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SYSTEMATIC REVIEW

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Diagnostic accuracy of artificial intelligence algorithms to predict remove all macroscopic disease and survival rate after complete surgical cytoreduction in patients with ovarian cancer: a systematic review and meta-analysis

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Abstract

Background Complete Cytoreduction (CC) in ovarian cancer (OC) has been associated with better outcomes. Outcomes after CC have a multifactorial and interrelated cause that may not be predictable by conventional statistical methods. Artificial intelligence (AI) may be more accurate in predicting outcomes. This systematic review aimed to determine the accuracy of AI compared to traditional statistics in predicting outcomes after CC in OC.

Methods PubMed, Scopus, Google Scholar, Embase, and Web of Science databases were searched with Mesh terms to find studies that investigated the role of AI in predicting outcomes after CC in EOC from the beginning of 2015 to February 2024. The outcomes included overall survival (OS), removal of all macroscopic disease (R0), length of hospital stay (LOS), and intensive care unit (ICU) admission. This systematic review was conducted based on the PRISMA guidelines. Heterogeneity between studies was evaluated using the I^2 test. Egger's test was used to check publication bias.

Results Ten studies (3460 participants) were included. The pooled estimate of 3 studies showed that the accuracy of AI for predicting OS was (Mean: 69.64%, CI 95%:66.50, 72.78%, I^2:0%). The pooled estimate of 4 studies showed that the accuracy of AI for predicting R0 was (Mean: 80.5%, CI 95%:71.46, 89.6%, I^2:47.9%). The use of AI in predicting outcomes, including ICU admission, urinary tract infection (UTI), and LOS was investigated in one study, and the AUC of AI for predicting all three outcomes was approximately 90%.

Conclusion AI may accurately predict the outcomes after CC in OC patients. Most studies agree that Artificial Neural Networks (ANN) and Machine Learning (ML) models outperform conventional statistics in predicting postoperative outcomes.

Keywords Artificial intelligence, Complete surgical cytoreduction, Ovarian Cancer, Outcomes, Prediction

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Introduction

Ovarian cancer (OC) is the eighth most prevalent and the most lethal gynecological cancer, with the majority presenting with advanced disease [1]. The majority (90%) of ovarian tumors are of epithelial origin and correspondingly cited as epithelial ovarian cancer (EOC), although a small portion originates from germ cells or sex-cord stromal tissues [2]. With an incidence of 3.4% and a mortality of 4.7%, over 300,000 women are stricken, and roughly 152,000 women die of OC each year, displaying the severe threat that this disease poses to the health and survival of women [3]. According to the GLOBOCAN study, there is a planned universal rise of 55% in OC cases and a 67% increase in mortality between 2012 and 2035 [4].

Cytoreductive surgery and platinum-based chemotherapy are the current first-line therapy for OC [5]. In the management of advanced ovarian cancer, two primary approaches are typically employed: primary debulking surgery and interval debulking surgery following chemotherapy. However, findings from the CHROUS trial have demonstrated that the overall survival outcomes associated with these two approaches are comparable [6–8]. As defined in previous studies, optimal cytoreductive surgery to define a minimal residual disease instead of complete resection has shown little association with improved overall survival in the recurrent status [9]. Thus, complete Cytoreduction (CC) is critical, which indicates a lack of macroscopically visible residual tumor cells in the tumor bed after surgical cytoreduction [10].

Also, surgical success rates hinge on the operating surgeons' experience, skill, and philosophical approach [11] For instance, AI can be used to monitor quality improvement and the delivery of modern OC care [12]. Accurate classification between benign and malignant ovarian neoplasms by developing a specific EOC prediction framework for clinical staging, disease burden, and prognosis based on multiple blood biomarkers have been the most critical applications of this technology in OC [13]. As technology advances, AI is poised to play a pivotal role in predicting ovarian cancer debulking outcomes.

AI is a valuable tool for crafting algorithms tailored to text-based inputs. This capability allows for predicting postoperative stay duration based on factors like comorbidities. However, its application in image processing presents challenges. The assessment of complete cytoreduction during primary surgery or interval debulking relies on CT scans or laparoscopic evaluations, demanding extensive computational power for high-resolution image analysis. Moreover, a rapid link to data centers is necessary for efficient image transfer and processing. The current technology limitations will not allow the prediction of debulking with image processing in the immediate future. A convolutional neural network is required to analyze the images and predict disease areas suitable for debulking. Overcoming these technical hurdles is imperative for AI development in this domain.

