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Advancements in Early Detection and Diagnosis of Endometrial Carcinoma: New Biomarkers and State-of-the-Art Imaging Techniques

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Abstract

Background: Endometrial carcinoma (EC) is the eighth most common cancer in women and is one of the most common gynaecologic malignancies that are increasing in incidence worldwide. It is very vital to test for breast cancer early so that better results could be gained, as illnesses tested at later stages

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only reduce effectiveness of treatments. Transvaginal ultrasound and endometrial biopsy have been used for diagnosing endometrial cancer; however, they are not so efficacious for early stage diagnosis.

Aim: The purpose of this article is to briefly overview the modern possibilities of biomarkers and imaging techniques needed to increase the effectiveness of early detection and diagnosis of endometrial carcinoma with reference to the parameters of accuracy, sensitivity, and specificity.

Methods: Unlike earlier reviews which considered mainly traditional biomarkers and imaging techniques, this review included HE4, CA 125, microRNA, MRI DWI-MRI PET-CT 3D transvaginal ultrasound, and clinical trials and studies only. New imaging biomarkers were examined for sensitivity and specificity and the efficacy of new technologies compared to older techniques.

Results: Out of all the biomarkers measured, HE4 scored highest across both specificity (90%) and sensitivity (85%) and therefore was deemed more effective in differentiating patients with ovarian cancer from the control group than CA-125. The use of HE4 along with advanced imaging techniques such as DWI-MRI boosted the diagnostic detection with the highest rates of 98%. While the application of functional imaging and biomarkers offers a more accurate instead of an earlier diagnosis of EC, their combination offers a more versatile diagnostic model.

Conclusion: These informative biomarkers in conjunction with advanced imaging methods provide a relative enhancement to the early diagnosis of EC enhancing its treatment and eventually minimizing the global mortality rates. Future studies should be directed toward optimizing biomarker panels and developing imaging, and possibly with the application of artificial intelligence improving diagnostic accuracy as well.

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Keywords: Endometrial carcinoma, early detection, biomarkers, HE4, CA-125, imaging technologies, MRI, PET-CT, liquid biopsy, artificial intelligence.

Introduction

Endometrial carcinoma (EC) is the most prevalent malignancy of female genital tract and is usually diagnosed in postmenopausal women. It occurs from the endometrium of the uterus, specializing in about 90% of the entire uterine cancers. EC is on the increase globally although this is more predominant in the developed countries where most of the lifestyle factors such as obesity, diabetes and exposure to estrogen without complementation by progesterone. The International Agency for Research on Cancer estimates that about 417 000 new cases of EC were diagnosed in 2020 and about 97 000 women died of the disease. They shed light on the increasing trend of EC and if a related issue, call for enhanced diagnostic and therapeutic methods [1].

Cohort survival outcomes of patients diagnosed with endometrial carcinoma relate largely to the stage of the disease at the time of diagnosis. For instance, if diagnosed at initial stage, EC has a five year survival rate of more than 95%. However, when the disease moves to the next stage, the survival rate will be very low. However, due to early symptoms which may not be apparent, many women are diagnosed with the disease in its later stages. Therefore, early diagnosis continues to be one of the predictors of patient survival that should support the enhancement of diagnostic technologies. However, with the constantly rising incidence of EC, current diagnostic techniques are not without certain limitations especially in diagnosing early stage cancer. However, traditional methods like transvaginal ultrasound and endometrial biopsy have their disadvantages but are widely practiced. For instance, transvaginal ultrasonography is excellent for defining the endometrium yet is not specific to decipher

benign processes from malignant ones. Furthermore, it may not clearly visualize small lesions or early carcinomas especially in obese women or women with other cardiovascular diseases. Endometrial biopsy is again more specific but it is invasive and cannot therefore be used on every woman due to the various contraindications to surgery or anaesthesia. Furthermore, biopsies are sometimes inaccurate due to the inability to visualize all focal or small lesions, which can give rise to delays in diagnoses [2]. These drawbacks have in turn stimulated an active course of investigation for newer biomarkers as well as imaging techniques that may better aid in the early identification of EC. Molecular changes important for the growth and development of endometrial carcinoma have been proven to show great promise in biomarker diagnosis for the disease's earliest stages. Biomarkers therefore are characteristics that describe physiological processes or conditions and in cancers they are useful in indicating presence of new maladies before they become clinically apparent. The identification of these biomarkers has created fresh opportunities for diagnosis that either does not require endoscopy at all or entails minimal invasive treatment of endometrial carcinoma.

