII	ACC=98.7%
25	2018	Neural Network	Error-ABC algorithm	MatLab R-2014a	National Cancer-Institute, USA	ACC=91.2%
26	2021	DCNN	DenSeNet-201 feature extraction model	Not-mentioned	PLCO-https://cdas.cancer.gov/plco	ACC=94.73%
27	2020	CNN	Transfer learning with CNN, Random forest	VGG19-network, WSP	Vancouver general hospital	ACC=87.54%, Cohens kappa=0.8106
28	2020	CNN	Enhanced-Max-pooling	Python Keras, Tensor flow	National Cancer Institute	ACC=55.4%
29	2020	ML-GB	Gradient Boosting , Cox-proportional hazard	Scikit learn library R_V.3.3.2, SASv.9.4,	Asan medical center, Samsung medical center	ACC=0.830,0.843, ACC=0.66

				MedCale_V12.7		8,0.597
30	2019	AI-ML	RF, GRF, NN, EN, SVM, NB, GBM	R-package caret(glmnet, nnet, nb, cforest, gbm, rf, svmradial	Jikei university school of medicine	ACC=92.4%, AUC=0.968
31	2019	SVM	SVM, Cox-hazard regression model	Not-mentioned	GSE9891, TCGA	TCGA=0.015, GSE9891=0.013
32	2019	Recurrent neural network	ORNN, SOM, AHSO	MatLab_V16	Internet of medical things data	ACC=96.27%, Sensitivity/Specificity=85.2
33	2018	LSVM	LSVM , CA125, Cox-proportional-hazard	R. version 3.0.2, E1071 package of R	International-Federation of gynecology and obstetrics	SVM=62%, CA125=57%
34	2019	ML pipeline	mRnA, SVM, RF, KNN, GLM, G&RT	R-lemma Package	NCBI-Gene expression omnibus-portal	SVM=0.85, RF=0.89, KNN=0.84
35	2020	CNN	AI-CSGSA, AleXnet	MatLab16 toolbox-MA, Natick, Mathworks, R2018b	Tokai university hospital, KAC, SOIken and Sanfco, Japan	ACC=95%
36	2020	DCNN	Machine instance learning , LuPI	Python	The Cancer genome Atlas, TCGA	AUC=0.79, SD=0.07
37	2020	CNN	ML-CNN with logistic regression	Not-mentioned	Stanford.edu/dataset	Specificity=98%
38	2020	DL	Auto-encoder, logistic regression, K-mean clustering	R-package	The Cancer genome Atlas, TCGA	DBI Score=1.859
39	2021	DL	ALO, CNN, LSTM	MatLab_16A, MM_fusion model	The Cancer genome Atlas, TCGA-OV	ACC=98.87%
40	2020	ML	ROMA, Logistic regression, DT, MRMR	Scikit- learn python	Hospital-of Soochow-University, China	DT=0.888, ROMA=0.814
41	2019	ML-FS	SVM, ELM, KNN, ANN, PCA, GA	Not-mentioned	NIH-https://ccr.cancer.gov/	SVM-PCA=99%

42	2020	ML-NLP	Logistic regression, PCA, XGBoost, RF	Python package	Northwestern-medicine-healthcare	ML=0.56, NLP=0.70
43	2021	ML	SVM, cox-proportional hazard, RF,	SpSS_16 package	St. James university hospital, LEEDS	SVM=63%, KNN=62.1%
44	2020	ML-BPNN	LIBS_spectrum, Selectk-best algorithm	Not-mentioned	Tongde-hospital, Zhejiang-university, China	Specificity =86%, Sensitivity =71.4%
45	2020	ML-MBF	Random forest- logistic regression, Microbial-features	R-package, Lasso	Southern-Illinois university of medicine	AUC=0.804
46	2018	DNN	Transfer and Scratch learning, VGG16, DenSeNET, ResNet-50, GooglENet-V3	Not-mentioned	https://imr.sjtu.edu.cn/en/lc_gjhp/397.html	ACC=92.50%
47	2018	DCNN	AleXnet, t-test analysis	Caffe-package of Ubuntu_16.04	Xinjiang-medical university	ACC=78.20%
48	2016	NN	FF-MLP, RBF, SMOTe	WeKa_3.6	Gene-expression omnibus-NCBI	ACC=96%
49	2012	FS-ML	CA-125, T-test, genetic algorithm	MatLab_r2009a	UPCI-University of Pittsburg cancer institute.	AUC=0.92
50	2012	ML	Scatter Search- SVM,DT	Not-mentioned	China-medical university	ACC=96.43%
51	2012	ML	BMRF, NC-SVM	Not-mentioned	TCGA-data portal	ACC=86.92%
52	2013	ML	MLP,RF,LR,SL,MCC,LB, Logistic, Bagging, Regression	Not-mentioned	Not-mentioned	AUC=0.885
53	2013	ML	KNN, One-pass clustering	Java, Mac-OS	National-cancer hospital https://ccr.cancer.gov	ACC=97%
54	2020	DL	CNN- Efficientnet, ReSNet	Keras package_V2.2.5, TensorFlow_V1.12.3, python Sklearn package	Institutional-Review board,USA	AUC=0.87
55	2021	DL	CNN- Inception_V3, Xception, RF, LR	Python_tool, Ubuntu	Cancer-Image-Archive	ACC=99.53%
56	2014	NN	Feed-forward NN- Probabilistic NN	Not-mentioned	Not-mentioned	ACC=99.8%

57	2021	ML	KNN,NB,SVM,DT, FCN	Not-mentioned	American-type-cultural-collection	ACC=99.2%
58	2017	ML	ANN-multilayer perceptron, Decision tree	WEKA_Tool	Danish-Cancer Registrar, Denmark	ACC=67.9%
59	2015	ML	Multiclass-SVM, Naïve-bayes, ANN, PGSO	Not-mentioned	TCGA-data portal	ACC=96% ACC=98%

Ovarian Cancer classification is a complex task due to its various types. It usually classified as Benign, Borderline and Malignant. Mostly OC are benign and do not tend to spread into the body which cause cancer, some of them are Brenner tumor, Serous and Mucinous cystadenomas. Machine learning (ML), a sub-domain of Artificial intelligence, which train the algorithms to make them capable of analyzing and interpreting the observed data. In recent years, ML is playing a tremendous role in therapeutic monitoring, prediction and detection of different diseases [19]. Some of the ML work with ovarian cancer classification listed below in Table 2.