A comprehensive study on AI evidence for predicting cytoreductive surgery outcomes in OC patients has yet to be conducted. Accordingly, this systematic review aimed to determine the current accuracy of AI compared to traditional statistics in predicting outcomes after CC surgery in OC patients.

Methods

Literature search

In this systematic review, we reviewed all observational and diagnostic accuracy studies that investigated the role of AI in predicting outcomes after CC in OC from the beginning of 2015 to February 2024. This study used the checklist for conducting systematic reviews (PRISMA) [14].

The PICO (population, intervention, comparison, and outcome) format determined the mesh terms to search the datasets. PubMed, Scopus, Google Scholar, Web of Science, and Cochrane Library databases were searched by two researchers. The last search was done on February 10, 2024. The search was conducted using the following mesh terms: ((" Ovarian Cancer" OR " Ovarian Neoplasms "OR" Ovary Neoplasm") and ("Complete Cytoreduction" OR" surgery/Cytoreduction " OR "Debulking") and ("Artificial Intelligence" OR" "Computational Intelligence" OR "Machine Intelligence" OR 'Computer Reasoning" OR "Machine Learning" OR " Artificial Neural Network")).

Inclusion and exclusion criteria

We reviewed all observational and diagnostic accuracy studies that evaluated the role of AI with at least one of its algorithms in predicting CC in OC patients. Studies show that at least one of the AI algorithms, including Artificial Neural Networks (ANN), Machine Learning (ML), k-nearest neighbor (k-NN), extreme gradient, and boosting (XGBoost), was investigated to predict CC. Studies published in a language other than English, review articles, letters to the editor, laboratory or animal studies, and lack of access to the full text were defined as exclusion criteria.

The outcomes included AI's diagnostic accuracy in predicting patients' survival, no macroscopically visible residual disease (R0), length of hospital stay (LOS) [15], and hospitalization in the ICU.

Study selection and data extraction

A checklist was designed to extract data based on the literature review. After the search, Endnote version 20 software was used to clean and remove duplicate studies. Two independent researchers initially screened studies based on title and abstract. In the initial search, 1013 studies were found. Then, 921 (Duplicate articles (n=274), lack of inclusion criteria (n=108), use of AI for other cancers (n=116), lack of relevance to research objectives and questions, review articles, case reports, and non-English (n=288) and other reason (n=135) studies were excluded. The full text of 92 studies was evaluated. Eighty-two articles, including out-of-scope (n=37), lack of access to full text (n=14), and lack of details (n=31)) were excluded. Finally, ten studies were included in this systematic review (Fig. 1).

Extracted data included authors, year, evaluated outcome (survival, R0, metastasis, LOS, total number of patients, mean age, country, study design, the study period, the AI method used, the accuracy of the