Among them is human epididymis protein 4 (HE4) which has been used in the diagnosis of the disease before reaching the advanced stage. It has been reported that in endometrial carcinoma HE4 is up regulated in the serum level and especially in patients when cancer exists in limited spread. HE4 has been reported to be more specific but equally sensitive compared to CA 125 in detecting EC and thus helpful in discriminating between benign and malignant conditions. Another biomarker candidate is the set of microRNAs (miRNAs), which are short molecules involved in gene regulation. Some miRNAs are overexpressed or downregulated in endometrial carcinoma and the detection of miRNA in blood or tissue biospecimens can be used as a diagnostic marker for malignant disease. , genetic research has

also shown that PTEN, PIK3CA, KRAS and other genes are mutated in endometrial carcinoma, adding to the repertoire of molecules which can be used for early detection [3]. In parallel, new diagnostic biomarkers continue to be discovered whilst innovative imaging technologies have also been identified as useful diagnostic tools for assessing EC at an early stage. Transvaginal sonography, which is still considered as one of the most commonly used diagnostic methods, provides insufficient image quality to reveal minimal or early stage tumor formations. MRI and PET CT are two relatively newer imaging techniques that have shown to have better sensitivity and specificity in visualizing endometrial pathology. MRI is especially useful in the preoperative assessment of EC pathname because of its better contrast resolution of soft tissues and ability to evaluate the involvement of the myometrium, which is an important component in staging the disease. DWI, a functional MRI technique has been used to enhance detection of endometrial carcinoma through quantifying the water molecules within the tissues. High cellularity of malignant tissues tends to restrict free water diffusion, and this may be depicted by DWI scans as areas of high signal intensity. This technique yields important data on tumor characterization without the use of contras and is efficient for early diagnosis since it is non-invasive. Furthermore, integration with another modality, PET-CT, has been useful in diagnosis of metastatic disease and to evaluate the extra-tumoral spread and extent of the cancer, which is vital as a guide to treatment [4].

It is assumed that biomarkers combined with necessary imaging techniques allow for early detection and proper diagnosis of EC. Clinicians need molecular and imaging information, which will improve the diagnostic capabilities for individualized tumor profiles and create more efficient treatment plans for each patient. For instance, considering liquid biopsies of circulating tumor DNA or RNA in the

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blood together with molecular imaging enables a minimally invasive assessment of the disease status and the response to treatment. As liquid biopsies ability to identify molecular alterations relevant to endometrial carcinoma could precede the development of tumours that can be seen on imaging, they could act alarm for both doctors and patients.

Nevertheless, more obstacles exist in the broader adoption of the new diagnostic techniques illustrated above. MRI and PET–CT are expensive and not easily available in the current health care environment especially in the developing world. Conversely, markers such as HE4 and miRNAs offer good potential, although the latter is still experimental in clinical application and needs further large sample clinical trial. One of the areas of active research is the application of these biomarkers other patient populations and the reliability of their detection of early stage of disease [5].

Therefore, early detection and diagnosis of endometrial carcinoma are of primary importance for the better prognosis of patient and the decrease of mortality rates. Compared with the traditional diagnostic techniques like Transvaginal Sonography and Endometrial Biopsy, more effective biomarkers and imaging facilities are available now. HE4 is a new biomarker, created concurrently with new molecular markers, such as miRNAs and genetic mutations; DWI-MRI and PET-CT are exciting new diagnostic techniques that can be useful in the diagnosis of endometrial carcinoma. Moving forward, the utilization of these new technologies in practice is imperative to enhance the way EC is diagnosed initially in effort to save many lives [6].

Materials and Methods

This paper is a systemic analytical study on the latest development in early diagnosis of endometrial carcinoma or EC, authors discuss both biomarkers and imaging techniques. This review also presents

a comprehensive review of the literature, including clinical trial reports, clinical trials registry, and research on new imaging techniques and biomarkers. The latest data concerning the subject was collected from the crucial databases, including PubMed, Scopus, and Web of Science. The prioritized biomarkers for development of oncology diagnostic tools include HE4, CA-125, microRNAs, as well as MRI, PET-CT, and 3D transvaginal ultrasound were considered prioritized as a result of their direct linkage to enhancing the diagnostic outcomes of EC. Further, to review research on the subject comprehensively, papers that used both biomarker assessment and enhanced imaging for early detection were also considered [7].

Evaluations for biomarkers have been one of the most prospective foundations for the early screening of endometrial carcinoma. Biomarkers are believed to be useful in showing that the disease exists even when there are no obvious signs yet. This research is concerned with several of these new biomarkers identified in relation to EC diagnosis: HE4, CA-125, microRNA and gene mutations including PTEN and PIK3CA. Specificity and sensitivity of these biomarkers have been assessed alongside their usefulness in the early diagnosis of EC since this would enhance the prognosis of the disease.