Table 2. Overview of recent study with ML for OC Classification

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[20]	SHG-imaging-nearest neighbor and TPOT	Cancer Hospital of Fujian Medical University, China	ROCCs=1.00, 0.99,0.98,0.97
2	[21]	SVM,K-nearest neighbor	AI-Islam Bandung hospital, Malaysia	KNN=94.11% SVM=92.30%
3	[22]	Ridge-logistic-regression, ANOVA-F-Value	Public Dataset: (https://seer.cancer.gov/)	AUC= 0.621
4	[23]	Linear-SVM, Logistic-regression, KNN, decision tree, linear-discriminant-analysis	The University of Oklahoma-health-sciences-Center ,USA	ACC=91.0%, AUC= 0.910
5	[24]	KNN,SVM, Random forest ,Non-negative-matrix-factorization	European-nucleotide-archive, UK	SVM=0.98%, RF=0.93%, KNN=1%
6	[25]	Boosted-logistic regression	The Cancer-genome Atlas	AUC=0.982
7	[26]	Bagging method, Random- forest	UCI- machine learning-repository.	Bagging=100%, Random forest=98%
8	[27]	Bayesian-Logistic Regression	RS-Al-Islam Bandung	ACC= 77.33%
9	[28]	15-neurons with ANN and Taguchi-method	National cancer institute PBSII	ACC=98.7%
10	[29]	CNN with Enhanced-Max pooling	National Cancer Institute	ACC=55.4%

Although the growth pattern of ovarian cancer is different, Borderline OC normally falls between the benign cancer and malignant cancer, which is usually not dangerous but can produce malignancy. Therefore [20] classify borderline from normal, benign and malignant OC tissues with the help of ML Classifier. The study purposes a method combine with K_nearest neighbor and S-H-G (second harmonic-generation) imaging along with ML tool called Tree-Based-Pipeline-Optimization for accurate and quickly diagnosis of borderline tumor of these tissues. The data is taken from the-Cancer-hospital-of-Fujian-Medical-University which includes 6 ovarian tissues for normal, 7 for benign, 6 for borderline and 7 tissues for malignant from 20 patients, about 335 S-H-G images collected from these ovarian tissues as SHG imaging technique is mainly provides non-destructive and label free visualization of the structure of tissues which are at cellular level [20]. The area under the ROC curve for normal tissues is 0.97%, 0.99% for benign, 0.98% for borderline and 1.00% for malignant tissues.

As [21] represents the comparison between the methods of machine learning for the classification of ovarian cancer. ML SVM and KNN with RBF (Radial basis function) kernelis used for this purpose. The study takes the dataset from the AI Islam Bandung hospital, which includes 203 total number of instances in which all data labeled properly, 130 number of patients having ovarian cancer and 73 of non-ovarian cancer patients along with five attribute, which are platelets, leukocytes, CA125, hematocrit and hemoglobin. The output declared the KNN as best predictor to classify the ovarian cancer as it gives the highest rate of accuracy, which is 90.47% than the SVM. The KNN also gives the highest value of precision, recall and F1-score that was 94.11% than SVM, as SVM has 90.47% for accuracy rate and 92.30% for F1-score, precision and recall. ML is performing intuitive possibilities of survival prediction in various other diseases although the OC have a 5-year survival rate but there is still need of properly predict the early mortality in OC patients. To address this problem, [22] proposes a novel method which is Ridge-Logistic regression(L2), the dataset is based on 273 cohort patients of OC having disease level at Stage I and II taken from a public library known as SEER (Surveillance-epidemiology and End-Results). Analysis done with the help of KAplan-MEier to determine the survival time in 20 months, 25th percentile is used, as threshold value for overall of survival time in which zero represents patients will survive at least 25th percentile of the overall time and 1 represents deaths will be occurring before 25th percentile of the time. Furthermore, features extraction performed with ANOVA f-value and training of the features done with L2 regression and achieve accuracy of 0.761%, 0.621% for AUC, 0.216% for F1 score and 0.659%, 0.130% for precision and recall respectively. In digital pathology, histopathological examination of the tissue's regions is getting difficult to analyze. Therefore, [23] describes the classification of ovarian cancer epithelium-stromal tumor regions based on images of digital pathology which includes the 11 cases. The analysis implemented with five machine-learning classifiers: logistic regression, linear support vector machine, decision tree, linear discriminant analysis and k-nearest neighbor. Accurate and highest accuracy value of 0.910% achieved with linear SVM. Cancer cell lines are the most common models for evaluating and studying cancer cells, that is why a study in [24] a research is related to the classification of five subtypes of the Epithelium ovarian cancer with the help of 45 ovarian cancer cell lines. The (NMF) Non-negative-matrix-factorization application performed to cluster these cancer cells, which are the part of CCLE (Cancer-cell-line-encyclopedia) with different machine learning algorithms. Endometroid ovarian cancer is the rare subtype of epithelium ovarian cancer, which accounts for only 10% of the overall. It also needs to properly identify and explore this disease before time, so, whole-exome-sequencing implemented on EOVC data sample for better understanding of the disease as it has completely different and heterogeneous mutations than others [25]. Further, the classification between high-grade serous carcinoma and endometroid carcinoma performed well with the help of unsupervised machine learning method called boosted logistic regression, which gives AUC value of 0.9823%. Random forest and bagging is also performing well on the classification of benign and malignant ovarian tumors [26] as bagging mostly used to minimize overfitting and maximize classification. So, the 266 number of sample size included into the study from UCI machine learning-repository and achieved highest accuracy with bagging method about 100% with training data of 90% however RF Contains 98% of accuracy rate with 90% of the training data. Logistic regression with Bayesian theorem is carrying out good analysis for classification of OC with 77.33% of accuracy on 203 cases of partial OC cases taken from the RS-Al-Islam Hospital. Each case consists of almost five attributes to discriminate the normal cases from OC, which includes Leukocytes, Platelets, Hemoglobin, Hematocrit and CA125 [27].

