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Original Article

Morbidity of metabolic syndrome in gynecologic cancers patients

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Abstract: Objective: To investigate the morbidity of metabolic syndrome (MS) in gynecologic cancers patients and explore the relationship between gynecologic cancers and MS. Methods: 359 cases of gynecologic cancers were enrolled as study group, 400 cases of gynecologic benign neoplasms were enrolled as control group. Clinical characteristics of the two groups were compared. Morbidity of metabolic syndrome in gynecologic cancers and benign neoplasms patients was calculated. Results: Compared with the control group, systolic blood pressure, diastolic blood pressure, body mass index (BMI), abdominal circumference, the fasting blood glucose, fasting blood insulin, plasma triglycerides, HOMA-IR, morbidity of metabolic syndrome (37.60% vs. 12.25%) in study group were significantly increased (all $P<0.05$). The level of high-density lipoprotein cholesterol in study group was lower than it in control group ($P<0.05$). Conclusion: The morbidity of MS in gynecologic cancers patients is higher than it in gynecologic benign neoplasms patients.

Keywords: Gynecologic cancers, metabolic syndrome, morbidity, insulin resistant, clinical characteristics

Introduction

Gynecologic malignant tumor is a serious threat to women's physical and mental health and the related factors of onset remains unclear. The metabolic syndrome (MS) is a cluster of risk factors for cardiovascular disease and type2 diabetes and constitutes a growing problem worldwide. MS includes obesity, dysglycemia, raised blood pressure, elevated triglyceride levels, and low high density lipoprotein (HDL) cholesterol levels [1, 2]. The incidence of MS is increasing year by year, on the other hand, more and more studies support the emerging hypothesis that MS may be an important etiologic factor for the development and progression of certain types of cancer [3-5]. So we aimed to investigate the morbidity of MS in Gynecologic malignant tumors patients and to explore the relationship between gynecologic malignant tumors and MS. This study was retrospectively analyzed the clinical data of patients suffered from gynecologic malignant tumors in our hospital and reported as follows.

Materials and methods

General information of patients

359 cases (study group) with gynecologic malignant tumors were completed surgical treatment and had full clinical and pathological data in our hospital from January 2008 to January 2015, of which 142 cases with ovarian cancer, 131 cases with endometrial cancer and 86 cases with cervical cancer. 400 cases (control group) with benign gynecologic tumors were randomly selected from the same period. Two groups had no family history of hereditary diseases, without hobby of smoking and alcohol, and had no history of exposure to sex hormones preoperative within 1 year.

Methods

Data of age at menarche, age of onset, gravidity and parity in two groups were retrospectively analyzed. All patients were measured and recorded blood pressure, weight, height, waist circumference, calculation of body mass index (BMI) according to the same criteria in the morning within a week preoperation by hand on quiescent condition. The fasting plasma glucose, insulin, and lipids were tested by sampled intravenous blood within 3 days preoperation. Insulin resistance was evaluated by homeostasis model assessment of insulin resistance (HOMA-IR), HOMA-IR = (fasting glucose × fasting insulin)/22.5. Metabolic syndrome was diagnosed reference to guidelines of the Inter-

Table 1. Comparison of the general conditions between two groups ($\bar{x} \pm s$)

Group	Cases	Age at menarche (years)	Age of onset (years)	Gravidity (times)	Parity (times)
Study group	359	11.28±3.09	49.71±8.09	4.66±2.91	2.34±0.75
Control group	400	12.54±2.76	48.43±7.36	3.71±1.74	3.19±1.48

Table 2. Results of physical examination in gynecologic cancers and benign neoplasms patients ($\bar{x} \pm s$)

Group	Cases	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	BMI (kg/m^2)	Abdominal circumference (cm)
Control group	400	112±14	75± 8	22.2±2.1	76±9
Study group	359	129±13[a]	87±11[a]	26.7±2.8[a]	88±7[a]

Note: compared with control group, [a]*P*<0.05. BMI: body mass index.

national Diabetes Federation criteria, namely, central obesity as the core of a group of metabolic syndrome, for Asian women, must comply with the waist circumference ≥ 80 cm, and at least meet 2 of the following four items: triglycerides ≥ 1.7 mmol/L or have received treatment, high-density lipoprotein cholesterol <1.29 mmol/L or have received corresponding treatment, blood pressure: systolic blood pressure ≥ 130 mmHg and (or) diastolic blood pressure ≥ 85 mmHg or have received corresponding treatment or have been diagnosed hypertension previously, hyperglycemia: fasting plasma glucose ≥ 5.6 mmol/L or have been diagnosed with impaired glucose tolerance, type 2 diabetes or have received treatment.