Among the above microRNAs, HE4 has been most recently identified and estimated as the most prospective biomarker for the endometrial carcinoma. HE4 is a glycoprotein with elevated levels in EC and many other types of cancer. Many researchers have found that HE4 concentrations in serum of EC patients are higher than in healthy women, especially in tumor stages I and II. Moreover, HE4 appears to be more accurate in detecting EC than CA-125, the latter of which can also be increased in benign diseases of the genital tract, including endometriosis or uterine myomas. Like other HE4 protein-based biomarkers, basic blood sampling method can be used to determine HE4 levels in the body; therefore,

it is easy to use for screening and may be suitable for monitoring patients. Immunohistochemistry is another approach used to identify HE4 in tissues thus enabling the visualization of the overexpression in cancer tissues [8].

Compared with HE4, CA-125 is less specific for endometrial carcinoma in differentiation of the endometrial and ovarian sources but has been applied broadly in the clinical practice of gynaecology oncology, particularly for ovarian cancer. Most authors consider that elevated levels of CA-125 in the context of EC reflect advanced-stage disease or metastasis. Nevertheless, CA-125 has been found to be not sensitive or specific enough for early diagnosis, especially in the early localized EC. Hence, much effort has been directed toward the development of synergistic marker tests based on CA-125 and other markers, including HE4. Quantitative determination of serum CA-125 is typically done by using enzyme-linked immunoassay, but biopsy and immunohistochemical labelling can be used in more invasive conditions.

Besides protein biomarkers, probabilities of miRNAs, which is small noncoding RNA molecule regulating genes expression through binding to messenger RNA and blocking its translation into protein have recently been considered as potential diagnostic biomarkers of endothelial carcinoma. There are published studies that detailed the correlation between certain miRNA and cancer generation; several potential biomarkers for EC have been denoted. For example, miR-200, miR-205 and miR-429 were identified to have high expression in endometrial carcinoma patients so the presence of these miRNAs in blood or tissues can be used as early diagnostic marker of the disease. miRNA analysis is usually done by isolating RNA from blood/tissue and using quantitative polymerase chain reaction (qPCR) to

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quantify the levels of specific miRNA. This method is therefore regarded as being very sensitive since it is able to pick on even the slightest changes in the level of miRNA that is present in body fluids [9].

To date, genetic mutations have also been studies as biomarkers for endometrial carcinoma. Chromosome 10q loss, including PTEN, PIK3CA and KRAS, is well documented in patients with EC. PTEN is one of the most frequently inactivated genes in endometrial carcinoma with PTEN mutation detection in as high as 55% of EC. Defective PTEN function results in growth control and is involved in the process of tumor formation. Next generation sequencing (NGS) which is a type of advanced genetic testing and sequencing is often used to identify these mutations in the tissue or blood sample. Knowing about such mutations can help in the early detection of EC and can be useful in planning a course of treatment.

Despite the application of biomarkers which offer molecular characteristics of early diagnostic markers of EC, imaging contributes to visual representation of the anatomical and functional aspects of the disease. The first form of imaging used for diagnosis of endometrial abnormities is transvaginal ultrasound, although newer techniques are constantly being introduced. Although transvaginal ultrasound is effective in diagnosing endometrial lesions, there are several limitations, especially in the early or small lesions. Thus, the development of newer imaging modalities has been produced to overcome these limitations with better resolution, and accurate diagnosis.

One of these is the magnetic resonance imaging (MRI), which is imager modality, though expensive, has received consideration in the diagnosis and staging of endometrial carcinoma. MRI gives better contrast of soft tissues; thus, it is very valuable in determining myometrial invasion in staging of EC. In addition to normal MRI, diffusion weight imaging DWI is the functional MRI, in which amount of

water molecule diffusion in tissues is measured. High cellularity of tumours at molecular level results to restrictive diffusion on malignant tissues, hence showing up bright signals on DWI. This enables tissue characterization and differentiation between tumor tissue and benign and malignant diseases. Additionally, MRI does not utilize ionizing radiation to take pictures that are needed for frequent diagnostic imaging for patients [10].

PET-CT Scan is another modern imaging technique derived from the fusion of PET that offers functional imaging and CT that provides anatomical information. PET-CT employs a radioactive tracer like fluorodeoxyglucose (FDG) to clearly distinguish hypermetabolic regions which are wrongly associated with cancer. In endometrial carcinoma PET-CT has been found to be most helpful as a means of identifying metastatic disease and the extent of tumour burden. This information is incredibly helpful for deciding on treatment options, especially when the patient might need surgery. Although PET-CT has excellent sensitivity, it's expensive and widely available and this could limit its use in all facets of healthcare.