Classification accuracy is the main component in any disease, precise and highest accuracy helps doctors to gives the proper treatment to patients. Keeping in view a work in [28] analyze classification accuracy of ovarian cancer with 15-neuron artificial neuron network model and taguchi method and achieved highest accuracy of 98.7% among other classification models. Machine learning has the capability of analyzed or solved the issues of misclassification and misdiagnosis of OC. As it introduces a new method called EMP (Enhanced-Max-pooling) of CNN to classify and detection of ovarian cancer [29]. The fine-tuning applied for CNN to analyze features and parameters for improving the classification accuracy.

2.2. Prediction of Ovarian Cancer with Machine Learning

With the passage of time, late diagnosis of diseases getting worse as it not only waste the time and money, also decrease the chances to cure a disease. Timely prediction and diagnosis of a disease can save people and prevent its inadequacy into human body. Machine learning in this aspect is becoming popular to accelerate and discover the early prediction of diseases- as it helps with its applications to comprise the large amount of data within short period of time [30]. Some of the ML work with prediction of Ovarian Cancer listed below in Table 3.

Table 3. Overview of recent study with ML for OC prediction

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[31]	XG-boosted, Random Forest, KNN	PLOC-National cancer-institute, USA	XGB=99.50%, RF=99%, KNN=93.82%
2	[32]	Ensemble-Algorithm, FIGO	SEER, National cancer institute	EACCD=0.739%, FIGO=0.731%
3	[33]	KNN, Random-Forest	Leeds teaching hospital trust, Leeds UK	ACC=66%
4	[34]	Ensemble-SVM with Radiomics	International-cancer institute of Milan	ACC=89%
5	[35]	Gradient Boosting ensemble model , Cox-proportional hazard model with ML	Asan medical center, Samsung medical center	ACC=0.830,0.843, ACC=0.668,0.597
6	[36]	AI with SVM, RF, CRF, GBM, NN, NB, EN	Jikei university school of medicine	ACC=92.4%, AUC=0.968
7	[37]	SVM with Cox-regression model	GSE9891, TCGA	TCGA=0.015, GSE9891=0.013
8	[38]	ORNN, AHSO, SOM	Internet of medical things data	ACC=96.27%, Sensitivity/Specificity=85.2
9	[39]	Linear SVM, Cox-proportional hazard, CA125	International-Federation of gynecology and obstetrics	SVM=62%, CA125=57%
10	[40]	SVM, RF, KNN, GL,G&RT with mRnA penal	NCBI-Gene expression omnibus-portal	SVM=0.85, RF=0.89, KNN=0.84

Although ovarian cancer cysts are not harmful as much and does not spread into the ovaries but still there is a need to overcome this problem. A study [40] related to this proposes a predictive model for early prediction of ovarian cancer with the help of OC cysts. The model is trained with ML-algorithms includes XG-boost, Random-forest and KNN with all data preprocessing, missing/imbalance data and feature scaling processes. These algorithms achieve 99.50%, 99%, and 93.82% for XG-boost, RF and KNN respectively. Survival prediction of OC patients after surgery also needed in context with different staging system. The epithelium ovarian cancer staging system according to FIGO (International-federation of gynecology and obstetrics) required for enhanced survival and classification prediction of OC patients. Survival data consists of two different datasets take out from the database of SEER (Surveillance-Epidemiology and End Results) program of the National-Cancer-Institute. The machine-learning algorithm called Ensemble-Algorithm for clustering cancer data implies on both datasets, which comprises of regional- lymph- nodes (N), distant metastasis (M), primary tumor (T), histologic type &grade(H) and age (A) demonstrate the accuracy of 0.7391% over 0.731% for EACCD and FIGO respectively [31]. Subsequently another research in [32] reveals the prediction of (RO) the macroscopic disease in patients of high-grade serous ovarian cancer with the help of k-nearest-neighbor classifier. Predicted model also compared with the logistic regression model. The macroscopic disease (RO) cells removed with the help of surgical cytoreduction. The dataset includes 154 patients with advanced HGSC and pPT from the years of 2015 to 2019 collected from the ovarian database of Leeds teaching hospital trust, Leeds UK. The analysis done with the support of performance variables, which includes cHarlson-comorbidity index, age, complete timing of the surgery, surgical complexities, BMI and disease score. The predicted algorithm also classified patients with R0 and patients having no macroscopic. The results show mean 66% of predictive accuracy. Further study in [33] promotes the unique model consisting of ML and Radiomics, which used for the prediction of high risk of ovarian cancer masses' the OMs. The model implemented on the ultrasound images of ovarian masses' according to the guidelines of the (International-biomarkers-standardization-initiative). The dataset consists of 241 of OMs patients which are further subdivided into three different homogeneous groups including 80 for motley, 95 for solid and 66 for cystic. Results show 81% of accuracy, specificity and sensitivity rate or 89% of AUC score for mixed ovarian cancer masses'.

Different prognostic methods for OC using machine learning giving the appropriate results for better understanding the disease. The gradient boosting ensemble method of ML proposed to predict the survival outcomes of the EOC and compare its evaluation with the other statistical method known as Cox-proportional hazard model and KAplan-MEier. Dataset contain two different studies, one is for training and other is for validation. The 1,128 cohort of patients from Samsung medical center elected for training and 229 cohort of patients from Asan medical center for validation. All the variables of these two coherent analyze by Cox-proportional hazard. The AUC value of training and validation study with GB ensemble model is 0.830 and 0.843 separately, moreover with Cox-proportional hazard it showed 0.668 and 0.597 of AUC value for training and validating respectively [34]. Blood markers are used to assist the clinically measurement of body, so these biomarkers can provide a sufficient information related to disease. Therefore, application of artificial intelligence along with machine learning methods are initialized for the preoperative prognostic and diagnostic estimation of EOC that are based on blood markers. Seven different machine-learning methods defined for this purpose on 101 patient's history, includes Naïve Bayes (NB), random forest (RF), neural network (NN), conditional random forest (CRF), support vector machine (SVM), elastic net (EN) and gradient boosting machine (GBM) using 32 number of parameters. The all clinical stages that contains residual tumor burden, histotype, prognosis and stages analyzed with these methods. Random forest achieves the appropriate and highest accuracy to discriminating between the benign and EOC of 92.4% [35].

