Iranian Journal of Blood & Cancer

Iran J Blood Cancer, 2026, 18(3), 64-76
https://ijbc.ir

Original

Explainable Deep Learning for Ovarian Cancer Survival Prediction: A Retrospective Analysis of Iranian National Data

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Citation Akbari A, Rahimi M, Asadi F, Akbari ME. Explainable Deep Learning for Ovarian Cancer Survival Prediction: A Retrospective Analysis of Iranian National Data. Iran J Blood Cancer. 2026 Sep 30;18(3): 64-76.

doi 0

Article info:
Received: 15 Jul 2026
Accepted: 20 Sep 2026
Published: 30 Sep 2026

Keywords:
Ovarian cancer
Survival analysis
Survival prediction
Machine learning
Deep learning

Abstract

Background: Ovarian cancer is one of the deadliest gynecological cancers, creating an urgent need for reliable prognostic tools to guide treatment decisions. With the growing use of deep learning in healthcare, this study aimed to predict ovarian cancer survival outcomes even when working with incomplete or low-quality clinical data.

Methods: We performed a retrospective analysis of 2,675 ovarian cancer cases with complete survival data from the Iranian National Cancer Registry (2008–2015). Survival probabilities were estimated using Kaplan–Meier analysis, and eight deep learning models, covering discrete- and continuous-time approaches, were compared using the concordance index (C-index). Model interpretability analyses were also conducted to identify key prognostic factors.

Results: Five- and ten-year survival rates were 54% and 42%, respectively. The discrete-time Logistic Hazard model achieved the best predictive performance (C-index = 0.69). Age at diagnosis and histological subtype were significant survival predictors ($p < 0.05$), and patients with epithelial type II tumors had poorer outcomes despite their higher prevalence.

Conclusion: Deep learning shows strong potential for survival prediction in ovarian cancer, even with imperfect data. However, improving data completeness and model transparency is crucial before these tools can be applied in clinical settings.

1. INTRODUCTION

Ovarian cancer (OC) is the seventh most common cancer among women globally and ranks eighteenth in overall cancer prevalence [1]. It accounts for approximately 5% of cancer-related deaths in women, with a particularly high mortality-to-incidence ratio compared to other gynecological cancers [2]. According to the World Health Organization (WHO), 2020 saw approximately 314,000 new OC cases and 207,000 deaths worldwide, with Iran reporting 1,966 new cases and 1,269 deaths [1, 3, 4]. The incidence and mortality rates vary significantly by region, with higher rates in European countries and lower rates in Africa. Notably, projections indicate that countries with low Human

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Development Index (HDI) values will experience a dramatic increase in both incidence (96%) and mortality (100%) by 2040, underscoring the need for targeted interventions and effective prognostic tools in these regions [3, 4].

Despite advancements in treatment, over 70% of OC cases are diagnosed at advanced stages due to the lack of effective screening programs and nonspecific early symptoms, resulting in poor prognosis [5]. Approximately 90% of OC cases are epithelial ovarian cancers (EOC), while the remainder are germ cell tumors or sex cord-stromal malignancies. Survival outcomes are closely tied to the stage at diagnosis, with a 5-year overall survival rate of approximately 90% for stage I patients but only 20% for those diagnosed at stage IV [6, 7]. Early and accurate prediction of survival outcomes is crucial for informing treatment strategies and optimizing patient management.

Survival analysis has traditionally relied on statistical models such as the log-rank test and Cox Proportional Hazards (CPH) model [8]. While these methods are effective for small, linear datasets, they struggle with the complexities of heterogeneous and nonlinear data distributions commonly encountered in cancer datasets [9]. For instance, studies have shown that traditional models often fail to fully utilize high-dimensional data, such as genetic and imaging features, which are increasingly available due to advancements in diagnostic technologies [10]. This limitation necessitates the adoption of more sophisticated approaches capable of capturing intricate patterns in large and complex datasets.

Machine learning (ML) and deep learning (DL) techniques have emerged as transformative tools in survival prediction due to their ability to model non-linear relationships and incorporate diverse data types, such as clinical, genomic, and imaging data [11, 12]. ML models, including random forests (RF) and logistic regression (LR), have demonstrated improved performance in handling censored survival data, particularly through the integration of survival-specific loss functions [13]. However, DL models, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), offer significant advantages in processing unstructured data, including medical images and sequential time-series data [12, 14]. Recently, attention mechanisms and transformer-based architectures have further advanced the field by allowing models to focus on clinically relevant features while reducing the influence of noisy or irrelevant variables [15, 16]. For instance, studies incorporating multi-modal DL approaches have successfully integrated imaging data with patient demographics and molecular profiles, achieving state-of-the-art results in survival prediction [16].

This study aims to leverage advanced DL models to predict and analyze the 5- and 10-year overall survival rates of OC patients in Iran using national data from 2008 to 2015. By examining key prognostic variables and employing both continuous-time and discrete-time DL approaches, this research seeks to address gaps in localized survival prediction models. Several valid evaluation metrics, including Harrell's concordance index (C-index) and integrated Brier score (IBS), will be used to assess the performance of these models. While ML models are effective for clear and simple datasets, the presence of missing key variables in this dataset necessitated the use of DL techniques to identify complex, non-linear relationships that could enhance overall survival prediction. DL models offer advantages in uncovering intricate and hidden patterns, making them particularly suitable for datasets where key prognostic variables may be incomplete or interact in complex ways. The findings are expected to provide valuable insights for clinicians, aiding in personalized treatment planning and resource allocation, while advancing the application of DL techniques in oncology.