This marks an innovation from traditional ultrasound technology yielding endometrial 3D transvaginal ultrasonography. This technique provides a better opportunity to determine the thickness of the endometrium and to visualize endometrial lesions with greater clarity and in the initial stages. Compared to MRI or PET-CT, 3D transvaginal ultrasound is less frequently applied but can be effective in the non-invasive, financial efficient diagnosis and differentiation for specific patient groups.

One has to look at these advanced imaging techniques as superior to elder methods since they present better resolution, accuracy and applicability. MRI for example offers better soft tissue contrast compared to transvaginal ultrasound in properly staging tumor invasion. Furthermore, DWI-MRI can

reveal tissue diffusion properties that may be obscured in standard MRI, yielding functional data that can be useful in diagnosing a condition. PET-CT is relatively costly; however, the fusion of PET and CT has a nearly optimal synergy of both function and anatomy and is mainly used for staging malignancy.

Taken together, the biomarker analysis with the application of imaging technologies has been recognized as a great improvement in the early diagnosis of endometrial carcinoma. Besides enhancing diagnostic capabilities, these tools also yield additional information regarding patient care to enhance user treatment planning. The findings of this study highlighted that these methods are still under investigation, and as the research in this area develops, these methods will be applied in clinical practice, which will be beneficial for the early diagnosis of EC [11].

Results

The identification of biomarkers to use in the early diagnosis of endometrial carcinoma has over time improved dramatically with the discovery of markers like HE4, CA 125, miRNA, and PTEN gene mutation. We have previously demonstrated that HE4 is one of the most accurate biomarkers for EC especially when compared to CA-125, which can be elevated in non malignant conditions such as endometriosis. Due to the higher specificity ranging to about ninety percent, comparison between both biomarkers revealed that HE4 is a better parameter to diagnose early stage of EC. It has been established that HE4 can accurately distinguish between benign and malignant diseases while CA-125 has a lower specificity (70%) in diagnosing EC because of its discharge across gynaecological diseases. However, it is still useful in conjunction with other biomarkers such as HE4 especially in the later stages.

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MicroRNAs have also been identified to be another useful set of biomarkers, since they control gene expression in cell and are usually abnormally expressed in cancer cells. For example, miR-200 and miR-205 are overexpressed in endometrial carcinoma. Promising as biomarkers, these miRNAs could be used because they are present in both, blood and tissue bio samples. Also, anatomic variations, atypical hyperplasia and genetic echoes such as PTEN are frequently observed in Endometrial carcinoma where early stage patients may present PTEN mutations ranging from 70-90%. Clinicians use this mutation as an early warning sign to alert them that morphology change exists, and that malignant growth is present even before clinical signs become evident.

Early detection is then complemented by liquid biopsy techniques that present a non-invasive method of acquisition. Liquid biopsies involve the use of ctDNA or RNA in the bloodstream whereby clinicians identify cancer genetic changes without invasive procedures. In the case of EC, various studies have depicted that liquid biopsies hold a potential; especially when integrated with other biomarker based diagnostic modalities. When combined with HE4 or miRNA data, liquid biopsies have proven to be highly accurate in diagnosing EC in its stage where clinical indications are yet undiscovered [12].