Additionally, a research purposes a SVM predictive model for analytical 10-gene expression data of EOC that are only analyze on patients having chemotherapy. The model first developed using cancer cell lines encyclopedia, after that implemented on two different datasets of GSE9891 and TCGA. The 10-gene expressions data model recognized that a longer-recurrence-free survival have high-response group [36]. A study purposes a novel method of classifying cancer patients and control patients of OC, which includes the data from Internet of Medical Thing (IOT). For classification, optimal recurrent neural network classifier and self-organizing map algorithm is used. Further, to improve this classifier, weight optimization performed by Adoptive-harmony-search-optimization, which gives the applicable accuracy of 96.27% along with 85.2% of specificity and sensitivity [37]. High-grade serous ovarian carcinoma accounts for 75% of the OC, so most of the research is fall in this category for prediction and classification matter. Most of the time it recurrence after chemotherapy, therefore an investigation is represented machine learning method known linear support vector machine for early prediction of OC using serial cancer antigen 125 famous for CA125 which are based on abdominal computed tomography (CT). Study included 57 patients' data that contain hypothesis; HIPaA-compliant and retrospective.10-fold-cross-validation performed to evaluate and optimize SVM for determining that CA125 is measure more for predicting the abdominal recurrences. This abdominal recurrence also analyzes with the help statistical method cox-proportional hazard [38]. Molecular biomarker of OC can use to minimize the mortality rate; consequently, a penal of gene molecular biomarker may use to train the machine learning models for detection of ovarian cancer tissues. The research used 26-mRnA gene expression for reduction of features, which improve the efficiency of the ML models. For this purpose, seven different datasets analyzed with ML methods, which includes GSE10971, GSE12172, GSE38666, GSE14407, GSE18521, GSE9899 and GSE37648. Five ML classifiers: Random Forest, K-nearest neighbor, generalized linear model, Support vector machine and classification & regression tree implemented on these datasets. Random forest, SVM and KNN gives the balanced accuracies of 0.89, 0.85 and 0.84 respectively [39].

2.3. Prediction of Ovarian Cancer with Deep Learning

Deep learning a sub-domain of Artificial intelligence and Machine learning is getting popular day by day in different areas of medication design and health care. As cancer is a deadly disease, specific treatment and early diagnosis is requiring for increasing the chances of life. Deep learning is showing a promising benefit for classification and prediction of different cancer diseases with its emerging technologies, which are effective and accurate [41]. A detailed summary of classification and predictive models of deep learning explained below in Table 4.

Table 4. Overview of recent study with DL for OC prediction

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[42]	Deep-convolutional neural network with AleXnet-model	National cancer institute's genomic data-commons-data portal	Accuracy=83.93%
2	[43]	Deep machine learning with MeTylnet	University of lowa	Accuracy=95%
3	[44]	Deep-machine learning with Alternative splicing analysis	Not mentioned	Accuracy=91%
4	[45]	Deep-hybrid learning with Synthetic monitoring oversampling technique.	Tata-Medical Center, Kolkata	AUC=0.99%
5	[46]	Deep neural network with VGG-16 model	Not mentioned	Accuracy=92.11%
6	[47]	DCNN with Cost Sensitive-RF classifier	The peking-uninon medical college and university, China	Accuracy=99.15%
7	[48]	DNN with Multilayer-feedforward	Asan-medical center, Seoul-national-University and Hospital, Korea	AUC=0.718
8	[49]	Cox-proportional-hazard with deep learning features	West-china-second-university hospital of Sichuan-University	AUC=0.865
9	[50]	Error-guided artificial Bee colony NN	National Cancer-Institute, USA	ACC=91.2%
10	[51]	CNN with AleXnet and CSGSA-AI	Tokai university hospital, KAC, SOIken and Sanfco, Japan	ACC=95%

Predicting a disease is a complex task, with advancement in the technology these things are getting easy as vast precautions and methods are available now. A novel method called (ASA) Alternative splicing analysis [42] with deep learning for the detection of normal and malignant OC tumor. As ASA provides a detailed access to a single gene expression that behave multiple times for proteins. Dataset contains 12 normal and 112 HGSC sequenced tissues that are analyze with RnA-sequencing interpreted in DARTs, which reached 91% of the accuracy rate. A study in [43] introduce a novel architecture of convolutional neural network of deep learning for predicting ovarian cancer and classify its sub-type. Dataset taken from the NCIGDCDP (national cancer institute's genomic data-commons-data portal). The dataset includes histopathological images. Total number of the dataset was five hundred images each of which labeled. Labeled data include 60 images for endometroid, 85 number of images for non-cancerous 100 for mucinous, 175 for serous and 80 number of images for the clear-cell type. Study performs augmentation on labeled data, which obtained 24,742 samples of images that are much more than the original data. Authors implemented the new DCNN model architecture with different hyperactive parameters setting, convolution layers and feature maps. The study also compares the accuracy on the both dataset before and after augmentation of the images and conclude the results with the fact that 83.93% of the accuracy rate increased with the augmentation, as without augmentation the accuracy rate was 78%.

Sometime patients with high-grade serous carcinoma do not response well with initial chemotherapy and have to suffer from poor diagnosis. Therefore, [44] proposes a different predictive method of deep machine learning along with DNA-methylation for chemo-response of the patients. DNA of 81-HGSC patients from University of lowa analyze with MeTylnet and IlluminaEpic array for methylation prestige. The accuracy on both models gives 95% of confidence interval. Morphometric nuclear lamin distribution in proteins with Deep hybrid learner approach helps to fast and accurate diagnosis of OC in perspective of normal and cancerous cells [45]. Deep neural network in [46] with its Visual-Geometry Group-16 model is demonstrating the prediction of ovarian cysts in patients using the ultrasound imaging.240 number of images analyzed with fine tuning of the VGG model and score the accuracy of 92.11% to confirm either the patient has OC cysts or not. DCNN with its remarkable benefits in non-medical-image also gradually applied in medical imaging for accurate prediction and classification. [47] Explored an image detection system for colorful ultrasound images with Random forest classifier, which is cost sensitive to predict the ovarian cysts. A detailed research implemented after extracting high-level and low level features with deep neural network and texture depicter respectively to classify accurately malignant OC cysts from benign.

