International Journal of
Science Inventions Today
www.ijsit.com
ISSN 2319-5436
Research Article

RELATIONSHIP BETWEEN POLYCYSTIC OVARY SYNDROME AND ENDOMETRIAL CANCER

Leila Mohamed Hussein MD[a*], Jianbin Zhou MD[a], Iqra Sharif Hashi Siad MD[b] and Nasra Mohamed Hussein MD[c]

The Second Affiliated Hospital, Department Of Gynecology & Obestetrics, Hengyang Medical School, University Of south China, Hengyang, Hunan, 421001, China.

ABSTRACT

Polycystic ovary syndrome (PCOS) is considered as a high risk factor for endometrial cancer (EC), but the exact mechanism of PCOS causing EC is still not completely clear. Endocrine and metabolic abnormalities and changes in various signal transduction pathways in PCOS patients may lead to the occurrence and development of EC. Risk factors such as persistent anovulation, androgen and insulin levels, inflammatory factors and tumor necrosis factor may affect the molecular and gene expression of endometrium by acting on different receptors and activating various signal transduction pathways. Therefore, future research should focus on the changes of EC-related signal transduction pathways in PCOS patients in order to prevent the occurrence of PCOS-related endometrial cancer.

Keywords: polycystic ovary syndrome; Endometrial carcinoma of submandibular organ; Hormone, receptor; signal channel

INTRODUCTION

Polycystic Ovary Syndrome, PCOS) is a common gynecological endocrine and metabolic syndrome, and its main features include long-term anovulation, hyperandrogenism and hyperinsulinemia, and insulin resistance [1]. Accompanied by complications such as abnormal lipid and glucose metabolism, such as type 2 diabetes, hyperlipidemia and cardiovascular diseases. The incidence of PCOS is about 6% among women of childbearing age in the world, and it is even higher among women aged 45, reaching 5.6% [2]. Endometrial Cancer, EC) accounts for 5% of the global incidence of female cancer, ranking sixth in the global incidence of female cancer [3]. Studies have shown that the risk of PCOS patients suffering from EC is more than three times that of healthy women [4], and the correlation with PCOS is more obvious among younger EC patients [5]. According to epidemiological investigation, the incidence of EC in women with PCOS complicated with endometrial dysplasia is as high as 0.1%, which is much higher than 0.025% in healthy people [6].

There are many similarities between the high-risk factors of EC and the clinical characteristics of PCOS. At present, it is clearly pointed out that the development of PCOS-related EC is not only affected by long-term estrogen stimulation, but also by hyperandrogenism, hyperinsulinemia, chronic inflammation, tumor necrosis factor-α, nicotinamide adenine dinucleotide phosphate and other related factors.

Future research should further explore the specific mechanism of these influencing factors and PCOS correlation EC. Early detection and evaluation of the risk factors of PCOS-related EC can help clinicians to better diagnose and treat this complication. In addition, it is also very important to find new potential therapeutic targets to deal with the risk of PCOS patients developing into EC more effectively. These research results are expected to provide more specific basis for guiding clinical work, provide more accurate prevention and treatment strategies for PCOS patients, and further improve their quality of life.

Persistent anovulation and EC:

Persistent anovulation is one of the main characteristics of PCOS. Long-term exposure of the endometrium of anovulatory PCOS patients to high estrogen environment without progesterone orange antibody leads to different degrees of endometrial proliferation, active mitosis and increased cell mutation rate.

Estrogen participates in EC:

Estrogen plays an important role in the pathogenesis of endometrial carcinoma (EC), especially in 70%~80% EC types. In addition, the close correlation with polycystic ovary syndrome (PCOS) and type I EC has also attracted wide attention [7]. This article will deeply discuss that estrogen participates in the occurrence of EC through various mechanisms.

1. The participation of obesity-related genes: Obesity is considered to be closely related to the risk of EC. Obesity-related genes encode a ketoglutarate-dependent nucleic acid demethylase, and its role in obesity-related diseases has been confirmed, and it also promotes the growth, self-renewal and metastasis of cancer cells [8]. These genes are highly expressed in EC tissues, and estrogen can induce the accumulation of obesity-

related genes through the signal transduction pathway of rapamycin target protein, thus further enhancing the proliferation of EC cells [9].