Statistical methods

SPSS 20.0 software was used for statistical analysis. The measurement data was presented as $\bar{x} \pm s$, and was compared using *t* test. The count data was compared using the X^2 test. P<0.05 was considered statistically significant.

Results

The general conditions in gynecologic cancers and benign neoplasms patients

As shown in the **Table 1**, there were no significant difference about age at menarche, age of onset, gravidity and parity between gynecologic cancers and benign neoplasms patients (all P>0.05).

Results of physical examination in gynecologic cancers and benign neoplasms patients

As shown in the **Table 2**, compared with the control group, systolic blood pressure, diastolic blood pressure, body mass index (BMI) and abdominal circumference in study group were significantly increased (all P<0.05).

Results of laboratory examinations in gynecologic cancers and benign neoplasms patients

Compared with the control group, the fasting blood glucose, fasting blood insulin, plasma triglycerides and HOMA-IR in study group were significantly increased (**Table 3**) (P<0.05). The level of high-density lipoprotein cholesterol in study group was lower than it in control group (**Table 3**) (P<0.05).

Morbidity of metabolic syndrome in gynecologic cancers and benign neoplasms patients

As shown in the **Table 2**, compared with the control group, morbidity of metabolic syndrome in study group was significantly higher than that it in control group (37.60% *vs.* 12.25%) (P<0.05). Morbidity of metabolic syndrome in ovarian cancer, endometrial cancer and cervical cancer patients in study group were 37.32%, 43.51% and 29.07% respectively.

Discussion

The metabolic syndrome (MS) is characterized by obesity, hyperglycemia, dyslipidemia and hypertension and it is a pathological condition of many kinds of abnormal accumulation of metabolites [6]. MS has been shown to increase risk of several common cancer types [7, 8]. The risk of gastrointestinal tract cancer, penile cancer and genital tract cancer in patients with MS was significantly higher than it in the general population. Adams et al [9] reported that, in the patients died from cancer prospectively, 14% of men and 20% of women were combined with the obesity. The risk of colon cancer, colorectal cancer, stomach cancer, pancreatic cancer and

Table 3. Results of laboratory examinations in gynecologic cancers and benign neoplasms patient ($\bar{x} \pm s$)

Group	Cases	Fasting glucose (mmol/L)	Fasting insulin (mU/L)	HOMA-IR	Triglycerides (mmol/L)	HDLc (mmol/L)
Study group	359	6.5±2.9[a]	9.2±4.7[a]	3.9±0.8[a]	3.21±1.96[a]	1.25±0.51[a]
Control group	400	4.7±0.9	5.2±3.0	3.1±0.6	1.56±1.22	1.65±0.47

Note: comparison of control group, [a]$P<0.05$; HOMA-IR: homeostasis model assessment of insulin resistance; HDLc: high-density lipoprotein cholesterol.

liver cancer in men with obesity and the risk of ovarian cancer, non-Hodgkin's lymphoma, breast cancer, uterine cancer and liver cancer in women with obesity were significantly higher than it in the general population. So the correlation between obesity and cancer is obviously.

