

An exploration of newly found risk factors, diagnostic tools, and potential treatments for endometrial cancer

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Key Words:

Endometrial cancer, genes, obesity, TTK, estrogen, ubiquitination

Endometrial cancer is the fourth most common malignant tumor in women in the USA, with cases continuing to rise each year. Several causes, diagnostic tools, and potential treatments are being researched as a result. Studies found that significant risk factors may include obesity, use of oral estrogen, diet, and lack of physical activity. All were explored to have a notable correlation with the incidence of endometrial cancer. Diagnostic tools being explored include many different genes as well as TTK. TTK is even being studied as a treatment option. All of this shows significant promise in their effectiveness after further research is conducted.

Introduction

Endometrial cancer is the most common malignant gynecological tumor. In fact, in terms of incidence of malignant tumors in American women, it comes in fourth. This number is only expected to get higher as its incidence rate climbs each year. As of 2023, endometrial cancer has been the cause of 12,940 deaths a year and there have been 66,570 total cases reported [4]. Endometrial cancer mostly affects post-menopausal women, but its prevalence, as seen, is rising, even in pre-menopausal women [1]. There are several potential causes including, but not limited to: obesity, age, hormone therapies, estrogens and progestogens, hormonal contraceptives, exercise, and diet [2]. Current treatment of endometrial cancer includes standard first-line chemotherapy, which can achieve remission ratios of around 43-62% [3]. Recently, causes of endometrial cancer have been further explored and newer ways for diagnosis, including early detection, have been discovered and are being studied.

Recent Progress

The many potential causes of endometrial cancer and their relevance was deeply studied in 2019 and detailed in the research article "Increased incidence of endometrial cancer

following the women's health initiative" [2]. A large finding was that obesity was a cause for 40% of endometrial cancer cases. Another important finding was the effect that estrogen has as a risk factor for endometrial cancer. The article further explored preventative measures including intrauterine device use, oral contraceptives, diet, and increased physical activity [2].

New early detection tools are also being explored due to this increased prevalence and risk of endometrial cancer. One study conducted in 2023 found that there are at least 5 genes that could be used for diagnosis and treatment for endometrial cancer in the near future [4]. These genes are UBE2S, ASB2, EBF2, TRIM9, and FBXO40. These specific genes were chosen through analysis by univariate Cox regression and LASSO regression and were found to be promising with further research needed.

Another study explored a potential new diagnostic option. The study found that 80 CTA genes were found abundantly in endometrial cancer compared to normal tissue samples/ In addition, they found that a high expression of TTK could be linked to a lower survival rate for those that have endometrial cancer [3]. After utilizing ROC analysis, the

researchers found that they could use TTK to distinguish between benign endometrial samples and stage one endometrial cancer. The researchers have even begun exploring the use of TTK inhibitors such as AZ3146 for treatment of endometrial cancer.

Discussion

The causes and diagnostic tools for endometrial cancer show promise in understanding the root of the issue and ability to find and treat it more effectively than ever before.

An important cause that was explored is oral estrogen when it is unopposed. Without proper balance, this estrogen greatly increases the risk of endometrial cancer development. Today, those taking systemic estrogen must also take progestogens to prevent this risk [2]. Furthermore, taking lower progesterone compared to estrogen causes this risk to stay prevalent, though slightly decreased. From these findings, researchers were able to conclude that oral contraceptives and intrauterine devices are able to reduce the risk of endometrial cancer developing [2].

Another risk factor studied is obesity which, as previously mentioned, may account for 40% of endometrial cancer cases [2]. Obesity causes inflammation, which increases risk; however, it also causes the levels of estrogen circulating in the body to be higher than normal, especially in post-menopausal women. In addition, there has been a positive association found between obesity-related pro-inflammatory biomarkers and the risk of endometrial cancer [1]. As discussed, this increase of estrogen in the body is a significant risk factor in the development of endometrial cancer; this as well as the inflammation seen in obesity is why obesity is an important factor to take note of [2].

Other causes found to be significant include hormone therapy, diet, and exercise. Hormone therapies, especially CBHT, has been proven with data to be a large risk factor for endometrial cancer [2]. Poor diet is also seen to be a cause, especially due to poor diet increasing inflammation and being a risk factor for obesity. On the other hand, Mediterranean or ketogenic diet is known to help have a lower risk of endometrial cancer [1]. In the same way lack of physical activity is a risk factor for the same reasons. Increased physical activity can even reduce the risk of endometrial cancer by 20-40% [2].

With causes and risk factors being explored, so are diagnostic tools and treatments. It is essential for new treatment and diagnosis options to be found as the current ones used are not as effective as they have the potential to be. With chemotherapy being the current treatment of endometrial cancer, carboplatin and paclitaxel are heavily

relied on [3]. This treatment, as previously discussed, has remission rates of 43-62%; however, 40-60% have chemoresistance [3]. This statistic is shocking as survival odds are significantly decreased and it shows why new, more effective, and more efficient options need to be found and are being explored. Even surgery, which is another treatment option, usually leads to poor prognosis as lymph node or distant metastases are likely to develop [4].

A study earlier discussed considered that 5 genes, UBE2S, ASB2, EBF2, TRIM9, and FBXO40, have great potential to be a diagnostic and treatment tool for endometrial cancer [4]. The researchers analyzed ubiquitination-related genes and identified 46 prognosis-associated ubiquitination-related genes. They then performed LASSO regression analysis on these genes and narrowed them down to 22 ubiquitination-related genes; the researchers did this as they found that the prognostic model formed from the analysis performed best with these 22 genes. Lastly, the 22 ubiquitination-related genes were intersected with the differential expressed ubiquitination-related genes they found, resulting in the 5 genes that show great promise for prognosis [4]. With further research done, this could become very effective for diagnosis and treatment of endometrial cancer.

TTK is another factor that shows promise for endometrial cancer diagnosis and treatment. In one study, high expression of TTK showed both strong positive correlation with EMT-related genes in endometrial cancer tissue and was also linked significantly with lower survival in those already diagnosed [3]. Using ROC analysis, the researchers found that they could use TTK as a biomarker for early diagnosis or detection of endometrial cancer. They found that they could utilize TTK to differential between benign tissues and stage one endometrial cancer tissues. Not only does it have this early diagnosis potentially, but it could also be used as a treatment tool. Using TTK inhibitors, specifically AZ3146, was effective in this study in reducing endometrial cancer cell growth, enhancing apoptosis of endometrial cancer cells, and reducing the invasion of these cancer cells [3].

References

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