2. The function of negative feedback loop of PTEN PL-miR-200c: Estrogen can increase the level of Mir-200c after binding with its receptor. This process can inhibit the expression of PTENPl and PTEN gene, and activate phosphatidylinositol -3- kinase-protein kinase B(PKB/Akt) pathway, thus promoting the occurrence of endometrial cancer [10]. In EC cells, the expression of PTENPl -miR-200c was negatively correlated. MiR-200c directly binds to PTEN and PTENPl, and PTENPl can reverse the inhibitory effect of miR-200c on PTEN. The intervention of estrogen can increase the level of miR-200c and decrease the level of PTEN, thus enhancing the gene expression of phosphatidylinositol -3- kinase -Akt pathway. In addition, the knock-out of estrogen receptor α also proved the regulatory effect of estrogen on miR-200c and PTEN [10], emphasizing the relationship between estrogen and miR-200c.

3. The role of Cyr61 in EC: As a member of CCN family, the protein encoded by cyr61 plays a key role in cell proliferation, migration and adhesion. In addition, Cyr61 is also involved in cell apoptosis and tumor formation and development. Studies have shown that the expression of Cyr61 in endometrium of PCOS patients is increased, and estrogen can rapidly regulate Cyr61 and affect the process of apoptosis [11]. This high level of Cyr61 expression suggests that endometrium is highly sensitive to estrogen, so estrogen may mediate endometrial cell proliferation or mutation through Cyr61.

To sum up, estrogen plays a key role in the process of EC. Obesity-related genes, PTENPl -miR-200c negative feedback loop and Cyr61 may participate in the development of EC through estrogen mediation. These findings not only help to understand the relationship between PCOS and EC, but also provide new potential strategies for prevention and treatment. In the future research, exploring the molecular details of these mechanisms and their relationship will provide more accurate intervention methods for clinic.

Progesterone participates in EC:

Progesterone plays an important role in protecting endometrium and preventing endometrial cancer (EC), however, its molecular mechanism in EC is not completely clear. There is progesterone resistance in endometrium of patients with polycystic ovary syndrome (PCOS), which may be related to the occurrence of EC. Huang et al.' s research [12] reveals the molecular mechanism of progesterone in EC, which provides clues for us to understand the EC mechanism of progesterone in PCOS patients.

It was found that the expression of nuclear-rich transcript 1(NEAT1) of long-chain noncoding RNA in EC cells was down-regulated after progesterone treatment. In addition, the expression of lymphoenhancer 1 was positively correlated with the expression of NEAT1. Similarly, hsa_miR-146b-5p can target lymphoenhancer 1 and NEAT1. The expression of miR-146b-5p in Ishikawa cells was up-regulated after progesterone treatment. In the signal transduction pathway of B-linked protein, lymph enhancer 1 or NEAT1 is overexpressed in EC cells, but the expression is down-regulated after progesterone treatment. The expression of downstream gene c-myc or matrix metalloproteinase-9 regulated by the upstream gene Lymphenhancer-1 increased significantly in Ishikawa cells, and the expression of c-myc gene was positively

correlated with NEAT1-1. These findings suggest that progesterone may play an inhibitory role in EC progress by regulating lncRNA NEAT1/miR-146b-5p mediated B-linked protein signaling pathway.

Therefore, it is considered that progesterone regulates the proliferation and progress of EC cells by affecting NEAT1, miR-146b-5p and B-linked protein signaling pathways. This mechanism may explain the possibility of EC in PCOS patients with progesterone resistance, and provide a new perspective for further study on the relationship between PCOS and EC. This study is helpful to understand the regulation mechanism of progesterone on EC, and also provides a potential target for future treatment and intervention.

Hyperandrogenism and EC:

Polycystic ovary syndrome (PCOS) is a common endocrine disorder, and one of its typical manifestations is hyperandrogenism. The abnormal content of androgen in PCOS patients is closely related to the occurrence of endometrial cancer (EC). This article will discuss the possible mechanism of androgen in PCOS-related EC, especially the interaction between androgen and bisphenol A and fibroblast growth factor 13(FGF13) in PCOS patients [13].

