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A review on endometrial cancer; artificial intelligence, imaging modalities

Una revisión sobre el cáncer de endometrio; inteligencia artificial, modalidades de imagen

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Abstract

Endometrial cancer is one of the most common cancers among women especially in urban areas. The appearance of symptoms such as abnormal uterine bleeding or infertility on clinical examination increases the risk of endometrial lesion. Vaginal ultrasound and diagnostic hysteroscopy are common gynecological examinations for endometrial lesions. Endometrial cancer is often diagnosed in the early stages, in which case surgical removal of the uterus often cures endometrial cancer. However, screening and treatment programs are important in the timely diagnosis and treatment of this disease. Due to the importance of the topic, the present study was conducted to investigate the prevalence of this disease, the relationship between artificial intelligence as well as various imaging methods and the diagnosis of endometrial cancer.

Key words: Artificial intelligence, endometrial cancer, imaging modalities.

Resumen

El cáncer de endometrio es uno de los cánceres más comunes entre las mujeres, especialmente en las zonas urbanas. La aparición de síntomas como sangrado uterino anormal o infertilidad en el examen clínico aumenta el riesgo de lesión endometrial. La ecografía vaginal y la histeroscopia diagnóstica son exámenes ginecológicos comunes para detectar lesiones endometriales. El cáncer de endometrio a menudo se diagnostica en las primeras etapas, en cuyo caso la extirpación quirúrgica del útero a menudo cura el cáncer de endometrio. Sin embargo, los programas de detección y tratamiento son importantes en el diagnóstico y tratamiento oportuno de esta enfermedad. Debido a la importancia del tema, el presente estudio se realizó para investigar la prevalencia de esta enfermedad, la relación entre la inteligencia artificial, así como diversos métodos de imagen y el diagnóstico de cáncer de endometrio.

Palabras clave: Inteligencia artificial, cáncer de endometrio, modalidades de imagen.