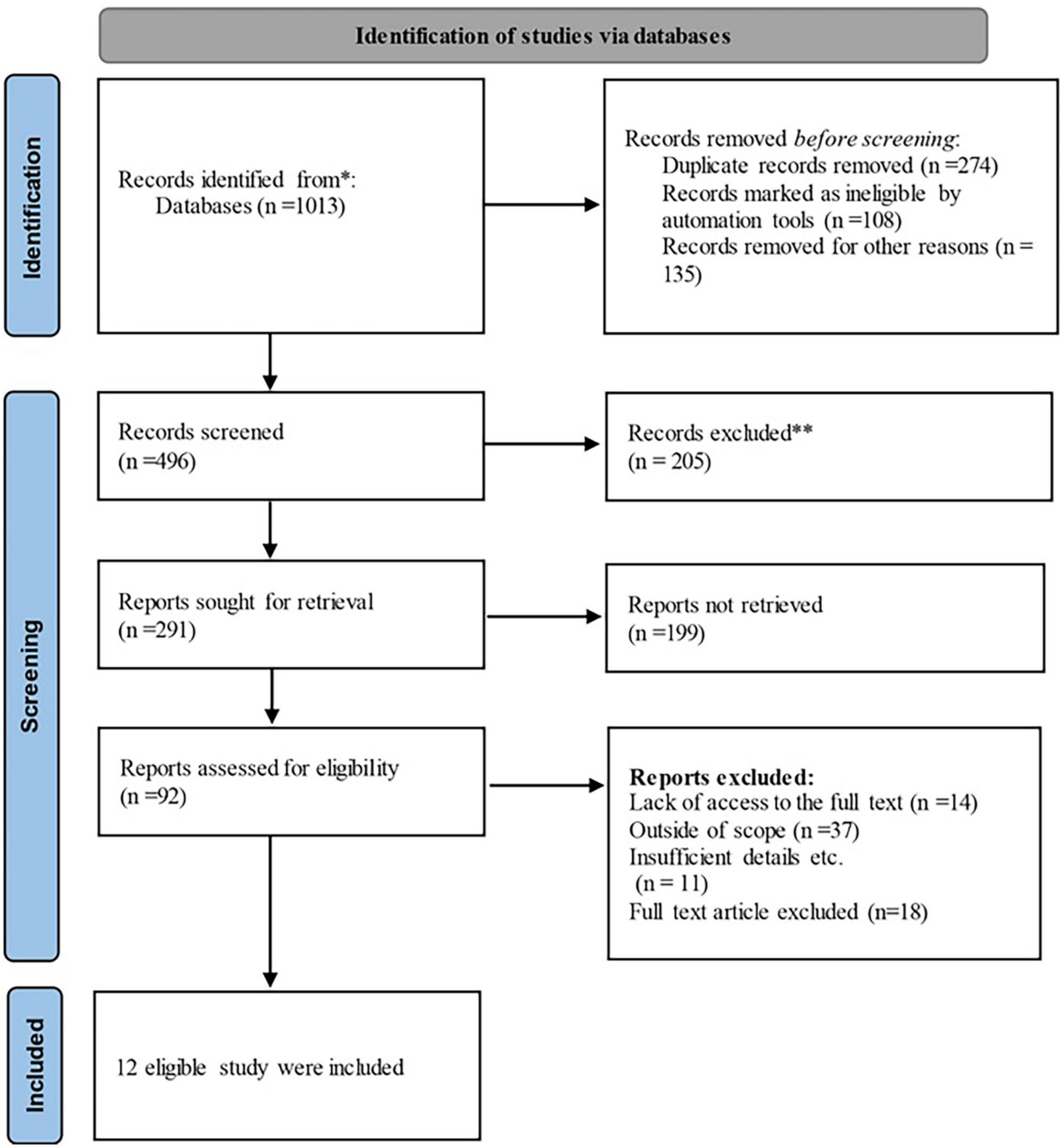

Fig. 1 Flowchart page of studies based on PRISMA 2020

technique, the confidence interval, the area under the curve (AUC), adjusted variables and the type of statistical analysis. Two independent researchers used Excel software to extract data. A third independent researcher resolved any discrepancies between the two researchers.

Quality assessment

We used the Prediction model study Risk Of Bias Assessment Tool PROBAST tool [16], which is a suitable method for assessing the risk of bias in the field of predictive algorithms (AI and ML-based models) [17].

Statistical analyses

The diagnostic accuracy for OS and R0 was reported as a pooled estimate. Pooled AUC estimates were presented with means and 95% confidence intervals (CIs) based on the Mantel-Haenszel random effects model. The I^2 test was used to estimate the heterogeneity between studies and algorithms. Egger's test was used to evaluate the publication bias, and the publication bias results were expressed with funnel plots. Sensitivity analysis was used to assess the individual effect of each study on the overall outcome. Meta-regression was used to control heterogeneity between studies. Due to the absence of publication bias in different studies, there was no need to use trim and fill analysis to resolve publication bias. $P<0.05$ was considered significant. Stata 17 software was used for analysis.

Results

This systematic review included ten studies (2,842 patients) [15, 18–26]. The mean age of the patients in this study was 61.4 ± 4.75 years. Based on the study evaluation checklist, most studies were of sound and moderate quality. Most of the studies were conducted in developed countries, including the USA. Seven studies reported data on the use of AI in advanced ovarian cancers. The application of AI to predict the outcomes of CC, including OS, R0, ideal LOS, ICU admission, and urinary tract infection after CC surgery in OC patients, was investigated. Different AI methods were used in individual studies. ML method was used in five studies. Three studies were conducted based on ANN. The characteristics of the studies included in this systematic review are reported in Table 1.

Outcomes

Overall survival

Three studies provided quantitative data for predicting survival [18, 20, 25]. The pooled estimation of the results showed that AI's prediction accuracy for overall survival was (Mean: 69.64%, CI 95%: 66.5, 71.92%) (Fig. 2). Based on Egger's test results, no evidence of publication bias was reported in the studies' results (Egger's test t = 1.2, 95% CI: – 1.11, 2.04, P: 0.087).