The role of bisphenol a and FGF13 in PCOS and EC;

The increase of serum bisphenol A: The study found that the serum bisphenol A in PCOS patients was significantly higher than that in healthy people. Bisphenol A is an endocrine disruptor, which may promote the synthesis of androgen by directly stimulating theca cells or binding globulin with sex hormones. This provides a potential mechanism for the formation of hyperandrogenism in PCOS patients [14].

The existence of FGF13: Fibroblast growth factor 13 exists in PCOS patients. This factor may promote the production of testosterone by activating mitogen-activated protein kinase pathway. This may further aggravate the increase of androgen in PCOS patients, thus affecting the physiological process of endometrial cells.

Possible mechanism of androgen and PCOS-related EC;

Androgen is transformed into estrogen: In PCOS patients, androgen contributes to the synthesis of aromatase mRNA in endometrial cells, leading to the increase of aromatase P450 expression. The expression of aromatase P450 in endometrial cells of PCOS patients is increased, which enables androgen to be converted into estrogen [15-16] by aromatase. The increase of aromatic androgen may increase the availability of precursors of estrogen formation in uterus, thus indirectly increasing the estrogen content in the body. The estrogen thus produced may stimulate endometrial hyperplasia and lead to EC.

Role of cytochrome P450-17a photochemical enzyme: The state of hyperandrogenism may promote the occurrence of EC. Cytochrome P450-17a photochemical enzyme is one of the key enzymes in steroid hormone synthesis. In the hyperandrogenic environment, the expression of cytochrome P450-17a light enzyme increased. EC cells may increase prostaglandin E2 through signal transduction and phosphorylated overexpression of activated transcription factor 3, thus further stimulating androgen synthesis, which may aggravate the invasive ability of EC [17].

Effects of collagen fiber tissue and aquaporin: The state of hyperandrogenism may have an impact on

the structure of uterus. Animal experiments show that the thickness of the subepithelial matrix and muscular layer in the uterus of rats simulating the hyperandrogenism environment of PCOS patients is increased. This change is related to the increase of collagen fiber tissue and the expression of aquaporin 3 and aquaporin 8. These results suggest that the state of hyperandrogenism may cause changes in uterine structure, which may be one of the mechanisms of PCOS-related EC [18].

In conclusion, the hyperandrogenic state of PCOS patients may play a key role in the occurrence of EC. Androgen may act on endometrial cells through many ways, including the transformation of androgen into estrogen, the participation of cytochrome P450-17a light enzyme, and the changes of collagen fiber tissue and aquaporin. These mechanisms may interact and jointly promote the development of PCOS-related EC. Further study of these mechanisms will help to better understand the relationship between PCOS and EC, and provide new ideas for prevention and treatment.

Insulin resistance, hyperinsulinemia and EC

In recent years, studies have confirmed that insulin resistance is involved in the process of endometrial proliferation in PCOS patients. PCOS patients often show different degrees of insulin resistance, which makes the body's insulin secretion compensatory increase, resulting in hyperinsulinemia [19]. Hyperinsulinemia and insulin resistance can promote cell proliferation and inhibit cell apoptosis, which can lead to excessive proliferation and even malignant transformation of endometrial cells.

Participate in the occurrence of EC by regulating cytokines:

Endometrial carcinoma (EC) is a malignant disease related to endocrine disorders, and many factors may be involved in its occurrence. The possible mechanism of three key transcription factors in EC development will be discussed in detail below.

1. FOXO1 adjustment:

Fork box protein 01(FOXO1) transcription factor plays an important role in cell proliferation and apoptosis. Mitogen-activated protein kinase pathway (MAPK) can negatively regulate FOXO1, but in high insulin environment, MAPK pathway is often active, resulting in low expression of FOXO1, thus promoting cell division and proliferation. Studies have shown that the activity of FOXO1 in endometrial cells of EC patients decreased significantly. FOXO1-1 may be the key factor in the occurrence of EC, and it may be a potential target for the treatment of EC [20].

2. IGF-1 participation:

Insulin-like growth factor -1(IGF-1) is a mitogen and plays an important role in cell proliferation. It is found that IGF-1 gene is the direct target of miR-323-3p, and the level of miR-323-3p in PCOS patients is significantly lower than that in healthy controls. The level of miR-323-3p in PCOS patients decreased, which led to the over-activation of IGF-1. This may promote the mitosis of endometrial cells, accelerate endometrial proliferation and even lead to cancer [21] by directly acting on IGF-1 receptor of endometrium by insulin.