2. MTERIALS AND METHODS

This study employed a systematic and data-driven approach to predict survival outcomes in ovarian cancer patients using advanced DL methodologies.

2.1 Characteristics of the dataset

The Cancer Research Center (CRC) conducted a comprehensive data collection effort targeting Iranian women diagnosed with OC between 2008 and 2015. The dataset was specifically curated for research purposes, capturing demographic, clinical, and pathological data. To enhance the dataset's depth and accuracy, trained CRC staff contacted patients in 2017 using their recorded contact information. This follow-up initiative successfully retrieved critical survival data, including exact dates of death or last follow-up. A detailed overview of the dataset is provided in Table 1, highlighting its scope and the variables collected to support advanced survival analysis.

2.2 Cleaning and preprocessing

The original dataset from the CRC comprised 15 variables and 7,977 records. A systematic cleaning process was undertaken to enhance the quality and usability of the data. Initially, 5,095 records lacking overall survival data were excluded, reducing the dataset to 2,882 entries. In the second step, records with missing pathology codes and undetermined causes of death were removed, resulting in a final dataset of 2,675 records. Six irrelevant columns were eliminated, leaving nine clinically and demographically relevant variables.

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Table1. Iranian national ovarian cancer dataset characteristics.

Variable	Attributes	Number	Percent	P-value
Age	Max	94		0.003638
	Min	10		
	Mean	50.62		
Grade	Grade I	258	10	0.000005
	Grade II	264	10	
	Grade III	294	11	
	Grade IV	33	1	
	Unknown	1826	69	
Histology	Clear cell carcinoma (CCC)	56	2	0.000000
	Endometrioid carcinoma (EC)	154	6	
	Germ cell carcinoma (GCC)	190	8	
	Mixed epithelial-stromal carcinoma (MESC)	19	<1	
	Mucinous carcinoma (MC)	205	8	
	Non-specific carcinoma (NSC)	474	18	
	Other specific non-epithelial (ONEC)	18	<1	
	Serous carcinoma (SC)	1021	38	
	Sex cord-stromal carcinoma (SCSC)	63	3	
	Squamous cell carcinoma (SCC)	15	<1	
	Transitional cell carcinoma (TCC)	30	1	
	Undifferentiated carcinoma (UC)	430	16	
Histological groups	EOC I	460	18	0.000000
	EOC II	1470	55	
	Others (GCC, NSC, ONEC, SCSC)	745	27	
Survival status	Censored	1288	48	
	Uncensored	1387	52	
Survival (month)	Min - Max	1 - 120		
Survival (year)	Min - Max	1 – 10		

To optimize the dataset, preprocessing and feature engineering techniques were applied. This refinement reduced the number of variables to seven by combining certain columns, as summarized in Table 1. Two new variables were derived: Histological Group (HG) and Survival (year). The HG variable grouped histological subtypes into two main categories: EOC I, encompassing Clear Cell, Endometrioid, Mucinous, Squamous, and Transitional carcinomas, and EOC II, including Serous, Mixed epithelial-stromal, and Undifferentiated carcinomas. The Survival (year) variable was calculated from the existing "Survival (month)" data.

Key input variables for the models included age, grade, histology, and HG. Depending on the survival prediction approach, three variables were used as labels. For the continuous-time approach, labels included overall survival (months) and censoring status, while for the discrete-time

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approach, labels were overall survival (years) and censoring status.

Categorical variables were preprocessed using a label encoding algorithm before being one-hot encoded into binary form. The age variable, a continuous feature, was normalized to a range of -1 to +1 using the standard scaler algorithm. These cleaning, preprocessing, and feature engineering steps resulted in a well-structured dataset, optimized for advanced survival analysis and predictive modeling.

2.3 Model structure

This study utilized Pycox, a specialized library in PyTorch, to implement advanced survival analysis and prediction models [17]. The models were based on Feedforward Neural Networks (FNN), designed with a three-layer architecture that integrated batch normalization, dropout layers, and fully connected layers with ReLU activation functions for optimal performance (Fig. 1).

The model architecture accommodated a 25-feature input tensor and produced outputs tailored to the prediction approach: a single feature for the continuous-time approach and ten features for the discrete-time approach.

The network's initial linear layer transformed the 25-feature input tensor into a 32-feature output tensor. This was followed by batch normalization to stabilize learning, and dropout layers to mitigate overfitting by randomly deactivating nodes during training. This process was iteratively applied across subsequent linear layers, with batch normalization and dropout ensuring robust model generalization.

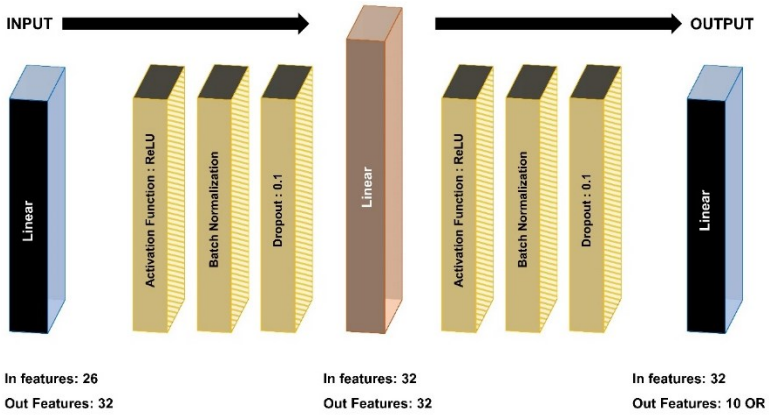


Figure 1. The Pycox library uses feedforward neural networks with three layers.