Remove all macroscopic disease (R0)

The pooled estimate of four studies [18, 19, 23, 26] showed that AI's accuracy for predicting R0 was 80.5% (Fig. 3). The study results did not report evidence of publication bias based on Egger's test (Egger's test t = -4.59, 95% CI: -14.6, 6.1, P: 0.58). The publication distribution of the studies for OS and R0 outcomes is shown in Fig. 4.

Other outcomes

In a study, Laios et al. [21] estimated the AUC of CCU prediction by the ML method in patients undergoing CC to be 95%. (93–97%) A Laios et al., [23] Showed the AUC of AI for predicting the LOS using the ANN method in patients undergoing CC was 93% (88–98%). J Ai et al., [24] evaluated the use of AI in predicting UTI after CC, based on the results of this study, the AUC of AI for predicting UTI was 86% (78 to 84%). Age, BMI, catheter, catheter intubation times, blood loss, diabetes, and hypoproteinaemia were the most important predictive factors.

Discussion

This systematic review and meta-analysis by examining ten retrospective cohort studies, including 2,842 patients, showed that the use of AI in treating OC patients and predicting the outcomes of its various treatment methods, especially CC, has increased significantly in the last decade. Almost all studies showed that AI has the potential to predict CC outcomes in OC patients, which conventional statistical methods and models cannot predict. The accuracy of AI for OS prediction based on the pooled estimate of five studies was approximately 70%, regardless of the method used for modeling. ANN and ML had the highest accuracy in predicting OS in OC patients. Also, the accuracy rate of AI for predicting R0 was almost 80%, which is much higher than other conventional forecasting models. The prediction accuracy of AI methods differed depending on the quantity and quality of the variables entered in the models. S Piedimonte et al. [26] showed that the AI based on the ML algorithm in the test model showed an AUC of 84% for predicting the prognosis of CC in patients with AOC selected for PCS, and this model may help in decision-making.

Compared to other methods and algorithms, ML and ANN models have the highest application in predicting the outcomes of CC and had a high accuracy of 70% in almost all studies. The use of AI to predict UTI after CC, LOS, and ICU admission, which were each investigated in one study, were 95%, 93%, and 86%, respectively, which shows that AI for predicting critical outcomes also has high accuracy. Almost all studies showed that age, BMI, Charlson Comorbidity Index, timing of surgery,

Table 1 Characteristics of patients in the studies and the quality of the included studies

Author (Year)	AI method	Country	Sample size	Mean Age	Outcome investigated	Histology	Predictors Outcomes	Design	Summarize key findings	Quality of studies
A Enshaei (2015) [18]	ANN	Northern	190	NA	OS/R0	ovarian serous	age, stage, grade, histologic type, and preoperative Ca125	Different ML techniques were compared with the data set by examining the models to discover the optimal stop-training point.	AI systems may play an important role in providing predictive data for the treatment and diagnosis of patients.	Low
G Bogani (2018) [19]	ANN	Italy	194	61.6	R0	secondary cytoreductive surgery (SCS)	NA	ANN analysis was used to weigh the importance of related variables, thus predicting each variable's impact on achieving CC and survival outcomes.	AI can help in the diagnosis, treatment, and decision-making processes needed.	Unclear
A Laios (2020) [20]	k-NN	UK	96	64.4	OS	serous ovarian	Age, BMI, Charlson Comorbidity Index, the timing of surgery, surgical complexity, and disease score.	K-NN models were used to classify R0 versus non-R0 patients.	The k-NN algorithm was a promising tool for predicting R0 removal.	Low
A Laios (2021) [21]	ML	UK	291	64	CCU Admission	advanced stage high-grade serous ovarian cancer (HGSOC)	pre-treatment albumin, surgical complexity score, estimated blood loss, operative time, and bowel resection with stoma	All patient data were used for ANN models in regression mode, and sample selection was varied using the Kennard-Stine method, with 60% for training and 40% for testing.	Predictive ML algorithms may improve the quality of modern care by improving diagnostic prediction accuracy.	Low

Table 1 (continued)