3. the influence of Pax 6:

Heterozygous pairing box 6(PAX6) is an important transcription factor, which is closely related to

insulin metabolism. PAX6 is highly expressed in endometrial cells of PCOS patients in high insulin environment. Overexpression of PAX6 increased insulin-induced S-phase accumulation in endometrial epithelial cells. PAX6 can also directly bind to the promoter of CDKN1B gene, and inhibit the transcription of CDKN1B gene stimulated by insulin, resulting in uncontrolled proliferation of endometrial epithelial cells [22].

Comprehensive discussion:

These three transcription factors (FOXO1, IGF-1 and PAX6) may play an important role in the occurrence of EC. MAPK pathway regulates FOXO1 activity. Insulin environment may affect the mitosis of endometrial cells through the regulation of IGF-1 and miR-323-3p, while PAX6 is related to insulin metabolism, and its overexpression may aggravate the proliferation of endometrial epithelial cells. These factors may work together to promote the occurrence and development of EC [23].

Studying the regulation mechanism of these transcription factors will help to better understand the pathological process of EC and provide new ideas for future treatment strategies. These findings may be helpful to develop therapeutic methods for these factors, so as to block or interfere with the development of EC and provide better treatment options for patients.

Participate in the occurrence of EC through TETI (ten-eleven-translocation 1) gene:

TETI gene is the key control point of DNA methylation and gene expression, and its expression is often out of balance in human cancer cells. Insulin can up-regulate the expression of G protein coupled estrogen receptor (GPER), but the mechanism of insulin up-regulating GPER to promote EC cell proliferation is still unclear. Xie et al. [24] found that insulin can up-regulate the expression of TETI gene, while the latter can up-regulate the expression of GPER and activate the phosphatidylinositol fighting kinase -Akt signaling pathway. The phosphatidylinositol -3- kinase -Akt signaling pathway is involved in the process of cell apoptosis, differentiation and proliferation, and is related to the metastasis and adhesion of cancer cells. Therefore, it is speculated that the up-regulation of GPER mediated by TETI gene is a mechanism of insulin promoting EC.

Obesity and EC:

Obesity has obvious correlation with the occurrence and development of EC. Meta-analysis of 26 studies by American Cancer Institute shows that the risk of EC increases by 50% [25] when the body mass index increases by 5 units. Obesity may lead to the occurrence of EC through the following mechanisms: ① Participate in the occurrence of EC by increasing circulating estrogen. Adipose tissue is an important synthesis site of estrogen, and preadipocytes, mesenchymal stem cells and adipocytes in adipose tissue are the main sources of aromatase. Aromatase can transform androgen into estrogen, and the level and activity of aromatase increase with the increase of fat. In addition, the level of sex hormone binding globulin decreases with the increase of fat, which indirectly increases the bioactive estrogen. As a stimulating factor, estrogen can promote endometrial proliferation and even canceration [26]. ② participate in the occurrence of EC through cholesterol regulatory element binding protein L. Cholesterol regulatory element binding protein 1

plays an important role in fatty acid synthesis and metabolism, and it can also activate phosphatidylinositol -4, 5- diphosphate 3- kinase pathway, thus promoting cell proliferation and growth synergistically. It was found that the expression of cholesterol regulatory element binding protein L gene in endometrium of PCOS and EC patients was significantly increased, and it was positively correlated with body mass index and serum triglyceride level [27]. Therefore, cholesterol regulatory element binding protein L may be involved in the occurrence of EC in PCOS patients, but further research is needed to confirm it. ③ Participate in the occurrence of EC through insulin pathway. Obese PCOS patients often have insulin resistance and hyperinsulinemia, and there is a complex relationship between them. Hyperinsulinemia and insulin resistance can make the endometrium of PCOS patients proliferate or even become malignant through various mechanisms.