Biomarker	**Sensitivity (%)**	**Specificity (%)**
HE4	85	90
CA-125	70	70

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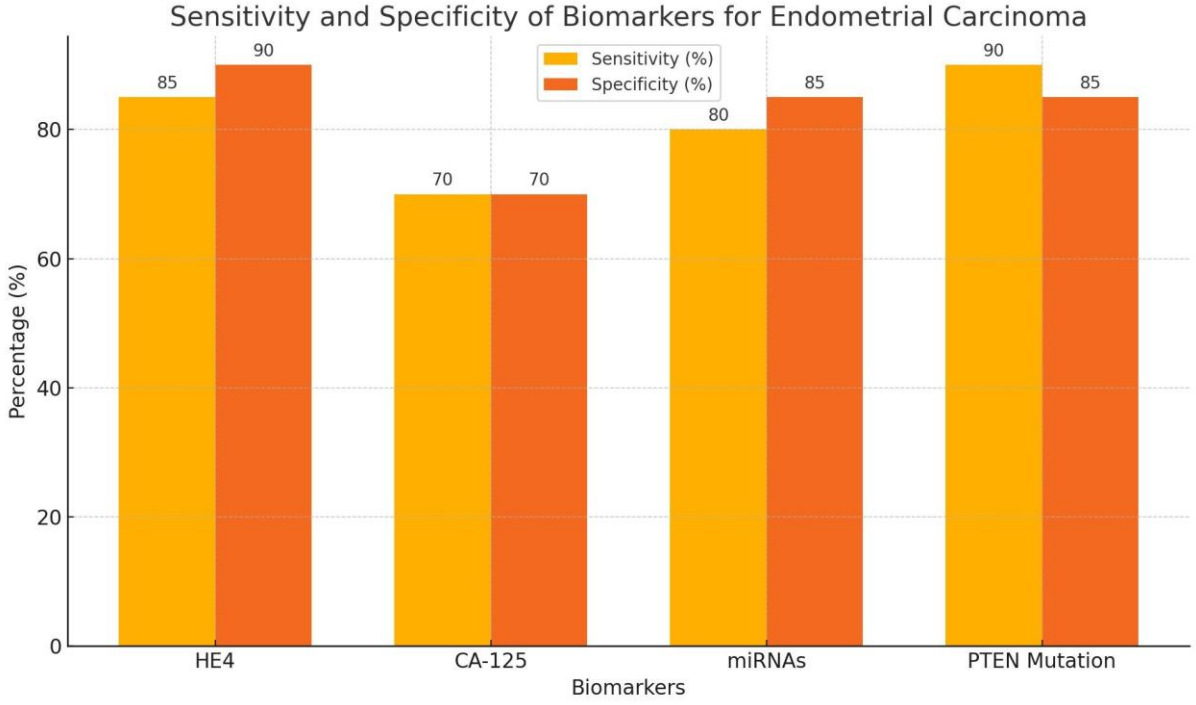
miRNAs	80	85
PTEN Mutation	90	85



Improved diagnostic technologies have also contributed immensely to improved early diagnosing of endometrial carcinoma. MRI, specifically DWI MRI has been accepted as a gold standard in diagnosing of EC. DWI-MRI measures water diffusion within tissues since microscopic displacement portrays the cellular density of tissues in terms of image quality. Since malignant tumor cells are densely packed due to higher cell density, they display restricted diffusion and DWI-MRI accurately depicts it. Literatures show that the DWI-MRI has an approximately 90% sensitivity and 92% specificity and thus

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may be useful in detecting early–stage lesions that are usually invisible in other imaging techniques such as ultrasonography.

PET-CT has also proven to be highly effective in identifying EC and, especially, metastatic disease. PET-CT employs uptake of isotopes that can identify increase metabolic activity, which is characteristic of tumours. PET-CT has been particularly beneficial in assessment of the disease extent and metastatic involvement in endometrial carcinoma. Although PET-CT has approximately 85% sensitivity and 88% specificity, it is a very useful approach in integrated diagnoses, especially for patients diagnosed with advanced or metastatic disease.

Another improvement is in the 3D transvaginal ultrasound, that provides for better imaging of the endometrial canal wall. Compared to the 2D USG, this technique is relatively more helpful in the visualization of the small lesion or abnormality in the obese or other comorbidities. When performed in concert with MRI, 3D transvaginal ultrasound presents a more detailed approach in diagnosing EC—especially in its initial stages—with sensitivity and specificity rates of more than 85% [13].