Author (Year)	AI method	Country	Sample size	Mean Age	Outcome investigated	Histology	Predictors Outcomes	Design	Summarize key findings	Quality of studies
A Laios (2022) [23]	XGBoost	UK	571	63.5	R0	Advanced-Stage Epithelial Ovarian	NA	A new AI-based predictive LOS score was developed for patients with HGSOC after CC. ANN was combined with ordinary logistic regression to predict continuous and binary LOS outcomes for HGSOC patients.	AI can help to predict LOS in EOC patients in the advanced stage after CC.	Low
J Ai (2022) [24]	ML	China	674	63.5	UTI	ovarian cancer after cytoreductive surgery	age, BMI, catheter, catheter intubation times, blood loss, diabetes and hypoproteinaemia	With the help of ML, five models using two-stage estimation methods of predictor variables were used to predict UTI.	The prediction model based on ML developed using random forest classification can help in treatment decisions, prevent postoperative UTIs, and improve clinical outcomes.	Low
Y Feng (2022) [25]	ML	Netherlands	98	54.2	OS	ovarian serous	CA125 level, white blood cell (WBC) count, presence of lymph node metastasis (LNM), MO count, the MO/LY ratio, differentiation status, stage, LY%, ascites cytology, and age.	A decision tree algorithm based on ML was used to predict survival.	AI can accurately predict the survival of patients with serous ovarian cancer.	Low
A Laios (2022) [23]	ANN	UK	201	64	LOS	advanced stage HGSOC	NA	ML and deep learning methods using ANN combined with ordinary logistic regression were used to predict continuous and binary LOS outcomes for HGSOC patients.	Quantitative and qualitative AI models can be highly accurate in predicting LOS in advanced-stage EOC patients after CC.	Low

Table 1 (continued)

Author (Year)	AI method	Country	Sample size	Mean Age	Outcome investigated	Histology	Predictors Outcomes	Design	Summarize key findings	Quality of studies
A Laios (2023) [15]	XGBoost	UK	576	NA	R0	advanced-stage EOC	NA	An explainable AI framework was used to explain trait effects associated with CC.	AI had adequate precision to explain the effects of the characteristics associated with CC.	Low
S Piedimonte (2023) [26]	ML	USA	151	58	R0	advanced ovarian cancer (AOC)	CA125, albumin, diaphragmatic disease, age, and ascites	A random forest model was used to predict the optimal CC (< 1 cm) and no gross residual (RD = 0).	The ML algorithm had high accuracy for predicting the optimal cell reduction in patients with AOC selected for PCS, and this method can help in decision-making.	High

K-NN: k-nearest neighbor; XGBoost: extreme gradient boosting, UTI: Urinary tract infection