Other relevant factors:

Chronic inflammation is involved in EC:

PCOS patients are often accompanied by chronic inflammation of different degrees, in which cells in the immune system (such as natural killer cells) are recruited to the inflammatory site. At present, natural killer cells in uterus are considered as endometrial markers [28] of PCOS. Natural killer cells in uterus are related to the synthesis of endometrial cytokines. Most natural killer cells in uterus have $CD56^+$ and $CD16^-$ phenotypes. Natural killer cells can help endometrial proliferation, differentiation and repair by releasing inflammatory factors. Because the number of natural killer cells in PCOS patients is obviously reduced during the secretory phase of cell cycle, the effect of natural killer cells is weakened, which may lead to the steady imbalance of female reproductive tract [29]. In addition, inflammatory cells can produce mitochondrial reactive oxygen species, which can break DNA. At this time, endometrial tissues with DNA mismatch repair defects may accumulate harmful mutant genes, leading to endometrial hyperplasia and even EC.

Leptin and tumor necrosis factor participate in EC development:

Leptin has anti-apoptosis and mitotic effects on cancer cells, and plays an important role in the process of angiogenesis, cell proliferation and apoptosis of EC. The content of leptin in EC patients is positively correlated with EC staging. Leptin can increase the synthesis of estrogen in vivo by increasing the expression of aromatase and protein [30]. Studies show that the expression of leptin receptor in EC cells is up-regulated, and leptin can activate phosphatidylinositol -3- kinase/Akt/ mammalian rapamycin target protein, tyrosine kinase 2/ signal transduction and transcription activation factor 3 and promote the expression of vascular endothelial growth factor, thus promoting inflammation and blood vessels, leading to EC [31]. Tumor necrosis factor-α plays a key role in the process of tissue injury repair and lysis. As a cancer cell growth factor, it can promote the proliferation of cancer cells, and it can also induce angiogenesis factors and promote tumor angiogenesis. The expression of leptin and its receptor, tumor necrosis factor-α and its receptor in endometrium of PCOS patients increased, which led to the change of insulin signal transduction in endometrium, insulin resistance, endometrial hyperplasia and EC [32]. It can be seen that leptin and tumor

necrosis factor-α participate in the occurrence and development of EC through various mechanisms.

Nicotinamide adenine dinucleotide phosphate is involved in EC occurrence:

Nicotinamide adenine dinucleotide phosphate, encoded by tyrosinase L gene, is an important coenzyme involved in many anabolic reactions, such as the synthesis of nuclein. Acyl oxidoreductase 1 gene is related to many cancers, and its expression is regulated by estrogen receptor and progesterone. As mentioned above, abnormal estrogen and progesterone signal transduction increases EC risk. It has been confirmed that the expression of Hanoxidoreductase 1 gene in PCOS and EC patients is out of balance, which may lead to an increased risk of EC in PCOS women [33].

CONCLUSION

Polycystic ovary syndrome (PCOS) is one of the most common gynecological endocrine diseases, and its complicated and multifactorial nature makes the pathogenesis still not completely clear. Existing studies have revealed a variety of potential mechanisms, among which hypothalamic-pituitary-ovarian axis disorder, androgen excess, hyperestronemia, insulin resistance (IR) and compensatory hyperinsulinemia are considered as the main factors. In addition, excessive secretion of adrenal androgen may also be involved.

In PCOS patients, endocrine and metabolic changes have a significant impact on endometrium. These changes are closely related to the changes of androgen levels. Although the effect on endometrium is different due to the research results, hyperandrogenism may be one of the high risk factors for PCOS with endometrial lesions.

In addition, more than 50% PCOS patients are accompanied by obesity, especially abdominal obesity. Visfatin, as an adipocytokine, is closely related to PCOS and is considered as one of the potential risk factors for endometrial carcinogenesis. However, its specific mechanism needs to be further clarified.

Moreover, inflammation may also play an important role in the process of endometrial lesions caused by PCOS. Studies have shown that there are abnormal chronic inflammatory factors in PCOS patients, especially IL-6. The presence of these inflammatory factors may stimulate endometrial lesions.

To sum up, the main risk factors of PCOS-induced endometrial lesions include endocrine and metabolic disorders, hyperandrogenism and hyperinsulinemia, elevated visfatin levels, and the influence of chronic inflammation. Although there are still limitations in the treatment of PCOS complicated with endometrial lesions at present, it is of great guiding significance for clinical prevention of endometrial lesions in PCOS patients to understand these influencing factors and explore their mechanism of action, and it also provides useful suggestions for making clinical treatment plans.