2.4 Model training and optimization

This study employed eight deep learning algorithms from the Pycox library to address time-to-event challenges in survival prediction, encompassing four continuous-time and four discrete-time survival analysis models. The Adam optimization algorithm was utilized to dynamically adjust model weights, minimizing bias and enhancing predictive performance. A learning rate of 0.01 was determined through an optimization process to regulate weight updates during training, ensuring stable convergence.

To maximize model learning while maintaining computational efficiency, 80% of the dataset was allocated for training. A minibatch size of 256 was selected to facilitate efficient memory usage and improve convergence stability through incremental weight updates. Training was conducted over 100 epochs, allowing the model to iteratively refine its parameters through repeated exposure to the dataset. An early stopping mechanism was incorporated to monitor validation performance and halt training when no further improvement was observed, mitigating overfitting risks. These strategies collectively ensured robust model generalization and computational efficiency in survival prediction.

2.5 Model evaluation

To evaluate the DL models' performance in predicting OS among ovarian cancer patients, three distinct metrics were employed: the concordance index (C-index), the inverse probability of censoring weighted (IPCW) Brier Score, and the IPCW negative binomial log-likelihood (NBLL). The C-index, ranging from 0.5 (no discriminative ability) to 1.0 (perfect concordance), assesses a model's capacity to correctly rank patients by risk, reflecting its ordinal predictive accuracy. In contrast, the IPCW Brier Score quantifies calibration by measuring the squared discrepancy between predicted and observed survival probabilities, with lower scores indicating superior performance, particularly in the presence of censored observations. Meanwhile, the IPCW NBLL addresses potential overdispersion in survival data while adjusting for censoring bias through inverse probability weighting; here, too, reduced values correspond to improved model reliability.

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Collectively, these metrics provide complementary insights into discrimination and probabilistic accuracy, offering a robust framework for assessing survival prediction models under real-world conditions marked by incomplete follow-up data.

3. RESULTS

3.1 Dataset characteristics and patient demographics

From the initial dataset of 7,977 clinical records, a total of 2,675 records were included in the final analysis. The demographic and clinical characteristics of the patients are summarized in Table 1. The mean age of the patients was approximately 50 years. Among the available data, the "grade" variable exhibited a high prevalence of missing information, with 1,811 cases labeled as "Unknown." In terms of histopathological subtypes, serous carcinoma was the most frequent, accounting for 1,021 cases. Analysis of the HG variable showed that the EOC II subgroup had the highest frequency, representing 1,470 records.

Nearly half of the records (47%, n = 1,288) were right-censored. The Kaplan-Meier survival analysis (Fig. 3) estimated a 10-year overall survival rate of approximately 42%, with the 5-year survival rate reaching 54%. Figure 2 illustrates the distribution of survival data based on years, offering insights into survival trends over time. Additionally, bar and pie charts visualize the number of patients in the dataset by survival year, providing a comprehensive view of the data distribution and survival outcomes. The included data serves as a representative sample of the entire dataset, with a comparison provided in the supplementary file.

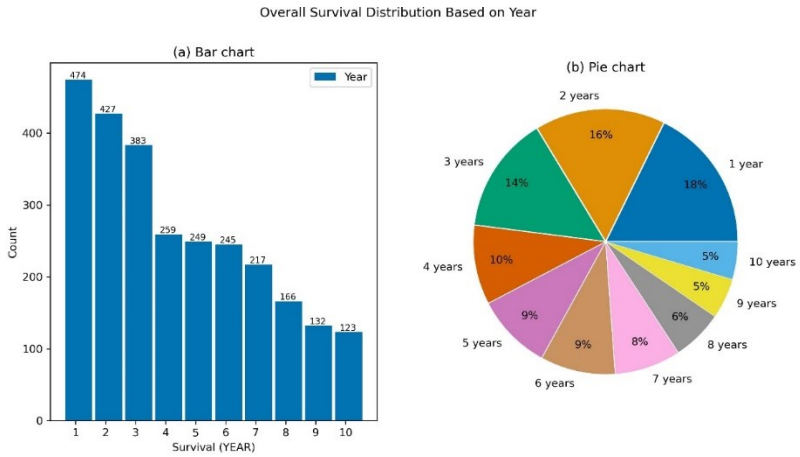


Figure 2. The figure presents the distribution of overall survival among patients over a ten-year period using two visualization methods. (a) Bar chart: The bar chart displays the frequency of patients surviving each year, with survival years on the x-axis and the corresponding count on the y-axis. Labels on top of each bar indicate the exact patient count for each survival year. (b) Pie chart: The pie chart illustrates the proportional distribution of patients across different survival years. Percentages are annotated to highlight the relative proportion of each survival duration. Both visualizations provide complementary insights into patient survival trends, aiding in the interpretation of long-term survival outcomes.