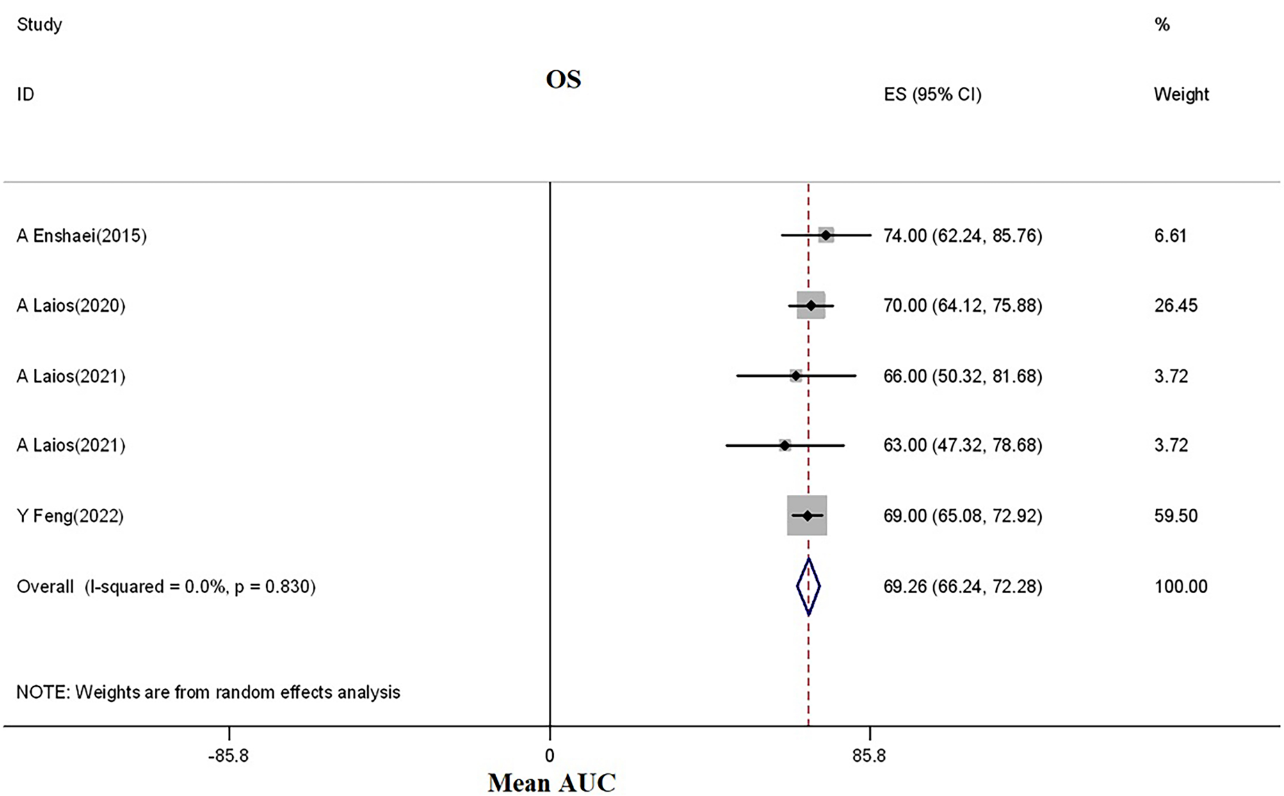

Fig. 2 Forest plot of the AUC of AI to predict OS

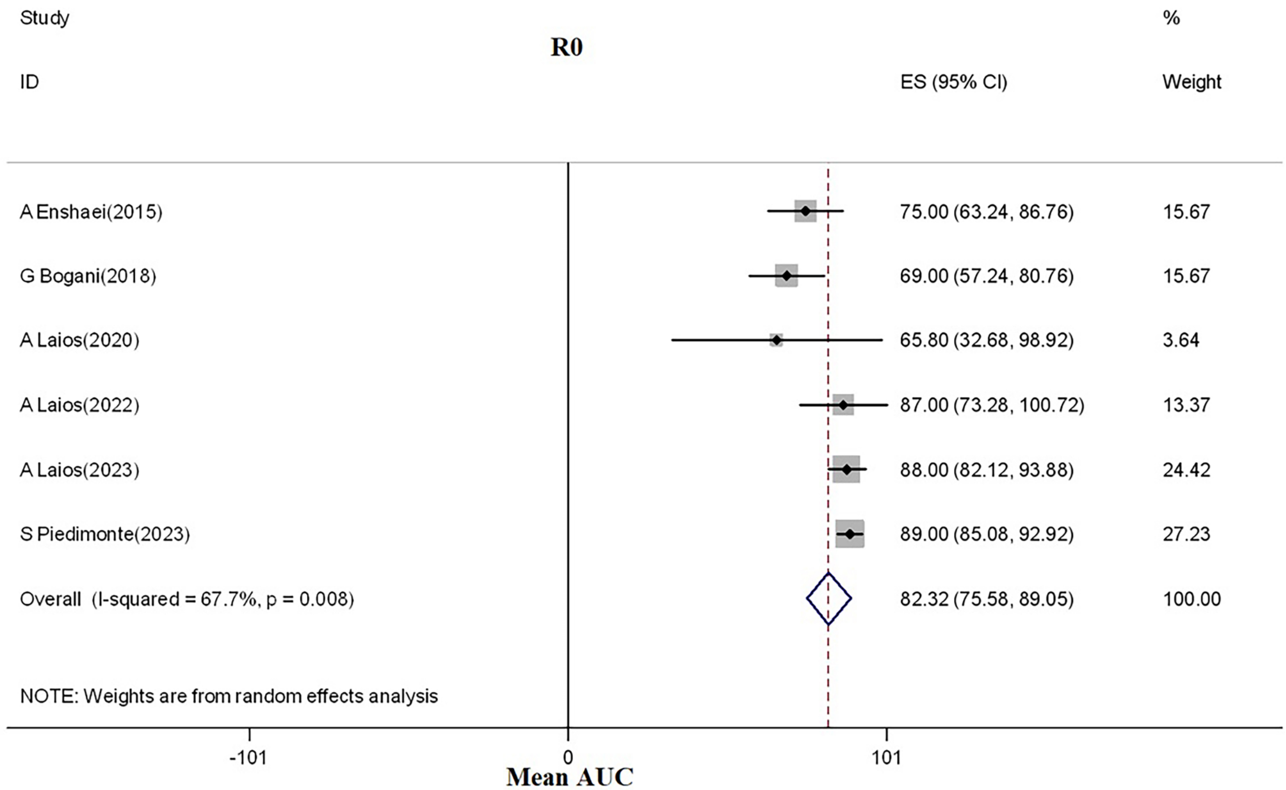

Fig. 3 Forest plot of the AUC of AI to predict R0

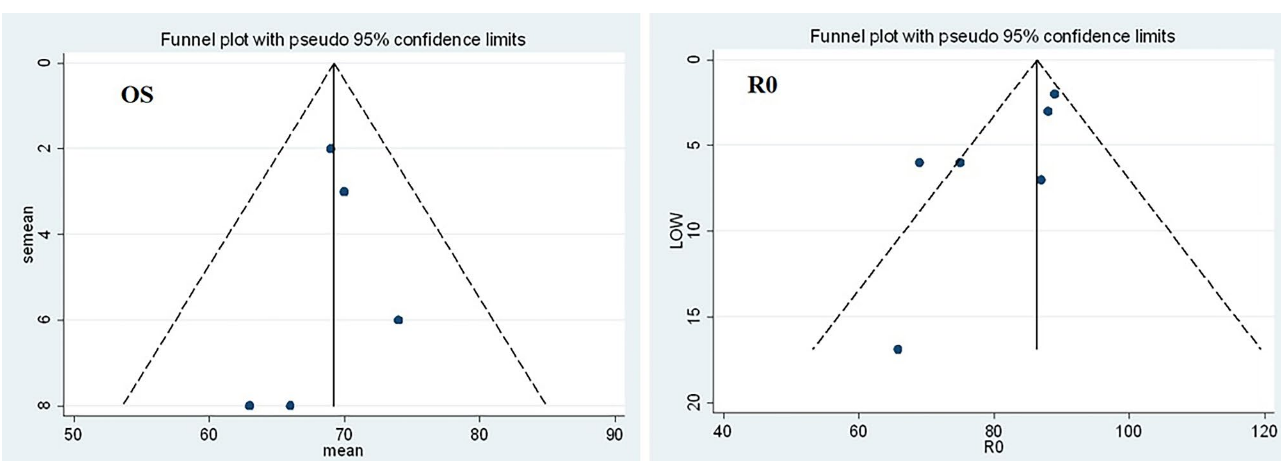

Fig. 4 Funnel plot of publication bias of studies-based outcomes

preoperative Ca125, and disease score were among the most important factors predicting all five outcomes of OS, R0, UTI, ICU, and LOS.

Heterogeneity was 0% for predicted OS and 47.9% for R0 resection. Heterogeneity between studies for RO in studies can be explained by differences in sample size, number of variables examined, patient characteristics, and follow-up patterns of the studies included in this meta-analysis.

We utilized a robust and theoretically sound explainable AI method to assess the significance of each feature in a patient's prognosis, delivering explanations in real time. This is crucial as it offers detailed and valuable insights customized to the patient's specific clinical profile. Proper visualization of these explanations could be presented in a concise visual format for gynecological and obstetric oncologists. This study establishes the foundation for an extensive clinical audit aimed at assessing OC surgeries across the National Health Service

(NHS). Predicting OC is one of the most important criteria for predicting treatment outcomes and providing more information to physicians in OC surgeries. Based on the literature review, conventional statistical methods are less accurate than AI methods. Anshai et al., [18] showed that AI methods have higher accuracy than conventional statistical methods, such as regression models, for predicting OS and R0.