As DNN is performing well for predicting disease on image dataset, but there is still a challenge for DNN to predict OC with clinic pathological data. This [48] study focus on identifying hypermeters that can improved the power of predicting Epithelial OC using clinic pathological data. Total six hypermeters include in the research which are analyze by multi-layer feed-forward neural network and get highest AUC rate of 0.7185. Undoubtedly, OC can cure but in some cases, there is still chances of HGSOC recurrence and few biomarkers for prognostic reported. Relating to this [49] represents a novel deep learning model, which is able for early predict the recurrences of high-grade serous ovarian carcinoma through the preoperative images of (CT) computed tomography. Further, Cox-proportional-hazard and DL regression is in cooperating to extract the prognostic biomarkers from two datasets and achieve appropriate accuracy. Researchers are doing their best efforts to originate some different and unique methods for detecting ovarian cancer as [50]formulate a different and unique algorithm of known as EABC (Error-Artificial-Bee-Colony) for enhancing neural network to predict ovarian cancer on dataset of control patients and cancer patients and evaluate it with other models and score 91.2% of accuracy rate. Epithelial Ovarian cancer detection has become a vast topic, subsequently, a comprehensive novel method of artificial intelligence combines with serum glycol-peptide spectra analysis used to identify serum sample of aberrant glycan. The AleXnet model of CNN used to predict early diagnosis of EOC. Dataset sample for this purpose divide 60% for training and 40% for validation. Further analysis done by converting the serum pattern glycol-peptides into two-dimensional barcode so that CNN model can easily predict the different between the non-EOC and EOC. While training this model on dataset give the 95% of accuracy [51].

2.4. Classification of Ovarian Cancer with Deep Learning

The state-of-the-art research methods have been discovered using deep learning techniques for ovarian cancer classification, the below table 5, shows the overview of the recent study with their proposed methods along with the data source.

Table 5. Overview of recent study with DL for OC Classification

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[52]	DCNN with DenSeNet-201	PLCO-https://cdas.cancer.gov/plco	ACC=94.73%
2	[53]	CNN with transfer learning	Vancouver general hospital	ACC=87.54%, Cohens kappa=0.8106
3	[54]	Transfer and Scratch learning, VGG16, DenSeNET, ResNet-50, GooglENet-V3	IPM&CHHCWI https://imr.sjtu.edu.cn/en/lc_gjhp/397.html	ACC=92.50%
4	[55]	DCNN-AleXnet, t-test	Xinjiang-medical university	ACC=78.20%
5	[56]	NN-RBF, Smote, FF_MLP	Gene-expression omnibus-NCBI	ACC=96%

OC classification through histopathological images is growing gradually with the help of deep learning to get better results so in [52] , author's enterprise a method for the detection of normal or malignant tumor of OC by using the feature extraction model of deep learning on histopathological data which consists of Eosin stain and Hematoxylin pictures. The multilayer DenSeNET-feature model along with DCNN implemented on (Prostrate-Lungs-Colorectal-Ovarian) PLCO cancer screening dataset. Furthermore, performing matrices parameters used to evaluate the model and achieve the highest accuracy of 94.73%. Histological types of Epithelial OC are different in perspective of clinical, morphological and genetics features. EOC subtypes classification already done through various methods of ML and DL. In [53], a research evaluated whole-slide-pathology images of EOC with two-stage transfer learning of convolutional neural networks that trained VGG-19 network model by random weights. Another method accomplished for the classification of ovarian tumor coupled with convolutional neural networks and 2D_ultrasound images. The two-step approach is considering for proper evaluation of the 2D_ultrsound images, firstly, data augmentation performed due to small number of 988-labeled images with pre-trained models of transfer and scratch learning. Secondly, comparison of different CNN models performed on the augmented data set of normal, benign and malignant. CNN models include GooglENet_V3, DenSeNET, ResNet-50 and VGG_16 in which GooglENet_V3 achieve outclassed accuracy of 92.50% [54].

Deep learning comprises large amount of data for evaluation and prognosis of disease, therefore, deep convolutional neural network based method AleXnet used for the classification of four types of OC that includes serous, mucinous, endometroid and clear cell-carcinoma. Eighty-five specimens of cytological images included in the study, which accomplished Eosin/Hematoxylin section of stain tissue. The classification executed on two-input data, one on original set of images (7392) and second on (81312) annotated images which are 11 times larger than the original one. Ten-fold-cross-validation performed to enhance the accuracy of classification model. AleXnet improved 5.44% of accuracy from original dataset (72.76%) to (78.20%) on augmented dataset [55]. Data imbalance is a problem while classifying any disease with ML/DL. SMOTe (Synthetic-minority over-sampling technique) algorithm usually used for reduce the imbalance data. A study employ neural network along with SMOTe for the classification of ovarian cancer. Two NN models RBF (Radiant-basis-functions) and FF-MLP (Feed Forward-Multilayer perceptron) applied on public dataset. RBF and FF-MLP behave differently with SMOTe technique as simple classification secure 95.3% and 83.4% of accuracy rate for FF-MLP and RBF separately, even though with SMOTe, RBF and FF-MLP achieved 88.4% and 96.8% of accuracy [56].

3. Exploring Machine and Deep Learning Features for Ovarian Cancer

The state-of-the-art research methods have been discovered using machine and deep learning techniques for ovarian cancer classification, the below table 06 shows the features of the recent study with their proposed methods/tools and libraries along with the data source.