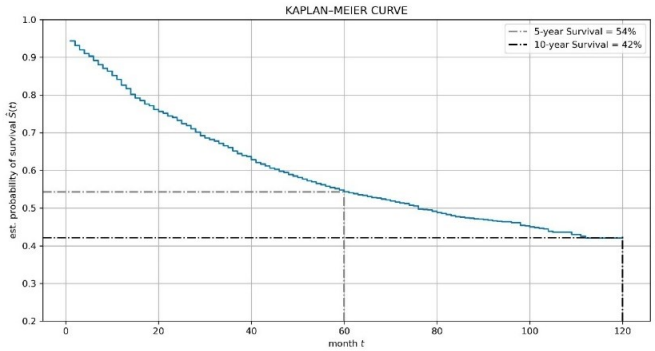


Figure 3. Kaplan-Meier survival curve illustrating the overall survival of ovarian cancer patients. The y-axis represents the probability of survival, while the x-axis indicates time in months. The estimated 5-year and 10-year overall survival rates for Iranian ovarian cancer patients are 54% and 42%, respectively

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3.2 Performance of deep learning models for survival prediction

Eight deep learning models were developed and evaluated to predict the survival outcomes of ovarian cancer patients using two distinct approaches: continuous-time and discrete-time (Table 2). The continuous-time models were trained on monthly survival data, whereas the discrete-time models utilized annual survival data.

In the discrete-time approach, the Logistic Hazard model demonstrated superior performance, achieving a C-index of 0.69, a Barrier score of 0.27, and an NBLL value of 0.75. Similarly, in the continuous-time approach, the COX-Time model emerged as the best performer, with a C-index of 0.67, a Barrier score of 0.19, and an NBLL value of 0.57. Conversely, the COX-PH model recorded the poorest performance across all models, with a C-index of 0.51.

Overall, the discrete-time approach outperformed the continuous-time approach, with an average C-index of 0.68 compared to 0.60. This finding highlights the potential advantages of discrete-time modeling for survival prediction in ovarian cancer patients.

Table 2. Outcome of deep learning models.

Approaches	Models	C-index score	Barrier score	NBLL score
Continuous-Time	COX-CC	0.66	0.29	0.80
	COX-PH	0.51	0.22	0.63
	COX-Time	0.67	0.19	0.57
	PC-Hazard	0.54	0.20	0.58
Discrete-Time	DeepHit	0.68	0.28	0.77
	Logistic Hazard	0.69	0.27	0.75
	MTLR	0.68	0.25	0.69
	PMF	0.67	0.27	0.75

3.3 Survival trends across histology, HG, and grade variables

In the histology subgroups, patients with GCC and SCSC exhibited the highest survival rates, whereas those with NSC and UC had the lowest. The HG variable revealed that patients classified under EOC I demonstrated better survival outcomes compared to those in EOC II.

Analysis of the grade variable highlighted that grade I patients had the highest survival rates, with survival progressively declining in higher grades, reaching the lowest in grade IV. Grades II and III exhibited comparable survival rates, suggesting a potential plateau effect in intermediate grades. Notably, subgroups with the highest frequency in the histology variable tended to have lower survival rates, a trend not mirrored in the grade variable, emphasizing distinct survival dynamics among these classifications (Fig. 4).

3.4 Impact of age and clinical variables on overall survival

The analysis reveals an inverse correlation between patient age and survival duration, with survival probabilities declining as age increases. The graph illustrates that patients aged 50 years or younger exhibit a notably higher likelihood of overall survival compared to older patients. Furthermore, the median age at which patients achieve survival rates of 1 year and 10 years is approximately 60 and 40 years, respectively. These findings underscore the heightened vulnerability of older patients and the potential for more favorable outcomes among younger cohorts, reflecting age's profound influence on survival dynamics (Fig. 5).

3.5 Age distribution insights among Iranian OC patients

The analysis of Iranian OC patients highlights several key demographic insights. As presented in Table 1, the mean age of patients diagnosed with OC in Iran is 52 years. Table 3 further breaks down the mean age of patients across different subgroups of histology, HG, and grade variables.

Within the histology category, the GCC subgroup exhibits the youngest mean age, averaging 29 years. Conversely, patients in the NSC, UC, MESC, TCC, and SCC subgroups have median ages exceeding the national mean of 52 years. Regarding the HG classification, the mean age of patients in the EOC I subgroup is 49 years, while those in EOC II exhibit a higher mean age of 53 years. Lastly, analysis by grade reveals that patients classified as grade I have the youngest mean age of 47 years, whereas those in grade III show the highest mean age of 53 years.

These findings provide a nuanced understanding of age distribution among Iranian OC patients and its association with clinical variables, emphasizing the variability in demographic patterns across subgroups.

3.6 Feature importance and impact on model predictions

The SHAP summary plot provides insights into the feature importance and directionality of their impact on model predictions. Among the analyzed features, histology exhibited the strongest influence, with higher values increasing the model's predicted outcome, suggesting a strong association with the target variable. Age also played a significant role, where older individuals tended to have higher risk predictions,aligning with clinical expectations. Grade and HG had relatively lower impacts, indicating their lesser but still notable contributions to the predictive model. These findings reinforce the biological and clinical relevance of key predictors and suggest that histology and age should be prioritized in predictive modeling for improved risk assessment (Fig. 6).