We assessed studies with the PROBAST tool, which is more comprehensive than other assessment tools for predicting AI models and assesses studies in four key areas—participants, predictors, outcome, and analysis. It also assesses the applicability of machine learning models in real-world, real-time clinical settings. As a result, implementing the PROBAST tool not only increases the accuracy of RoB assessment, but also directly addresses reviewers' concerns about the interpretability and explainability of AI models [17]. The superiority of PROBAST over NOS for ML-based models has been reported in recent studies [27, 28].

In 2023, G Parpinel et al. [29] evaluated the accuracy of AI for CC Prediction in epithelial ovarian cancer in 6 studies (1899 patients) in a narrative review. Their study examined quantitative survival data in only two studies, presenting the results qualitatively. They showed that AI had adequate accuracy to predict OS. In our study, we reported an accuracy for predicting survival based on the data of 3 studies and as a pooled estimate, which was nearly 70%. We also estimated the predictive accuracy of AI for R0 based on the findings of 4 studies, which showed a high accuracy of 80% of AI for predicting R0. In their study, they reported the accuracy of AI for predicting R0 between 65 and 77% based on the data of two studies. They showed that the use of AI compared to the data of logistic regression models was more accurate for predicting the outcomes of CC, which was in line with the results of our study. In a systematic review, J Breen et al. [30] 2023, by evaluating the role of AI in the histopathology of ovarian cancer, showed that AI is more accurate than conventional models for predicting diagnostic or prognostic models in the histopathology of ovarian cancer. However, the results had high heterogeneity and should be interpreted with caution. In our study, most studies were of high quality, and the heterogeneity rate was low.