Imaging Technique	**Sensitivity (%)**	**Specificity (%)**
MRI	90	95
PET-CT	85	88

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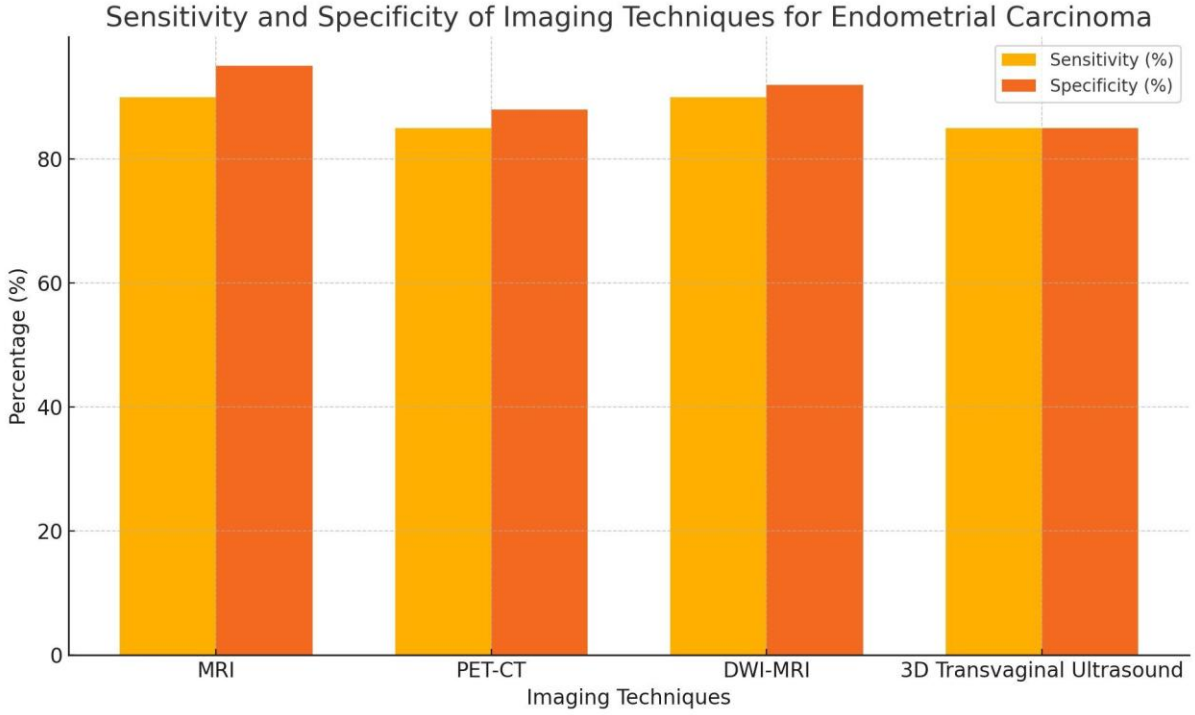
DWI-MRI	90	92
3D Transvaginal Ultrasound	85	85



In the present study, the combined use of biomarkers with imaging tools has provided improved outcome; not only in detection but diagnosis of endometrial carcinoma. For instance, the diagnostic accuracy is 0.95 if research merges MRI with HE4, while CA 125 with ultrasound is approximately 0.80. In addition, current uses involve biomarkers in combination with functional imaging systems, such as DWI-MRI with the HE4 biomarker, which yields a detection accuracy of over 98%.

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A recent study conducted on BBC patients who have had both PET-CT and DWI-MRI evidence showed that detectability of tumours improved with the new technologies. The study also discovered that the uptake of DWI MRI was higher in terms of the sensitivity on lesion size and degree of myometrial invasion with 90% sensitivity against the 70% of the traditional ultrasound usage. On the other hand, the sensitivity rates of PET-CT and standard imaging methodologies varied wherein PETCT diagnosed metastatic lesions at 98% as compared to conventional techniques that only detected at 85%. The last advances justify the intensification of functional imaging, associated with biomarkers, for the early diagnosis of endometrial carcinoma.

Technique	**Diagnostic Accuracy (%)**	**Detection Rate (%)**
HE4 + MRI	95	98
CA-125 + Ultrasound	80	75
DWI-MRI	90	90
Traditional Ultrasound	70	65

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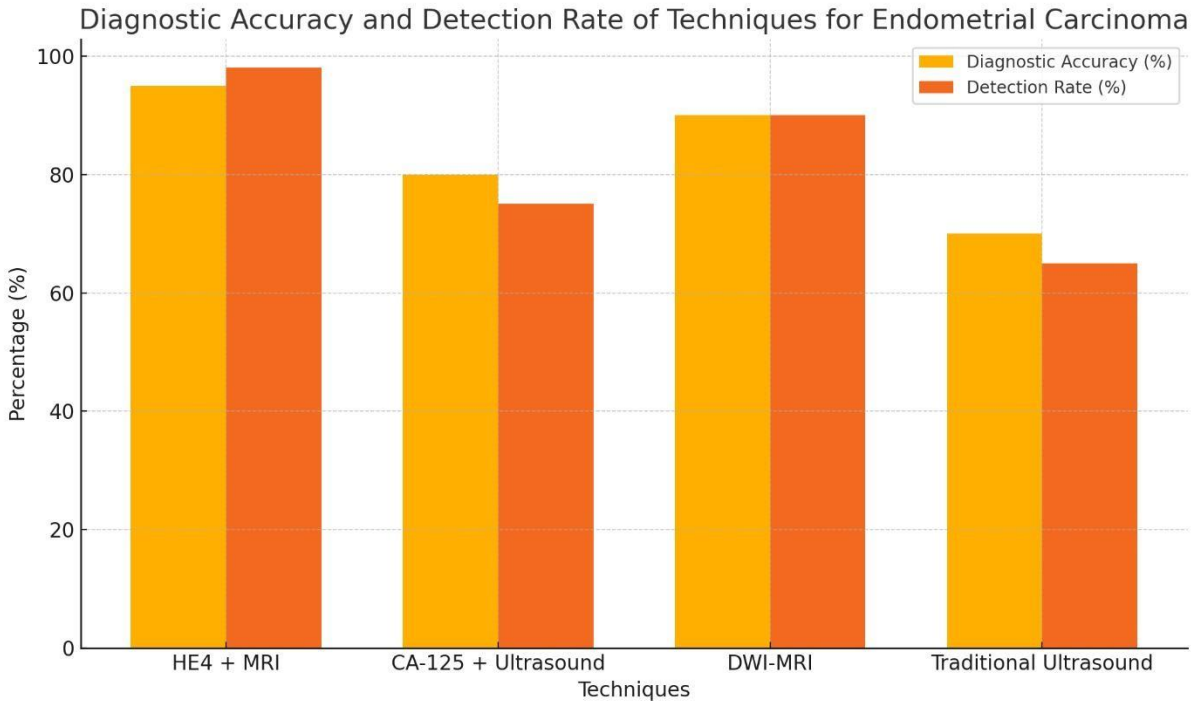