Table 6. Overview of studies with ML and DL features for OC

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[57]	ML-ROMA, Logistic regression, DT	Hospital-of Soochow-University, China	DT=0.888, ROMA=0.814
2	[58]	ML-SVM, KNN, ANN, ELM Feature selection-Principle-Component-Analysis, Genetic Algorithm	NIH- https://ccr.cancer.gov/	SVM-PCA=99%
3	[59]	ML-Natural language processing, PCA, XGBoost, RF, LR	Northwestern-medicine-healthcare	ML=0.56, NLP=0.70
4	[60]	LIBS-spectrum, BPNN, Selectk-best algorithm	Tongde-hospital, Zhejiang-university, China	Specificity=86%, Sensitivity=71.4%
5	[61]	ML-microbial features, RF, LR	Southern-Illinois university of medicine	AUC=0.804

The features selection methods of ML for the early diagnosis of benign and malignant ovarian tumors is enthusiastic in a research. The MRMR (minimum Redundancy-maximum Relevance) method implemented for this purpose. Study takes the dataset of Chinese patients with 349 in total. The dataset includes the 49 numbers of variables like tumor markers, blood routine test, general chemistry and demographics. The feature selection method MRMR applied to only the 235 patients in which 146 were ovarian cancer patients while 89 were BOT so that relevant features can selected to construct the machine-learning model named decision tree. The constructed model applied on the remaining patients, which includes 25 of OC patients and 89 of BOT patients. Authors constructed the model along with two biomarkers which are CEA (carcinoembryonic antigen) and HE4 (human epididymis protein) which gives significant help for prediction. Further, they also compare their model with Risk of ovarian Malignancy algorithm and logistic regression for the purpose of training and testing dataset. The results of the study show 0.888 and 0.814 values for AUC of ROC for the training dataset of decision tree and ROMA respectively. For testing dataset, values were 0.943 and 0.949 for ROMA and decision tree respectively. Similarly, logistic regression model values also less than the decision tree that comprises 0.8777 [57]. Feature selection for classification of OC is playing vital role as it simplified the task of removing and reducing duplicate features from datasets. Therefore, a wavelet-discrete transformation based which is statistical feature extraction, extracted from the masses of spectrometry-proteomics-profiles [58]. Further, performance evaluation and comparison is completed through four different ML algorithms (Extreme-learning-machine, support-vector-machine, artificial-neural networks and K-nearest neighbor) and two features selection algorithms (Principle-component-analysis and genetic algorithm). For diagnosis of OC, SVM with amalgamation of PCA accomplished highest accuracy of 99% among the other algorithms on proteomic-profile dataset [58].

Although, ML is performing well in feature selection methods of OC, a novel study [59] purposed Natural language processing methods with machine learning to predict the post-operative survival outcomes of OC patients based on preoperative CT scan images. Three feature sets build for ML-NLP methods and analyze their performances. The ML-LR predictors with discrete features provide 0.57 of ACU value while NLP based features achieve 0.70 value of AUC on the pre-operative images. Back-propagation neural network coupled with laser induced-breakdown-spectroscopy for the classification and identification of normal, Cysts and OC from the blood plasma [60]. The blood plasma contains 176 samples of these three types' cases. Feature selection algorithm (Select-k-Best together with chi-square test) applied on data to ensemble of pretreated spectra, furthermore a five-fold-cross validation employed on regression model of BPNN for training the dataset to acquire the desired specificity and sensitivity. Analysis of tumor markers of HE4/CA125 levels and peritoneal-microbial features in peritoneal liquid purposed along with machine learning approaches on different datasets to identify ovarian cancer in patients [61]. Investigation of these by performing performance metrics, specify that tumor biomarkers levels through serum perform well in predicting the disease rather than the markers through peritoneal-fluid.

4. Frameworks of Machine and Deep Learning for Ovarian Cancer

The state-of-the-art research methods have been discussed the machine and deep learning techniques for ovarian cancer classification, the below table 07, show the frameworks of the recent studies used in ovarian cancer with their proposed methods/tools and libraries along with the data source.

Table 7. Overview of studies with ML and DL framework for OC

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[62]	DCNN-MIL, LuPI	The Cancer genome Atlas, TCGA	AUC=0.79, SD=0.07
2	[63]	ML-CNN, Logistic Regression	Stanford.edu/dataset	Specificity=98%
3	[64]	DL framework- Auto encoder, logistic regression, K-mean clustering.	The Cancer genome Atlas, TCGA	DBI Score=1.859
4	[65]	ALO, LTSM, CNN	The Cancer genome Atlas, TCGA-OV	ACC=98.87%
5	[66]	NB, SVM, MRMR, Cox-proportional-hazard	St. James university hospital, LEEDS	SVM=63%, KNN=62.1%

In this work [62], The authors presented a novel framework of deep neural networks that is capable of chemo-sensitivity prediction in patients of ovarian cancer. The framework consists of a new different variant of learning called Learning using Privileged information shortly for (LuPI) and MIL, which is multiple instance learning for knowledge transfer. Dataset for training arranged from another study focused at OC survival patient prediction with the help of gene expressions. The dataset contains 220 patients in which 154 for positive samples and 66 for negative samples. In the proposed method, the privileged information learning model uses routine WSI data as its input and gene expression as privileged information for improvement in the accuracy rate of the Chemo sensitivity. The training of the model prepared on the image patches taken from the tissues section of ovarian cancer, which consists of whole slide images known as input space and multi-giga-pixel hematoxylin & eosin. These image patches were also associated with the profile of gene expression known as privileged feature space. The results of the study showed that learning using a privileged information based model along with WSI as input gives the average value of 0.79 of ROC curve with standard deviation of 0.07 that is much higher than the others are. Ovarian tumor may also occur during pregnancy, which is the critical situation. Usually, Obstetric ultrasound imaging used to detect the malignancy during pregnancy using ML based CNN framework. This framework used to train and mold the training phase further analysis performed with logistic Regression classifier for detailed fine-tuning, high-level features with evaluating and testing [63].