This study analyzed retrospectively the clinical data in our hospital in recent years. The age at menarche, age of onset, gravidity and parity in study group and control group were compared and there were significant difference the differences between study group and control group. Systolic blood pressure, diastolic blood pressure, BMI, waist circumference, fasting glucose, fasting insulin, HOMA-IR and triglycerides in study group were significantly higher than it in control group. High-density lipoprotein cholesterol in study group was significantly lower than control group. The incidence of MS in study group was significantly higher than it in control group. Those results suggested that excluding the contribution of age and female hormones, MS might play an important role in onset and development of gynecologic malignancies. Insulin resistance (IR) is considered to be the most important initial to MS. A large number of studies indicated that IR was related to multi-organ tumor cell proliferation, and overexpression of receptor of insulin-like growth factor -1 (IGF-1) promoted the tumor cells proliferation [10]. Growth hormone is the initial stimulating substance of IGF-1 synthesized in the liver, insulin stimulates the synthesis of IGF-1 by up regulation of growth hormone receptor. While hyperinsulinemia may increase the biological activity of IGF-1 by reducing the concentration of IGF-binding protein in liver [11, 12]. IR occurs with the promotion of proliferation and inhibition of apoptosis in tumorigenesis, on the other hand, IGF-1 stimulate tumorigenesis by increasing the synthesis of vascular endothelial growth factor [13, 14]. Hyperinsulinemia and IGF-1 may elevate free sex hormone level in blood plasma by inhibiting the synthesis of sex hormone-binding proteins, and promote the occurrence of breast cancer, endometrial cancer, prostate cancer and other hormone-dependent tumors [15-17]. IR plays an important role in onset and development of some obstetric and gynecological diseases, and is highly related to gestational diabetes, gestational hypertension and polycystic ovary syndrome [18, 19]. In this study, the morbidity of MS in the patients with ovarian cancer, endometrial cancer and cervical cancer were significantly higher than it in control group, it suggested that MS may be a potential contributing factor of occurrence and development of gynecological cancers. Bjørge et al [20] recorded the height, weight, blood pressure, blood glucose, total cholesterol and triglyceride levels of 290 000 female cases since 1974 to 2005 year and the relative risk of MS and ovarian cancer was analyzed by Cox proportional hazards regression. 644 cases of epithelial ovarian cancer were found, and 388 cases were died from the ovarian cancer. Those results showed that MS was not associated with all pathological types of ovarian cancer. The hypercholesterolemia and hypertension increased the risk of ovarian mucinous cancer and ovarian endometrial cancer, MS increased the mortality of ovarian cancer in women younger than 50 years, high BMI increased the mortality of ovarian cancer in women older than 50 years [20]. Endometrial cancer is considered to be the most closely associated with MS in all gynecological malignancies, Rosato et al [21] analyzed 454 cases of endometrial cancer and 798 cases of healthy control, and the multivariate OR values of endometrial cancer with type 2 diabetes, hypertension, hyperlipoidemia and BMI >30 kg/m were 22.18, 1.77, 1.20 and 3.83 respectively, and there was a direct correlation between MS and endometrial cancer. Bjørge et al [15] analyzed the relationship between MS and the risk of endometrial cancer

through a large prospective cohort study and found that MS increased the risk of endometrial cancer and the risk of death due to cancer, and other indexes of MS besides cholesterol also increased the risk alone. Ulmer et al [22] analyzed 425 cases of invasive cervical cancer, and found that the risk of cervical cancer was associated with BMI, blood pressure and triglycerides, the risk of cervical squamous cell carcinoma associated with triglycerides was significantly higher than it in cervical adenocarcinoma, the results suggested that obesity, hypertension and hypertriglyceridemia increased the risk of cervical cancer. Nagel et al [23] researched 288,834 women with an average follow-up for 11 years, a total of 82 cases of vulvar cancer, 26 cases of vaginal cancer and 43 patients with other rare gynecological cancer were found, the results showed that MS increased the risk of vulvar cancer and vaginal cancer. In all the indexes of MS, the risk of BMI was one standard deviation higher than the others, levels of blood glucose and triglyceride increased the risk of vulvar cancer. So MS and its various indexes had an effect on the occurrence of aforementioned rare gynecological malignancies. Our results were similar with the relevant literature, the incidence of MS in gynecological malignancies patients was significantly higher than it in control group. Our results suggested that MS increases the incidence of gynecologic malignancies, and possibly plays a potential role in occurrence and development of gynecologic cancer. So large sample studies may be helpful for increase evidence-based evidences, but further research remains to be confirmed to reveal the underlying mechanism in the future.

In a word, there is a relevance between gynecological malignancies and MS. The clinicians should fully understand that the incidence of gynecologic malignancies may be increased with enlarged of MS, and should be aware of the importance of control weight, blood pressure, blood glucose, lipids and insulin resistance of female. Gynecologists should give counseling to high-risk group, and detect a variety of risk factors associated with MS. So those measures should have positive significance to prevention and control of gynecological malignancies.

Disclosure of conflict of interest

None.

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