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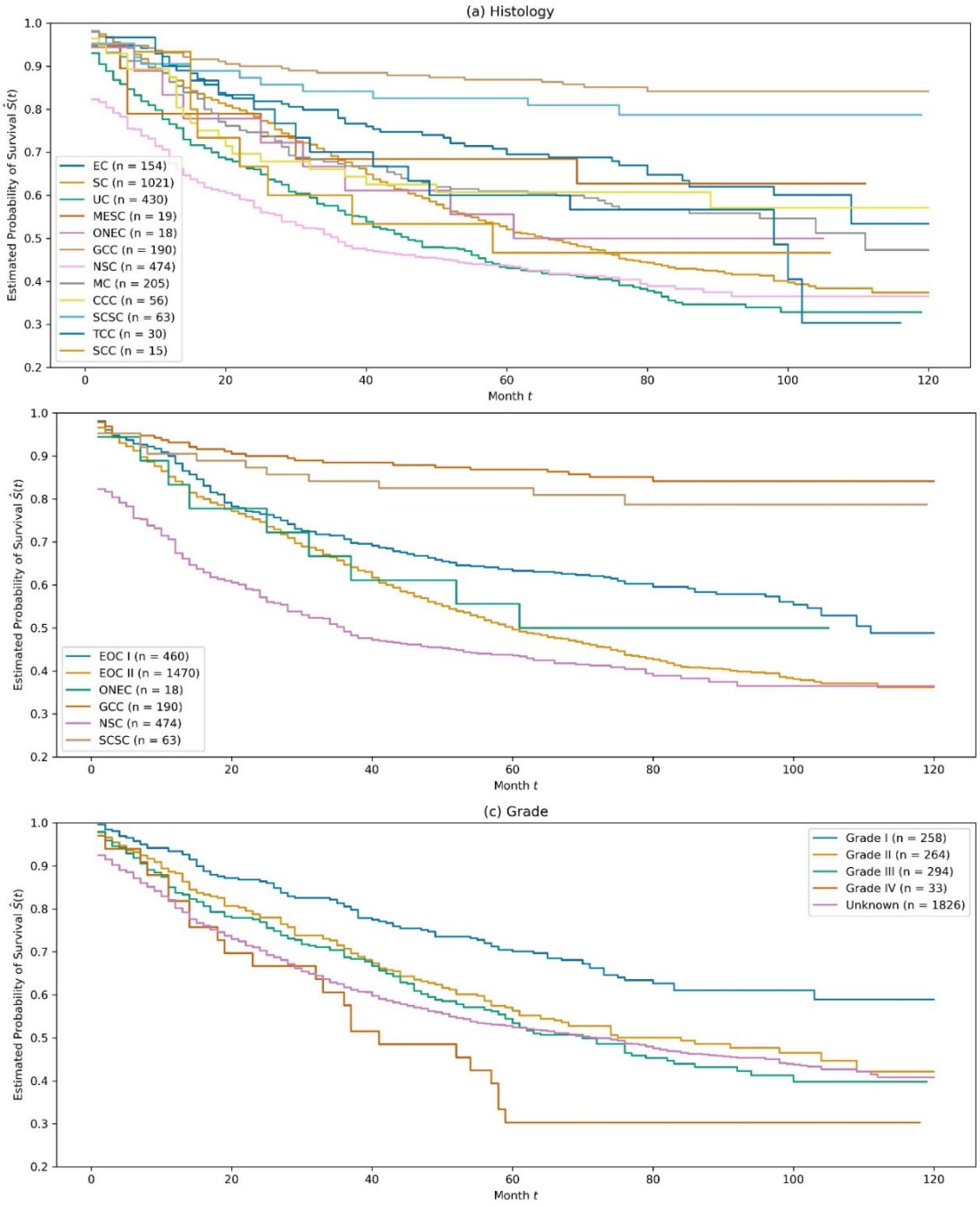


Figure 4. The figure illustrates the Kaplan-Meier survival curves stratified by three key factors in ovarian cancer. (a) Histology: Survival probabilities are compared across different histological subtypes, highlighting variations in prognosis. (b) Histology Groups (HG): The survival curves depict differences among broader histological classifications, offering insights into group-based prognostic trends. (c) Tumor Grade: The survival probability is analyzed based on tumor grading, demonstrating its impact on patient outcomes. The stepwise curves indicate the estimated probability of survival over time, with each category represented by a distinct color and sample size (n) indicated in the legend.