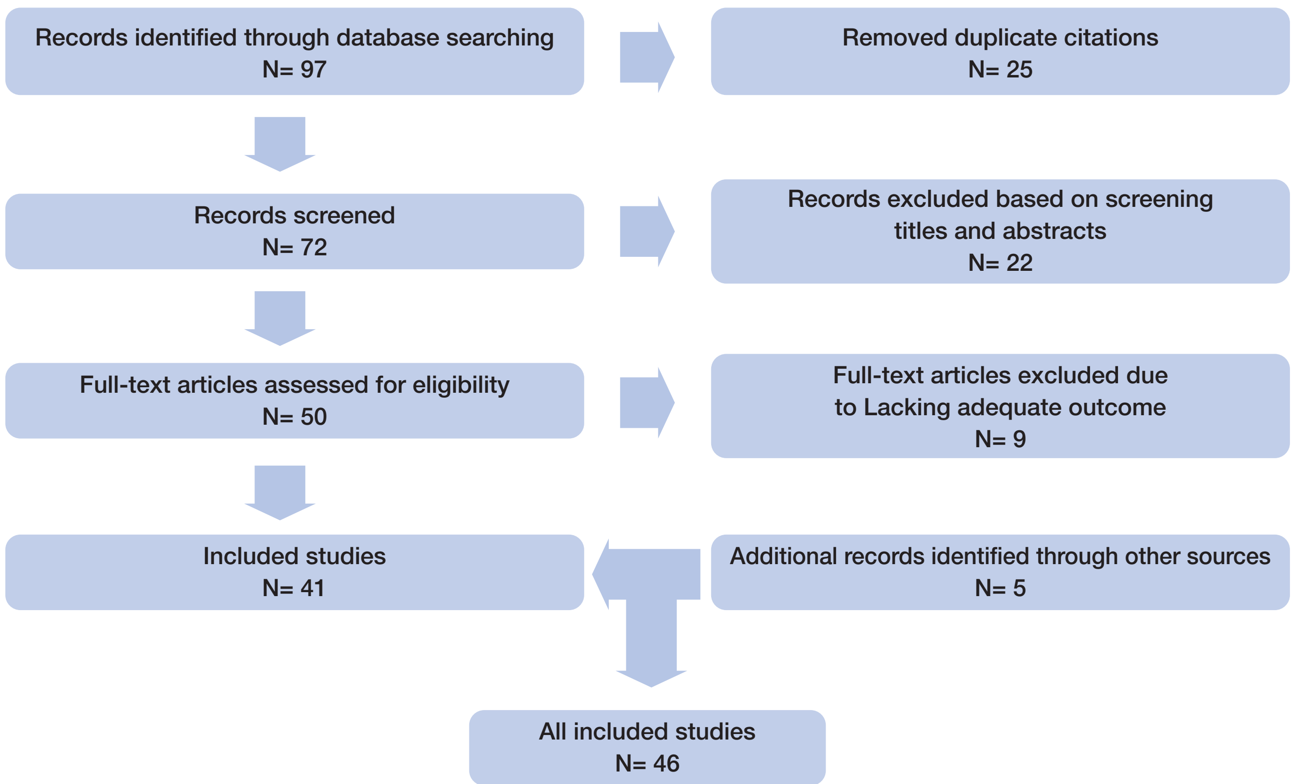
Introduction

Endometrial cancer (EC) is the fourth most common cancer among women, and its prevalence has increased steadily, especially in urban areas, due to the increase in obesity (BMI > 30) and longevity[1,2]. EC is the most common genital cancer, with about 320,000 newly diagnosed cases reported worldwide each year[3]. A total of 61,880 new cases and 12,160 EC-related deaths were estimated in the United States in 2019[4]. In general, the appearance of symptoms such as abnormal uterine bleeding or infertility on clinical examination increases the risk of endometrial lesion[5]. Vaginal ultrasound and diagnostic hysteroscopy are common gynecological examinations for endometrial lesions[6]. Due to abnormal vaginal bleeding, endometrial cancer is often diagnosed in the early stages, in which case surgical removal of the uterus often cures endometrial cancer[7]. Although uterine cancer is highly preventable, it is still one of the most common causes of cancer death in women of developing countries, therefore screening and treatment programs are important in the early diagnosis and treatment of this disease. Nowadays, the use of artificial intelligence technology will be beneficial about endometrial cancer. However there have not been many publications about artificial intelligence applications in endometrial cancers. In the present paper we summarized the characteristics of studies on the use of artificial intelligence, imaging methods and clinical factors for the diagnosis of endometrial cancer.

Literature search

We conducted a comprehensive review of the English-language literature involved endometrial cancer. The electronic databases MEDLINE, PUBMED, and EMBASE were searched on July 2021 for reporting the outcomes of endometrial cancer. Reference lists of published papers were then also hand-searched in an attempt to identify further reports. The following key words were used: endometrial cancer; artificial intelligence; deep learning; imaging modalities. The search terms were then entered onto Google Scholar, to ensure that articles were not missed. Papers were excluded if they were case reports or had a patient cohort, were not written in English, lacked documentation, non-human studies, narrative reviews, studies without clinical outcomes data, systematic reviews that did not pool data or perform a meta-analysis, and technique articles without outcomes. We then obtained full manuscripts for those studies that met the inclusion criteria. Search algorithm of articles included in the literature review is presented in **figure 1**.

Figure 1: PRISMA flow diagram.



Artificial intelligence (AI) features

Radiologists use artificial intelligence (AI) to read medical images for different diseases[8]. Artificial intelligence includes a set of algorithms, mathematical functions, interconnected practical approaches, and areas of mathematical and statistical overlap that are very suitable for radiology because the pixel values of the MRI image are measurable[9]. Although literature on artificial intelligence assistance in the diagnosis of endometrial cancer focuses on the function of "postoperative" diagnosis made by convolutional neural network-based classification[10], however research that examines the "preoperative" MRI stage, the function of interpreting AI in endometrial cancer are limited. Although current AI technology may not be able to replace the expertise and experience of physicians, it can be used as an auxiliary tool[11]. Due to the probability of human active errors and passive errors, the use of AI technology will be beneficial about endometrial cancer. There have not been many publications about AI applications in endometrial cancers. The research of Dong et al.[11] was the first attempt to use AI technology in order to evaluate the invasion depth of myometrium in early stage of endometrial cancers. However, creating a deep learning model is necessary to increase the precision. Generally, artificial intelligence as an appropriate option for preoperative assessment has the ability to help radiologists.

Deep learning is a discipline that has recently played an important role in areas such as computer vision and speech recognition. Deep learning as an important branch of artificial intelligence made outstanding contributions in the clinical prediction models and radiomics[12]. Based on the review of literature, artificial intelligence technologies have significant clinical applications. Each technology has a different role in predicting and detecting clinical outcomes. Zhang et al.[13] conducted a study, in order to create a convolutional neural network model that can automatically classify endometrial lesions using hysteroscopic images as input. After the images were preprocessed, a training set of 6478 images was input into a tuned VGGNet-16 model; and 250 images were used as the test set to evaluate the model's performance. They compared the model's results with the diagnosis of gynecologists and concluded that the VGGNet-16 model performs well in classifying endometrial lesions from hysteroscopic images and can provide objective diagnostic evidence for hysteroscopists. Chen et al.[14] used the deep learning model for detecting myometrial invasion depth in endometrial cancer and compare with radiologists for evaluating clinical application. In their study two stages CNN based deep learning method - trained with YOLOv3 for detection then used Resnet for classification. They concluded that diagnosis and classification of myometrial invasion depth by radiologists improved with deep learning method for lesions >2cm, radiologists better accuracy for lesions <2cm and false positive error most common for both radiologists and computer.