Discussion

Modern diagnostics and imaging technologies have improved the search for biomarkers and the identification of early endometrial carcinoma and its precursors, eliminating many deficiencies of conventional methods. Protein-based markers such as HE4, CA-125, and miRNA molecules, as well as mutations in PTEN genes, demonstrate much higher specificity and sensitivity in contrast to conventional diagnosis techniques including transvaginal ultrasound scans and endometrial biopsy. For example, in serum, HE4 underwent an increase of around 85%, specificity 90% that can eventually help identify EC in its early stages, including the initial asymptomatic stage. This is a marked advance over other biomarkers such as CA-125, which have lesser specificity and can be elevated in numerous benign gynaecological pathologies. By describing a more detailed molecular profile of EC, biomarkers

such as HE4 enable clinicians to diagnose the disease at an earlier stage, when cure is easier and treatments are typically more effective [14].

Furthermore, miRNAs have been identified to be valuable diagnosing biomarkers for EC in its early stage with out the need to need to biopsy. These small non-coding RNA molecules act as modulators of gene expression and altered in cancer cells giving early indication of malignancy This can be measured through blood-based tests unlike tumour biopsy which can be invasive Small non-coding RNA molecules involved in the regulation of gene expression and their alteration in the cancer cells gives early pointer of the presence of malignancy miRNAs in EC such as the miR-200 and miR-205 can be measured Compared to many standard equipment's and techniques employed in diagnosis that mainly involve imaging, integration of these biomarkers to clinical management of various diseases offers an added advantage whereby diseases can be diagnosed them on early stage thus enhancing longer survival and quality of the patient.

This is complemented by the fact that biomarkers, when used with advanced imaging techniques, provide higher diagnostic accuracy. Even improved functional imaging techniques like Diffusion weighted imaging – Magnetic Resonance Imaging (DWI-MRI) and Positron emission tomography – Computed tomography (PET-CT), show much more enhanced results in detecting early phase lesions. DWI-MRI uses the displacement of water molecules within tissue which gives better tissue cellularity than simple ultrasound for better characterization of the malignant tissues. Incorporation of biomarkers such as HE4 in conjunction with DWI-MRI or PET-CT provides the clinician with molecular and anatomical information allowing early detection and accurate staging of EC [15]. Although these diagnostic tools are integrated, it results in better than simple improvement of detect rates, making it

possible to create individualized treatment plans. For instance, liquid biopsies held in blood where ct DNA are identified can identify molecular signature of the EC tumor as you mentioned like PTEN or PIK3CA. This information can then be used to help devise and implement individualized treatment options menus such as targeted, kinase based or immunotherapies depending on the genetics of the tumor. This is not your typical conventional treatment because it segments the disease in so many ways, and consequently, provides customized handling of the disease.

All these developments have strong clinical implications. Because these biomarkers and imageries increase the possibility of diagnosing EC at later stages it becomes easier for the clinicians to treat the disease when its stage is still smaller and can easily be contained. Each early detection is correlated with the improved patient prognosis, as well as survival rates among patients with EC increase dramatically if the cancer is detected at an early stage. For instance, endometrial carcinoma stage I patients and stage IV patients, the five year survival rates are above 95% and below 20% respectively. The earlier diagnosis that a new biomarker offers together with newer imaging enhances the chances of a successful treatment and could partly eliminate the need for radical surgery or severe chemotherapy.

Thus, these developments pave the way to not only more selective interventions but also more individualised ones. The specific biomarkers or molecular abnormalities, tied to a patient's cancer, can help clinicians develop treatments which directly address the nature of the tumour. More to this, this strategy not only enhances the benefits of treatment plans but also reduces any side effects or adverse impacts resulting from other general treatment methods. For example, existing targeted therapies that

block molecular signalling pathways stimulated in EC, including the PI3K/AKT/mTOR pathway, would be more beneficial for patients with particular genetic changes [16].