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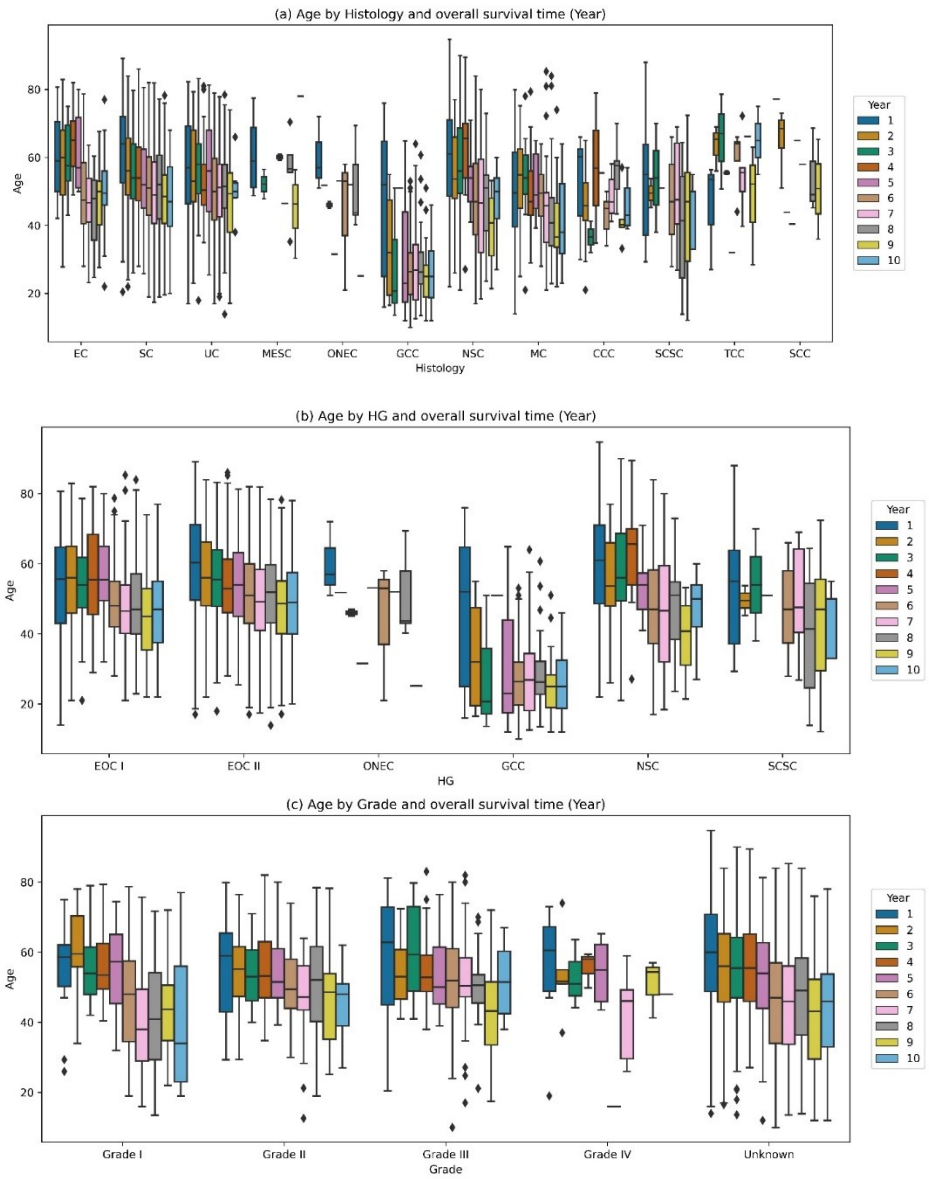


Figure 5. The Box plots depicting the relationship between the continuous variable *Age* and categorical variables *Histology*, *HG* (Histology Groups), and *Grade* with overall survival time (*Year*) as the target. The panels (a), (b), and (c) represent comparisons across different categorical variables, with *Age* plotted on the y-axis and each categorical variable on the x-axis. The plots are color-coded based on survival time groups, and the legends are placed to the right for clarity. These visualizations allow for the assessment of the dispersion of *Age* across different histologic and grade categories, providing insight into potential patterns associated with overall survival.

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Table 3. 5- and 10-year survival of ovarian cancer patients with age mean and numbers of incidence.

Main variables	Sub variables	5 years OS (%)	10 years OS (%)	Age (mean)	N (%)
Histology	CCC	60	57	47.86	56 (2)
	EC	69	54	51.58	154 (6)
	GCC	86	84	29.10	190 (8)
	MC	60	49	47.35	19 (<1)
	MESC	-	63	55.33	205 (8)
	NSC	43	38	53.32	474 (18)
	ONEC	55	-	48.45	18 (<1)
	SC	52	39	52.98	1021 (38)
	SCC	46	-	57.37	15 (<1)
	SCSC	-	78	46.31	63 (3)
	TCC	60	35	55.60	30 (1)
	UC	43	34	53.11	430 (16)
HG	EOC I	63	50	49.69	460 (18)
	EOC II	49	38	53.05	1470 (55)
Grade	Grade I	70	61	47.22	258 (10)
	Grade II	56	42	51.34	264 (10)
	Grade III	53	41	53.09	294 (11)
	Grade IV	30	30	50.76	33 (1)
	Unknown	52	42	50.61	1826 (68)

The table provides information on the 5- and 10-year overall survival rates of patients with OC based on the mean age and the incidence of different subgroups within the variables.