Imaging modalities

Magnetic resonance imaging (MRI) is widely used to determine and classify female malignancies[15]. Sensitivity and specificity related to the evaluation of the myometrial invasion depth in MRI reported varied (sensitivity of 42 -100 and specificity of 85-93) in various studies[14]. The accurate pre-operative assessment of the depth of myometrial invasion depends on MRI, especially T2-weighted imaging (T2WI) and contrast-enhanced T1-weighted imaging[16]. Some findings suggested that diffusion-weighted imaging (DWI) may have good diagnostic accuracy for assessing myometrial invasion[17]. However, in pre-operative MR examination the uterine cavity is often filled with polypoid tumors and tumors located in uterine cornu may lead to incorrect evaluations on myometrial invasion[18]. Han et al.[19] by evaluate whether whole-uterine MRI radiomic features can predict myometrial invasion depth in endometrial cancer (EC), reported that whole-uterine MRI radiomic features based on sagittal T2WI and axial DWI show potential in predicting myometrial invasion in endometrial cancer.

Ueno et al.[20] in a study aimed at building diagnostic radiomic model and evaluate its accuaracy for assessment of deep myometrial invasion, lymphovascular space invasion, histologic high-grade endometrial cancer, concluded that diagnostic accuracy of the random forest model was 81%, 76.6% and 78.1% to predict deep myometrial invasion, lymphovascular space involvement, and high-grade tumors, respectively, as well as random forest model performance analogous to diagnosis by three radiologists. Luo et al.[21] also reported that the radiomic-based machine-learning model using a nomogram algorithm achieved high diagnostic performance for predicting lymphovascular space invasion of endometrial carcinoma preoperatively, which could enhance risk stratification and provide support for therapeutic decision-making. Performance evaluation of MRI based radiomics model for detection of deep myometrial invasion in endometrial cancer by Stanzione et al.[22] showed that radiologist diagnostic accuracy improved with the aid of machine learning compared to without, however not statistically significant and model aided radiologists in diagnosing deep myometrial invasion on MR T2w images. Yan et al.[23] reported that the MRI-based radiomics model could be used to assess the status of pelvic lymph node and help radiologists improve their performance in predicting pelvic lymph node metastasis in endometrial carcinoma. Yan et al.[24] also showed that the radiomics nomogram achieved the highest diagnostic performance compared with the radiomics signature and the clinical parameters models. Bereby-Kahane et al.[25] reported that there was no association between apparent diffusion coefficient and high grade or lymphovascular space invasion.

Clinical features and sample sizes

This section of the present paper summarizes information on clinical factors and sample sizes used in studies. The study of Yan et al.[23] was a multi-center study on 622 endometrial cancer patients (age 56.6±8.8 years; range 27-85 years), which 358 features extracted and 37 features used to build the model. Stanzione et al.[22] conducted a single center study by analyzing 54 patients that preprocessed images randomly split to training and test sets. Bereby-Kahane et al.[25] also performed a single center study on 73 patients to evaluate the capabilities of two-dimensional MRI-based texture analysis features, tumor volume, tumor short axis and apparent diffusion coefficient in predicting histopathological high-grade and lymphovascular space invasion in endometrial adenocarcinoma. The sample size of a study by Xu et al.[26] as the first subgroup analysis on different sized lymph nodes with preoperative nomogram study in EC (benign vs. malignant) was 200 patients. Fasmer et al.[27] and Chen et al.[28] enrolled 138 and 102 patients, respectively, in their studies. A total of 163, 78 and 115 patients were analyzed in the studies by Han et al.[29], Gillen et al.[30] and De Bernardi et al.[31], respectively. Summary of studies and reviews conducted on endometrial cancer is presented in **table I.**

Conflict of Interests

The authors have no conflict of interest.

Table I: Characteristics of studies conducted on endometrial cancer.