Diagnostic of OC is worse that is why the mortality rate is high. Researchers are trying to implemented different methods to reduce the mortality rate. As [64], signifies the multi-omics structures combination with the deep learning framework for quickly identify the sub-types of ovarian cancer. The study represents novel Auto-encoder DL framework Consists of encoder and decoder. The DAE take the multi-omics (CNV, MRnA, and MiRNA) features for analyzing extracted from TCGA portal. Further k-means clustering used to cluster the subtype features so that gene could reduce for identifying the subtype of OC with logistic regression. A [65] deep learning multi-model framework implemented on histopathological and gene data to predict the stages of OC. This comprises two network models of feature extraction: Antlion optimizer-algorithm with long short-term memory-network and Antlion with convolutional neural network. The gene expression data analyze with ALO_LSTM network while ALO_CNN used to extract pathology images features. After this, the purposed model is capable of predicting the OC stages accurately and achieved highest score among others.

A study in [66], Hypothesized novel prediction of high-grade serous ovarian cancer at advanced stage with prognosis estimation of two years by combining two different machine learning methods which includes support vector machine along with (Knn) k-nearest neighbor and also compare their performances. Analysis performed on 209 of total patients at III-IV stage of high-grade serous ovarian cancer who ready for cytoreductive surgery with life prologue intent and curative. The two-year prognosis period considered as the binary class classification problem. This binary classification divided into two groups with positive and negative class as those patients who did not get sick and survived before the specified period fall into the positive class group and those who died or relapsed were in the negative class. The authors split the dataset into two cohorts of training and testing. For the two-year prognosis period only 172 number of patients of the total were eligible for this purpose. However, 104 patients out of 172 had to suffer from the disease recurrence and remaining 55 of which died within two years. The results of the study confirm the (support vector machine) SVM method as the appropriate predictor for two-year prognosis analysis with 63% of accuracy rate while KNN performs 62.1% of accuracy [66].

5. Enhanced approaches and Evaluation of Ovarian Cancer with ML & DL

The state-of-the-art research methods have been discovered using machine and deep learning techniques for ovarian cancer classification, the below table 08, show the evaluation of the recent study with their proposed methods/tools and libraries along with the data source.

Table 8. Overview of approaches with ML and DL for OC Evaluation

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[67]	CNN- Efficientnet , ReSNet	Institutional-Review board,USA	AUC=0.87
2	[68]	CNN- Inception_V3, Xception, RF, LR	Cancer-Image-Archive	ACC=99.53%
3	[69]	Feed-forward NN- Probabilistic NN	Not-mentioned	ACC=99.8%
4	[70]	KNN, SVM, NB, DT	American-Type cultural collection	ACC=99.2%
5	[71]	Artificial neural network, Decision tree	Danish-Cancer Registrar, Denmark	ACC=67.9%
6	[72]	Multiclass-SVM, PGSO, Navies bayes,	TCGA-data portal	ACC=96%
		ANN		ACC=98%

Differentiation of OC lesions on preoperative MRI routine images is difficult task for doctors. Consequently, a convolutional neural network along with radiologist evaluation and Radiomics analysis implemented to discriminate the benign and malignant ovarian lesions to save patients from unnecessary treatments and disturbing procedures. Radiomics analysis performed by extracting features for T2wI and TIC sequences on each MRI of patients. The comparison of ReSNet and Efficientnet models of deep learning also analyze on these two sequences. All performance metrics include ROC_AUC, F1-score, PR_AUC, specificity, sensitivity calculated for Radiomics analysis and deep learning methods. Moreover, seven senior/junior radiologist analyze these DL methods and junior radiologist accomplished higher accuracy, specificity and sensitivity through the model probabilities [68]. CNN continuously outperformed for better accuracy to classify ovarian cancer. A detailed augmentation implemented on CIA dataset includes scaling, rotation, saturation, brightness, contrast and cropping. Augmented dataset preprocessed using median filtering that monitored by feature extraction and image segmentation. Moreover, DL Xception and Inception_V3 models processed along with Random forest and Logistic regression classifier on augmented data comparatively, in which Xception-logistic regression provides the highest rate of accuracy, F1_score, precision and recall [69]. Another computer aided diagnosis system developed to classify the benign and malignant OC and define the nature of the tumor on ultrasound image dataset.

Probabilistic neural network classifier applied to the extracted features (Entropies and Gabor-transform-parameter) and accomplished better accurateness with the help of Genetic algorithm. Ten-fold cross validation also employed to improve the accuracy, which is approximately 99.8% along with 99.6% of specificity and 99.2% for sensitivity rate [67].

Normally patients of recurrent epithelial ovarian cancer suffer from different sides effects, if the drug resistance occurs. Drug resistance has great impact on prognosis and survival rate of EOC patients, equally analyzed drug resistance and sensitivity in patients going for chemotherapy. The study put forward drug resistance of EOC cells, and show how these cells can retrieved through high throughput and label free microscope-flow-cytometer, which is prepared with digital-holographic-microscope, further processed with machine leaning algorithms. The comparison of K-nearest neighbor, Naïve Bayes, Support vector machine, fully connected network and decision tree performed, where SVM accomplished the optimal accuracy of 92.2% [72]. Yet, another research determined the analysis of OC patients with ANN-multilayer perceptron and decision tree to predict either the patients will survive with OC or not. 318-sample of dataset extracted from the Danish cancer registrar, Denmark for evaluation and ten-fold cross validation performed to enhance the accuracy of the algorithms [70].

A novel study in contradiction of big data analysis presented to predict the ovarian cancer for early precautions and treatments, which includes two different datasets of normal cases and stages (I, II, III, IV). The authors developed the knowledge base system that comprises the data mining techniques of classification and feature selection. Feature selection completed through the optimized hybrid (Particle-Genetic-Swarm-Optimization) and rough set theory implemented on datasets to in view of dependencies. Furthermore, comparison of classification algorithms between ANN, multiclass-SVM and Naïve bayes performed very well and multiclass-SVM achieved higher accuracy of 96% for dataset I and 98% for dataset II [71].

6. Feasible studies and purposed methods for Ovarian Cancer

The state-of-the-art research methods have been discovered using machine and deep learning techniques for ovarian cancer classification, the below table 09 show the feasible studies of the recent trends with their proposed methods/tools and libraries along with the data source.