REFERENCES

1. Yao Qing, Shi Linqian, Ma Haiyan, et al. Expression of secretory curl-related protein 4 in serum of patients with polycystic ovary syndrome and its relationship with insulin resistance [J]. International Journal of

Laboratory Medicine, 2023,44(16):1925-1928+1933.

2. Yang Huijuan, Wang Yu, Hu Zhuangwen. Effects of propofol combined with different doses of ropivacaine on hemodynamics and coagulation function in patients with endometrial cancer [J]. China Maternal and Child Health Care, 2023,38(17):3222-3225.
3. Yan Tengying. Effects of Diane -35 clomiphene citrate and vitamin E on endometrial thickness and ovarian reserve function in patients with polycystic ovary syndrome [J]. China Maternal and Child Health Care, 2023,38(17):3277-3280.
4. Qiao Jiang, Guo Qing, Zhong Yi, et al. Based on network pharmacology and molecular docking, the mechanism of modified Tantan recipe in treating polycystic ovary syndrome [J]. journal of traditional chinese medicine, Hunan, 2023,39(08):174-181.
5. Zeng Xiaojie, Lei Lei. Lei Lei's experience in treating polycystic ovary syndrome infertility by applying the academic thought of Gynecological Economics [J]. journal of traditional chinese medicine, Hunan, 2023,39(08):64-67.
6. Yan Ming, Wendy Wang Xuan. Correlation analysis between ultrasonic blood flow parameters and pathological stage and prognosis of endometrial cancer [J]. Medical Theory and Practice, 2023,36(16):2807-2809.
7. Wang Yixian, Ray Zhang, Wu Quansheng, et al. Clinical observation on 50 cases of polycystic ovary syndrome with kidney deficiency and blood stasis treated by Bushen Huayu recipe [J]. Journal of Gansu University of Traditional Chinese Medicine, 2023,40(04):44-48.
8. Yang Zheng, Zhang Chunren, Li Juan. The effect of five-tone therapy combined with TCM syndrome differentiation on negative emotions and quality of life of patients with polycystic ovary syndrome of kidney deficiency and liver depression [J]. journal of traditional chinese medicine university of hunan, 2023,43(08):1450-1454.
9. Song Lianjin, Pang Mingmin. Clinical observation on improving endometrial receptivity of PCOS patients complicated with infertility with Wenshen Huoxue decoction [J]. Guizhou Medicine, 2023,47(08):1245-1246.
10. Zhao Fangyuan, Zou Hong, Shi Simao, et al. Correlation analysis between parameters measured by Doppler ultrasound and levels of sex hormones and inflammatory factors in patients with polycystic ovary syndrome [J/OL]. biomedical engineering and clinical medicine: 1-5 [August 30, 2023].
11. Lin Tao, Liu Jingjing. Analysis of the use of compound oral contraceptives in the outpatient department of Putuo District Maternal and Infant Health Hospital in Shanghai and the current situation [J]. Shanghai Medicine, 2023,44(16):10-13+25.
12. Yan Wan, Hao Yang. Research progress of metformin and drospirenone ethinyl estradiol in the treatment of polycystic ovary syndrome [J]. Clinical rational drug use, 2023,16(24):170-173.
13. Li Xia, Chen Ruolan. Analysis of influencing factors of threatened abortion in patients with polycystic ovary syndrome [J]. Clinical medical research and practice.