In a 2022 systematic review, WT Stam et al. [31], evaluated the role of AI in predicting surgical complications in patients undergoing major abdominal surgery. They showed that AI algorithms can accurately predict postoperative complications, which confirmed the results of our study. Despite the high accuracy of these algorithms, they reported that the algorithms should be tested and validated internally and externally.

The use of AI methods in predicting clinical outcomes, especially cancers, is not without limitations. Accurately estimating outcomes with AI methods requires a larger number of variables and more stringent criteria for diseases, which is one of the most important challenges in using these methods and constitutes an interesting prospect for the application of AI.

Many authors have stated that internal and external validation of machine learning models are necessary preconditions in addition to managing data imbalance. External validation is crucial to ensure the stability of the machine learning model by assessing its performance on unseen data. Only after external validation can we determine the generalizability and, hence, its applicability in clinical practice. However, creating a test set for external validation may reduce the training data, leading to the loss of important trends that could increase errors in the model. Grass et al. [32] suggested that a machine-learning model should be developed using data from individual institutions for optimal predictive performance. However, assessing the model's performance using an external dataset or a new cohort is recommended to enhance its generalizability. This approach provides greater confidence in the model's ability to perform well on data not used for model training, as these data were collected and recorded by different researchers and may have different characteristics compared to the training data.

Optimizing data sets is crucial when developing AI methods. Medical research frequently encounters imbalanced data due to the rare occurrence of clinical endpoints such as mortality, OS, and R0. To avoid having a training set that contains no events, imbalanced data must be addressed during model training. A model trained on imbalanced event distribution will result in a less useful or unusable prediction model because it must be adequately trained or overstrained to predict an event. AI-based predictive models can significantly change and improve postoperative outcomes if the previously described requirements are carefully implemented in daily clinical practice.

The initial studies included in this meta-analysis may have been conducted on specific populations with specific characteristics that may have amplified the role of selection bias. Publication bias in the studies was assessed using the Egger test, and publication bias did not significantly affect the results. However, several residual confounders that may not have been estimated in the initial studies could affect the results. Evaluating the effect of using AI methods on the prediction of clinical outcomes by designing prospective studies and by including a large number of variables that affect the final results of the study can help control biases and confounders for more accurate estimates of the results.

Strengths and weaknesses

Our study had limitations that need to be mentioned. The heterogeneity of the algorithms used in the included studies was the most important limitation of our systematic review and meta-analysis. The strength of this study is that the literature review on the current evidence for the use of AI in CC surgery in OC patients is properly and thoroughly conducted and is the first of its kind. As a result, all available information and outcomes after CC in OC patients were included in this systematic review and meta-analysis. Comparability of studies was low due to high variability in outcomes. Therefore, it is impossible to conclude which algorithm and model are superior in predicting outcomes after CC in OC patients.

Implications for practice and Future Research

Different studies have reported varied algorithm performance levels. Despite this, most authors agree that ANN and ML models outperform conventional statistics in predicting postoperative outcomes. The clinical implications of AI's ability to predict postoperative outcomes are significant. However, healthcare providers must be able to trust the predictions made by AI and use their experience to make clinical decisions based on their outcomes. With this prerequisite fulfilled, AI's potential to contribute to the shift toward personalized medicine and its predictive value will continue to be realized.

Conclusion

Our meta-analysis showed that AI may accurately predict the outcomes after CC in OC patients. AI has demonstrated better predictive accuracy than conventional algorithms because it can handle more data and more complex interactions.

Abbreviations

CC	Complete Cytoreduction
OC	Ovarian cancer
AI	Artificial intelligence
OS	Overall survival
R0	Remove all macroscopic disease
ICU	Intensive care unit
ANN	Artificial Neural Networks
ML	Machine Learning
k-NN	k-nearest neighbor
XGBoost	extreme gradient, and boosting
AUC	Area under the curve
CI	Confidence interval

Supplementary Information

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Supplementary Material 1

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Author contributions

Somayyeh Noei Teymoordash: ConceptualizationHoda Zendehdel: Drafting the manuscript and data collectionAli Reza Norouzi: Data collectionMahdis Kashian: Statistical analysis.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Dual publication

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Third party material

None.

Competing interests

The authors declare no competing interests.

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