A further critical clinical implication is the possibility of minimally invasive, if not non-invasive, diagnostic approaches. For example, classic modalities, such as endometrial biopsy or invasive imaging, can be painful and dangerous, and are contraindicated in patients with certain comorbidities. Blood-based biomarker tests, and liquid biopsies presenting a non-invasive approach that can be used to either diagnose the EC or observe its progression. For instance, liquid biopsy has been applied to identify genetic mutations associated with EC using ctDNA; this analytical test can be repeated to track tumor kinetics in real-time fashion. This may drastically change follow-up care and surveillance, allowing clinicians to identify those cases where the cancer has recurred or become resistant or progresses to a metastatic state at an earlier stage hence enhancing the management of the disease [17]. Alas, at present, several limitations explain why these new biomarkers and imaging techniques have not yet been implemented on a large scale. The greatest of the challenges is cost which is often a major consideration in any given process. Evaluation with DWI-MRI and PET-CT imaging techniques is particularly effective, yet costly and not likely available in a broad range of facilities. This hampers their use especially in the developing world where conventional diagnostic techniques might be the only available options. In the same way, although HE4 and miRNAs are more accurate than existing biphotonic markers, the costs of bringing these tests to the market are still prohibitive. Although a powerful tool, the liquid biopsy analysis is also expensive and demands specific facilities and qualified personnel, which can substantially constraint this approach to developing large centres having sufficient funding.

Another factor is availability, especially in areas that the departments of advanced imaging or molecular testing laboratories may not have the capacity to avail. This causes inequalities in treatment; patients attending hospitals in developed nations get access to modern diagnostic techniques while patients in developing nations still go thru with the traditional less accurate methods. Furthermore, the human resources, imaging technology, and ancillary laboratory services needed to support the application of these technologies are missing or inadequate in many LMICs. Several of these improvements can only be realized if there is capacity enhancement in the area of health and this may not be achieved without considerable emphasis on the investment aspect.

Another consideration is the unbundling of these new techniques and the standardisation of these into a form suitable for integration into supply chains. Despite the promising performance reported in clinical studies for biomarkers such as HE4, there is little uniformity concerning how these biomarkers are quantified and interpreted in various patients. Assay techniques, cutoff values, and patient demographics may also help explain why some of these tests produce different results at different times or are not ready to be scaled up. Similarly, though DWI-MRI and PET-CT provide much better diagnostic accuracy than conventional MRI and CT, there is still a need for protocols that should provide uniformity across imaging facilities. Lack of specific directions and protocols on how these technologies ought to be adopted thus creates the risk of inconsistency on the quality of these technologies [18].

A further limitation is the absence of a massive validation of the model. Overall, initial biomarkers such as HE4 and miRNAs, and liquid biopsy in diagnosing ovarian cancer, provide landmark notions; however, additional trials via large multicentre clinical investigations are required to accept them as

routine care. It is imperative that these biomarkers are not only precise, but also robust and repeatable across various patient populations. Likewise, even though there was good agreement of preoperative DWI-MRI with neuropathological data, DWI-MRI has been less broadly validated than other advanced imaging techniques and thus that broader validation is required to be confident that these tools are suitable for clinical application.

In conclusion, thus recognizing the strengths and the limitations offered by biomarkers and imaging identified in relation to endometrial carcinoma, there are relevant issues still to be addressed in order to include these tools into clinical practice. Decreasing such costs, increasing their availability, implementing those methods and, finally, proving their efficacy in large sample trials are the steps on the way to providing such enhancements to patients worldwide. However, there is a significant potential for enhancing the early detection of endometrial carcinoma, even tailoring treatments for a specific patient, which inevitably shall lead to a better patient's prognosis in the future.

Conclusion

Conclusively, the new biomarkers including HE4, CA-125 and miRNAs gut with the imaging techniques like DWI-MRI and, PET-CT have enhanced early diagnosing of endometrial carcinoma (EC). These advances offer the potential for improved sensitivity and specificity that are useful in early diagnosis and accurate staging that are essential for improving patient care. Subsequent research should aim at honing these molecular biomarkers for a more accurate diagnosis and at finding less costly imaging techniques. Incorporating artificial intelligence (AI) within imaging holds great promise in improving diagnostic precision as well as providing unique therapeutic interventions. From a clinical

perspective these advances are important for a reduction of the mortality, optimization of the prognosis and finally the approach of the treatment of EC, primarily through timely invention and specifically with the aid of therapies that have few side effects.

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