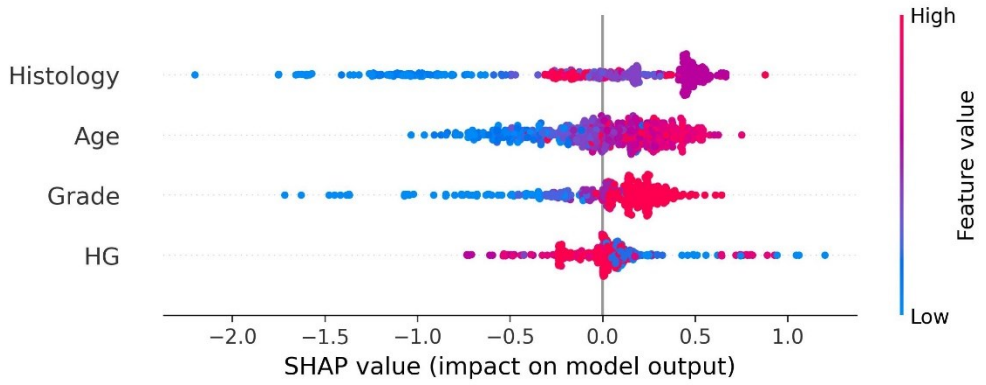


Figure 6. SHAP summary plot illustrating feature importance and impact on model predictions. Each point represents a SHAP value for a given feature in an individual prediction. The horizontal spread of points indicates the range of impact on the prediction, where values further from zero denote stronger effects. The color gradient represents feature values, with higher values shown in pink and lower values in blue. Positive SHAP values indicate a higher predicted risk, while negative values lower the prediction. This visualization highlights the relative contributions of input variables, reinforcing the significance of histology and age in risk assessment.

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4. DISCUSSION

This study aimed to provide a comprehensive analysis and prediction of overall survival rates for OC patients in Iran. The dataset, comprising 7977 patients diagnosed with OC between 2008 and 2015, was obtained from the Ministry of Health and Medical Education of Iran. The Kaplan-Meier analysis revealed 5- and 10-year survival rates of 54% and 42%, respectively. To model survival outcomes, eight DL algorithms were employed, with the Logistic Hazard, DeepHit, and COX-Time models achieving the highest performance as measured by the C-index.

This study predicted overall survival in OC patients, with the Logistic Hazard algorithm demonstrating the highest performance (C-index = 0.69). This finding aligns with a study on cervical cancer, where a DL model outperformed the Cox proportional hazards model in predicting overall survival and progression-free survival (PFS), achieving a higher accuracy as more clinical and laboratory features were incorporated (C-index = 0.795) [18].

Similarly, a DL-based model for hepatocellular carcinoma integrating multi-omics data achieved a comparable C-index of 0.68 across multiple external datasets [19]. Additionally, a machine learning model for epithelial OC that leveraged ultrasound imaging and clinical variables demonstrated high accuracy (AUROC = 0.92) in predicting 12-month PFS [20]. These results suggest that multimodal machine learning approaches combining clinical, imaging, and molecular data may enhance survival predictions.

While our model performed well using structured clinical variables, further improvements could be achieved by expanding feature sets, improving dataset quality, and addressing interpretability challenges.

The five-year survival rates for ovarian cancer vary significantly across countries, reflecting differences in healthcare infrastructure, early detection programs, and treatment accessibility. In our study, the five-year survival rate was 54%, placing it between the lower rates reported in India (23.8% and 22.8%) [21, 22] and the notably higher rate observed in Japan (91.7%) [23].

Comparable survival rates were recorded in South Korea (65.9%) and Singapore (64.7%), both slightly exceeding our findings, while China also demonstrated a modestly higher survival outcome at 63.5% [24]. The exceptionally high survival rate reported in Japan by Higash et al. (91.7%) may be attributed to advanced treatment protocols and early detection strategies [23].

Conversely, India's significantly lower survival rates highlight challenges in timely diagnosis and access to care. Notably, a recent 2021 study from South Korea reported a sharp increase in survival to 83.9%, likely driven by advancements in healthcare technology and accessibility [24, 25]. These disparities underscore the need for country-specific strategies to enhance ovarian cancer prognosis and improve patient outcomes.

Age was identified as the most influential factor affecting patient survival rates. Among histopathological subgroups, GCC had the lowest mean age (29 years) with 5- and 10-year survival rates of 86% and 84%, respectively, while SCC, with the highest mean age (57 years), showed a 5-year survival rate of 46%. For the grade variable, most subgroups had a mean age aligning with the dataset average of 50 years, except for Grade I, where the mean age was 47 years, and survival rates were 70% at 5 years and 61% at 10 years. These findings highlight the interplay between age, histology, and grade in determining survival outcomes.

In Asia, ovarian cancer incidence increased over 40 years while mortality remained steady, indicating improved survival rates. In Europe, survival rates were stable from 2000 to 2004, with modest improvements observed in Denmark, the UK, and Canada, likely reflecting advancements in treatment methods [26].

The mean age of OC in Iran was 50 years, with GCC and SCC subtypes having the lowest and highest mean ages, respectively. In Iran, the SC, NCS, and UC subgroups, with the highest incidence, had a mean age of approximately 53 years [27, 28]. Compared to global averages, the mean age in Iran was lower, aligning with findings in Asia, where OC onset tends to occur earlier than in countries like Germany (66 years) and Romania (57 years) [28].

The study found that the 5-year and 10-year overall survival rates for OC in Iran were 54% and 42%, respectively. A prior national study using statistical methods reported slightly higher rates of 55% and 45%, with differences likely stemming from variations in data cleaning and preprocessing techniques [4]. Among histopathological subtypes, NSC, UC, and SCC had 5-year survival rates below 50%. In the HG variable, EOC II, the most prevalent subgroup, had a mean age of 53 years and 5-year and 10-year survival rates of 49% and 38%, respectively. Consistent with findings from Japan and Australia, CCC and mucinous epithelial cells demonstrated better survival outcomes than serous epithelial cells, while EOC I showed higher survival rates compared to EOC II, despite the latter's higher incidence [29, 30].