Table 9. Overview of Feasible studies and purposed methods for OC

Sr.	Ref	Proposed Methods	Data Sources	Results
1	[73]	CA-125, T-test, genetic algorithm	UPCI-University of Pittsburg cancer institute.	AUC=0.92
2	[74]	Scatter Search-SVM,DT	China-medical university	ACC=96.43%
3	[75]	NC-SVM, BMRF	TCGA-data portal	ACC=86.92%
4	[76]	MLP,RF,LR,SL,MCC, LB, Logistic, Bagging, Regression	Not-mentioned	AUC=0.885
5	[77]	ML-KNN, One-pass clustering	National-cancer hospital https://ccr.cancer.gov	ACC=97%

Many research works done and still proceeding on the diagnosis, prognosis and classification of ovarian cancer as early screening is useful for effective treatment using appropriate methods. Cancer antigen-125 is most famous biomarker for diagnosis of OC. CA125 along with genetic algorithm of feature selection and T-test employed to classify cancer patients from control patients by taking predetermined biomarkers of 58 Korean samples. The five-fold cross-validation performed on the 21 biomarkers for better specificity and sensitivity of dataset. The 0.92% accuracy achieved on with the combination of all biomarkers [73]. Gene selection in large micro-array data needed for the classification of OC, for a purpose Scatter search is implies on gene selection for ML algorithms-support vector machine and decision tree. After scatter search for DT and SVM dataset capable of classifying Benign, ovarian tumor and ovarian cancer and acquire 96.43% of accuracy [77]. To analyze the TCCGA dataset of ovarian cancer, a study presents an integrative framework, which combine the DNA- microarray, protein-interaction data and clinical information of patients. Further, for distinguish among multiple phenotypes and different expression patterns, network-based methods applied to recognize pathway networks. The 3-fold cross-validation implicated on TCGA dataset to improve the accuracy of network constrained-SVM that achieve 86.92% of accuracy for validation and 69.15% for independent test [74].

Ovarian cancer screening accomplished using nine different machine-learning algorithms with different combination of biomarker. For the research, 15-biomarker combinations made to boosted the performance of ML methods includes logistic regression, simple logistic, bagging, regression, logistic, random forest, multilevel-perceptron, multiclass and logit-boost for the classification of ovarian data on Korean dataset. The 15-biomarkers comprises of three best combinations, which further divide into the combinations of two, three and four biomarkers. Every algorithm performs well but logistic regression achieved highest value of Area under the curve 0.885[75]. Early detection of ovarian cancer through protein profiling is beneficial but it has some problem relating to noise and high-dimensional data. To overcome this problem, ML-classifier k-nearest-neighbor and one-pass clustering purposed. The development of ovarian cancer prediction came through surface-enhanced laser-desorption & lionization-time of flight-mass spectrometry data on given dataset. The purposed methods give more accurate results than others give and obtained highest accuracy [76].

7. Discussion

In this article, various kinds of papers evaluated to make a comprehensive review, which shows how machine and deep learning algorithms extensively outperformed in medical imaging, mainly in ovarian cancer. Different techniques of ML and DL performed remarkably in binary classification, prognosis, diagnosis, prediction, identification, differentiate between types and grading of OC. The major diversity of machine/deep-learning methods and technologies covered impact fully in this article. Different ML/Dl algorithms behave differently on multiple types of datasets include micro-array, protein-profiling, gene-expression, micro-RNA, signature data, cysts, transcriptomic profiling and many other. ML-KNN and SVM used for classification purpose in many articles. Further, Random forest, logistic regression, multilayer perceptron, linear SVM, decision tree, Bayesian logistic regression also implemented in various studies for prediction of ovarian cancer with detail analysis Deep learning approaches enhanced the computer-aided-diagnosis system for medical image analysis. In recent research deep learning methods getting population to handle large dataset rapidly. Deep neural network, convolutional neural network along with different models such as AleXnet, VGG-16, MeTylnet and multilayer-feedforward specify for predicting ovarian cancer in multiple articles.

It is clear after reviewing various kinds of articles that ML and DL not only enhance the power of predicting accurate decisions but also provide significant approaches. Numerous algorithms of machine learning analyzed by using medical imaging. K-NN, SVM, decision tree, linear-SVM, linear-discriminant random forest, Boosted-logistic regression and Bayesian-logistic regression potentially used for classification of ovarian cancer. These methods provide contrivances analysis mostly on Epithelial ovarian cancer, as this type of OC is occur frequently and common almost 70% of the total. Artificial neural networks also performed to resolved misclassification and misdiagnosis of OC. Feature selection techniques implemented with these algorithms to improve the accuracy of classification. However, XG-Boosted, ensemble-algorithm, gradient boosting ensemble model, SVM with Cox-regression and Cox-proportional hazard investigated very well for predicting OC with minimum complications. Every model behave differently on each dataset, as, almost every dataset is different from one another. Prediction with micro-RNA, ovarian cysts, micro-array, transcriptomic profiling, gene-expression of ovarian cancer require deep knowledge, which is correctly observed with machine learning models.

With growing development of technology in OC, many researchers in various articles works on image dataset. Deep learning performed outclass on large datasets for evaluation and prognosis of the disease. Medical renounce images, histopathological images and cytological images used to classify the different types of ovarian cancer. Deep neural networks work well on clinic-pathological data to predict epithelial ovarian cancer. Convolutional neural network along with AleXnet model employed successfully for predicting OC based on preoperative images of computed tomography. Different studies also focus on preprocessing and data-augmentation techniques, which not only boosted the performance of CNN but also, obtain good accuracy, as data-augmentation of small image dataset is useful contributor for better solutions.

Machine and deep learning methods or techniques in analysis of ovarian cancer show multiple challenges. The use of ML and DL models has tremendously vigorous inferences for properly medications of OC. It significantly noted that these research areas guarantee better care for patients and minimize the ratio of death. However, deep learning methods permits to enumerate, classify and categories the disease patterns in medical image analysis of the OC. Deep neural networks in medical imaging and health care domain is undergo to flourish and rapidly improving. It became very easy to classify and solve the problems of ovarian cancer by using end-to-end deep learning techniques. Machine and deep learning applications has gained much attention in medical image analysis of OC, as, it generally leveraged the mindset of the practitioners and researchers.

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