Author (s)- Ref.	Characteristics: AI method Imaging modality Cohort size Center Classification task	Objective	Year	Conclusions
Yan, et al. (23)	Deep learning Preop MRI 622 patients Multi center Positive vs negative lymph nodes	Build MRI radiomic model and assess performance compared to radiologist to diagnose PLNM also, evaluate correlation with immunohistochemical indices	2021	glcm_Correlation feature from T2WI best for differentiating positive vs negative PLNM AUC, CDC, MRI, IDI measures showed higher diagnostic performance and net clinical benefits with radiomics aid than radiologists alone
Jacob et al. (32)	Machine learning MRI 338 patients Single center N/A	Build RPI model for survival prediction and assess association with gene expression profiles.	2021	High RPI associated with advanced FIGO, deep myometrial invasion, LN metastasis and poorer 5 year survival RPI not associated with age, histological subtype, grade. High RPI associated with 46 genes – mainly COMP and DMBT1, with poorer disease survival Linking radiomic and transcriptomic tumor profiles potential for more tailored and targeted treatment strategies in EC pts
Yan et al. (24)	Classical machine learning MRI 717 patients Multicenter study High risk vs low risk EC	Radiomics nomogram developed with MRI-based radiomic feature selection and clinical parameters	2020	11-15 per 100 patients were found to have better surgical planning with radiomics nomogram model compared to actual surgical procedure the radiomics nomogram achieved the highest diagnostic performance compared with the radiomics signature and the clinical parameters models
Stanzione et al. (22)	Classical machine learning MRI 54 patients Single center DMI + vs -	Performance evaluation of MRI based radiomics model for detection of Deep Myometrial Invasion in EC	2021	Radiologist diagnostic accuracy improved with the aid of ML compared to without, however not statistically significant Model aided radiologists in diagnosing DMI on MR T2w images
Bereby-Kahane et al. (25)	Classical ML 2D MRI 73 patients Single Center High grade vs low grade and LVSI +/-	Evaluate MRI based texture features, tumor volume and short axis and ADC for prediction of high tumor grade and LVSI in endo adenocarcinoma	2020	Tumor vol >14.3 cm^3 and SA >20 mm : High vs low grade Tumor vol > 26.3 cm^3 and SA > 26 mm : LVSI +/- association between ADC and high grade or LVSI SA >20 mm: best predictor
Xu et al. (26)	Classical machine learning? MRI 137 patients single center study NA	Build diagnostic radiomic model and evaluate its accuaracy for assessment of deep myometrial invasion, lymphovascular space invasion, histologic high-grade endometrial cancer	2017	Diagnostic accuracy of the RF model to predict DMI was 81%, LVSI 76.6% and high-grade tumors 78.1% model performance analogous to diagnosis by three radiologists
Fasmer et al. (27)	Classical machine learning MRI 138 patients Pathology confirmed Single center study Outcome of interest acc to set cut-off.	To develop MRI-based whole-volume tumor radiomic signatures for prediction of aggressive EC disease	2021	MRI-based whole-tumor radiomic signatures yield medium-to-high diagnostic performance for predicting aggressive EC. The signatures may aid in preoperative risk assessment and guide personalized treatment strategies in EC.

Author (s)- Ref.	Characteristics: AI method Imaging modality Cohort size Center Classification task	Objective	Year	Conclusions
Chen et al. (28)	Classical machine learning MRI 102 patients Pathology confirmed Single center study Low risk vs intermediate to high risk	to establish a model based on magnetic resonance imaging (MRI) and clinical factors for risk classification of Preoperative EC	2021	MRI-based radiomic model has great potential in prediction of low-risk ECs. the combined model had a robust predictive value for patients of low risk or intermediate-high risk EC The nomogram based on this model a noninvasive and applicable tool for the clinical diagnosis and optimal decision-making of EC
Luo et al. (21)	Classical machine learning Pre-operative MRI 144 PATIENTS Pathology confirmed Single center study Prediction of Lymphovascular space invasion	To develop a multiparametric MRI-based radiomics nomogram for predicting LVSI in EMC and provide decision-making support to clinicians.	2020	The radiomic-based machine-learning model using a nomogram algorithm achieved high diagnostic performance for predicting LVSI of EMC preoperatively, which could enhance risk stratification and provide support for therapeutic decision-making.
Gillen et al. (30)	Deep learning CT 78 patients multicenter study Treatment survival with Bevacizumab	To examine associations of body mass index subcutaneous fat area and density visceral fat area and density and total psoas area to outcomes among patients receiving chemotherapy with or without bevacizumab for advanced or recurrent endometrial cancer (EC).	2019	Obesity has been associated with increased levels of vascular endothelial growth factor (VEGF), the main target for bevacizumab therapy. Imaging measurements of VFA may provide prognostic information for patients with EC but no adiposity marker was predictive of improved response to bevacizumab
Han et al. (29)	Classical ML Preop T2WI/DWI MRI 163 pts Center Classification task	Assess whole uterine MRI based radiomic model in EC pts for detection predicting depth of myometrial invasion	2020	Models performances – no significant diff Combined model vs subjective diagnosis – no significant diff Single-sequence models vs subjective: lower specificity and accuracy but higher sensitivity
Chen et al. (14)	Deep Learning MRI 530 patients Single Center Deep vs shallow MI	DL model for detecting MI depth in EC and compare with radiologists for evaluating clinical application	2020	Diagnosis and classification of MI depth by radiologists improved with DL method for lesions >2cm. Radiologists better accuracy for lesions <2cm False positive error most common for both radiologists and computer

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