Environmental and geographic factors influence the incidence and mortality of OC, with risk factors including lifestyle behaviors, environmental pollutants, hormonal therapies, reproductive history, genetic predisposition, and infections [31]. While tumor type and grade influence survival, the strong impact of ovarian cancer stage underscores the importance of enhancing early detection to improve survival rates [32]. These factors highlight the complex interplay between biological and external contributors to OC development.

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Some studies suggest that chemotherapy regimens such as cisplatin and paclitaxel are most likely responsible for prolonging patient survival [33]. The results show that infertility in women is associated with a 51% increased risk of OC [34, 35]. The Total Fertility Rate (TFR) in Iran fell from 2.05 in 2011 to 2.01 in 2016, coinciding with the increase in the prevalence of OC [4]. This trend can be attributed to the fact that pregnancy has been shown to decrease the frequency of ovulatory cycles and gonadotropin secretion, thereby reducing the risk of OC [26].

The K-Nearest Neighbors imputation algorithm was applied during preprocessing to handle missing data and minimize errors in data allocation. Effective outlier and noise management is crucial for developing reliable models, particularly in health datasets, where unique class data can significantly impact model accuracy and performance [36].

The C-index, barrier, and NBLL scores assessed the generalizability and performance of eight deep learning models for survival prediction. While the C-index is a standard survival metric, machine learning studies also use AUC, accuracy, precision, and sensitivity [37]. Data heterogeneity is crucial for model robustness [38]. This study used internal validation, which, though useful, may be limited by dataset similarity. In contrast, external validation with diverse datasets offers a more robust performance assessment [39].

The superior performance of models like Logistic Hazard (C-index: 0.69) and DeepHit (C-index: 0.68) can be attributed to their ability to capture nonlinear relationships and complex feature interactions. Unlike traditional Cox models, which assume proportional hazards, these models provide greater flexibility in survival prediction.

Discrete-time models generally outperformed continuous-time approaches by effectively handling censored data and estimating event probabilities within time intervals. In contrast, the Cox proportional hazards model (C-index: 0.51) underperformed due to its restrictive assumptions, whereas Cox-Time (C-index: 0.67) showed better performance by allowing time-varying coefficients.

Additionally, regularization techniques such as dropout and batch normalization in deep learning models helped prevent overfitting, further enhancing predictive accuracy. These findings highlight the importance of selecting appropriate survival models that account for data complexity and time-dependent effects.

5. LIMITATIONS

This study has several limitations that warrant consideration for future research. Notably, 67% of the original dataset lacked complete survival outcome labels, primarily due to incomplete follow-up data in the Iranian National Cancer Registry. As a result, only 33% of the dataset was used for training the deep learning model. While statistical comparisons confirmed that the included subset was representative of the broader dataset in terms of demographic and clinical characteristics, this reduced sample size may limit the model's generalizability. Additionally, the dataset contained incomplete clinical and demographic information, including missing details on disease history, cancer stage, genetic profiles, treatment types, medications, and medical imaging, which could further enhance model performance if available. The study also lacked external validation, an essential step to ensure the stability and generalizability of the deep learning models across diverse populations. Future research with more complete datasets and external validation could address these limitations and improve the robustness of survival predictions for ovarian cancer.

6. CONCLUSION

This study applied deep learning techniques to predict overall survival in ovarian cancer patients using a retrospective dataset from the Iranian National Cancer Registry. In spite of the dataset's missing survival outcome labels, we trained models using the 33% of cases that had complete labels. The Logistic Hazard algorithm achieved a C-index of 0.69, demonstrating reliable predictive performance comparable to or better than prior studies with similar data constraints. This result highlights the feasibility of applying deep learning to real-world clinical datasets with significant missing data, a common challenge in retrospective studies. Using SHAP analysis, we identified histology and age as the most influential predictors of survival, with all evaluated features showing statistical significance. Among histopathological subtypes, EOC II exhibited poorer survival outcomes than EOC I, despite its higher incidence, providing valuable insights into prognostic differences that may inform clinical risk stratification.

The observed 5-year and 10-year overall survival rates of 54% and 42%, respectively, are consistent with established benchmarks for ovarian cancer, supporting the validity of our dataset and findings. The study's strength lies in its use of a large, nationally representative dataset and rigorous evaluation of prognostic factors, despite the limitations. Furthermore, the interpretability of deep learning models remains a challenge, though our application of SHAP analysis offers a step toward addressing this issue. Future research should focus on validating these findings with external datasets, incorporating additional clinical variables, and exploring explainable AI methods to enhance model transparency. This study contributes to the growing field of deep learning in oncology by demonstrating its applicability to imperfect datasets and identifying key prognostic factors, laying the groundwork for improved survival prediction and personalized treatment strategies in ovarian cancer.

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Acknowledgment

We thank and appreciate the financial support of Cancer Research Center of Shahid Beheshti University of Medical Sciences.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical statement

All procedures were conducted in accordance with the guidelines provided by the Iran National Committee for Ethics in Biomedical Research. This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.CRC.REC.1401.035). Verbal or written informed consent was provided by all participants prior to their participation.

Informed Consent Statement

Written or verbal consent was obtained from all patients prior to their participation in the study.

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