14. Jiang Yanzi, Zhang Juan, Fang Qian, etc. Summary of Professor He Chengyao's experience in treating polycystic ovary syndrome [J]. Research on Integrated Traditional Chinese and Western Medicine, 2023,15(04):278-281.
15. Song Yuanzi, Song Xiaoling, Gao Haixia. The value of dydrogesterone combined with hysteroscopic electrotomy in the treatment of early endometrial cancer [J]. Clinical Medicine, 2023,43(08):59-62.
16. Wei Jiajia, Lin Jiajing, Zheng Fengque, et al. Observation on the therapeutic effect of Dihuang Daotan decoction combined with external treatment of traditional Chinese medicine on obese PCOS with insulin resistance [J]. Journal of Hubei University of Traditional Chinese Medicine, 2023,25(04):29-32.
17. Xu Dongchen. Clinical efficacy of letrozole combined with clomiphene citrate in the treatment of patients with polycystic ovary syndrome and its influence on ovulation and pregnancy [J]. guide of china medicine, 2023,21(23):94-96.
18. Zeng Genping, Miao Yuxi, Li Peiyin, et al. To explore the correlation between the intestinal-ovarian axis and polycystic ovary syndrome based on "spleen governing transport and transformation" [J/OL]. Clinical Modern Chinese Medicine: 1-10[2023-08-30].
19. Ge Chang, Gao Yue, Chen Jiao et al. Research progress of chronic inflammation and polycystic ovary syndrome with insulin resistance [J]. Journal of Reproductive Medicine, 2023,32(08):1270-1274.
20. Wang Jingna, Zhao Xin speed skater, Jiang Shanshan, et al. Effects of comprehensive weight management on melatonin and oxidative stress in obese PCOS patients [J]. Journal of Reproductive Medicine, 2023,32(08):1166-1171.
21. Ren Yihua, Huang Haitao, Bu Xiaoling. A case of clinical pregnancy was successfully treated by Chinese medicine combined with low-dose CC+HMG micro-stimulation [J]. Journal of Reproductive Medicine, 2023,32(08):1266-1269.
22. Yuan Chenyi. Research progress on pathogenesis of polycystic ovary syndrome in TCM [J]. China Urban and Rural Enterprise Health, 2023,38(08):60-63.
23. Liang Ruining, Jin Jing, Ding Zhiling, et al. Zishen Qingre Lishi Huayu Recipe regulates granulosa cells mediated by C/EBP β signal to improve polycystic ovary syndrome [J]. Jiangxi Traditional Chinese Medicine, 2023,54(08):61-67.
24. Liu Yichao, Guo Ying, Ji Xiaobin, et al. Expression and mechanism of c-Fos and MAPK in patients with polycystic ovary syndrome complicated with endometrial cancer [J]. guide of china medicine, 2023,21(19):5-8.
25. Zhou Rong, Wang Yiqin, Lu Qun, et al. Expert consensus on fertility-preserving therapy for early endometrial cancer (2022 edition) [J]. China Clinical Journal of Obstetrics and Gynecology, 2023,24(02):215-219.
26. Sardonar Lee, Yang Dongzi. Interpretation of Chapter 1 (Diagnosis and Risk Assessment) of International Evidence-based Guidelines for Assessment and Management of Polycystic Ovary Syndrome in 2018 [J]. Journal of Practical Obstetrics and Gynecology, 2023,39(02):113-116.

27. Cai Lijun, Han Huanmei, Pang Tongliang, et al. Correlation between abdominal visceral fat and risk of endometrial cancer in patients with polycystic ovary syndrome [J]. China Sexology, 2022,31(06):95-99.
28. Ma Dandan, Zhou Yufei. Risk factors of endometrial cancer in women with polycystic ovary syndrome in childbearing age [J]. Modern Diagnosis and Treatment, 2022,33(07):954-956+1038.
29. [29] Qin Lang, Study on early preventive intervention and new treatment methods for patients with polycystic ovary syndrome in the population. Sichuan Province, Sichuan University, January 14, 2022.
30. Zhang Duojia, Chen Jingxin, Li Mubai. Study on PI3K/Akt/mTOR signaling pathway and the pathogenesis of endometrial cancer in patients with polycystic ovary syndrome [J]. modern journal of integrated traditional chinese and western medicine, 2021,30(29):3284-3288.
31. Zhang Xin, Wang Jiandong. Research progress of epidemiological high-risk factors related to endometrial cancer [J]. Medical Review, 2021,27 (15): 1995-2999.
32. Huang Zhiling. Value of hypothyroidism in the pathogenesis of endometrial cancer [D]. Jilin University, 2021.
33. Chang Hui, Zhu Mengyi, Fu Xin, et al. Research progress on the mechanism of berberine on polycystic ovary syndrome [J]. China Journal of Integrated Traditional Chinese and Western Medicine, 2021,41(06):764-768.