A Cohort Study of genetic ovarian cancer risk prediction models and pathogenesis exploration

NCT06564428

2025-06-03

Program design

[Design of the study methodology]

The aim of this project is to establish a bidirectional multicenter cohort of hereditary ovarian cancer and to describe the clinicopathologic features of hereditary ovarian cancer patients in our country. The risk prediction model of ovarian cancer for Chinese was established by following-up analysis of clinical and pathological information, genetic test results and detailed family history, to predict the risk of cancer in first-degree relatives of carriers of pathogenic/suspected pathogenic mutations, and to guide the intervention management of high-risk population of cancer.

The study will identify novel tumor-causing mutations/predisposing genes by gene sequencing in a special family with hereditary tumor.

[Eligibility, exclusion and withdrawal criteria]

Topic 1: The clinicopathological features and gene mutation characteristics of hereditary ovarian cancer

Case Group (hereditary ovarian cancer) inclusion criteria:

1) Epithelial ovarian cancer, age ≥18 years

2) The pathological diagnosis was clear, and the germ line pathogenic/suspected pathogenic mutations were detected in the gene (the mutation interpretation was based on ACMG genetic variation classification standard and guide)

Control Group (non-hereditary ovarian cancer) inclusion criteria:

1) Epithelial ovarian cancer, age ≥18 years

2) The pathological diagnosis was clear, and no germ line pathogenic or suspected pathogenic mutation was detected by gene detection

Exclusion criteria:

1) Non-epithelial ovarian cancer was confirmed by pathology

2) No gene detection was performed

Topic 2: To construct a genetic ovarian cancer risk prediction model (to predict the risk of ovarian cancer in first-degree relatives)

Case Group (hereditary ovarian cancer) inclusion criteria:

1) Female first-degree relatives of patients with hereditary ovarian cancer (Case Group 1).

2) The first-degree relatives were tested for pathogenic or suspected pathogenic mutation of germ line.

3) Ovarian cancer.

Control Group (non-hereditary ovarian cancer) inclusion criteria:

1) Female first-degree relatives of patients with hereditary ovarian cancer.

2) The first-degree relatives were tested for pathogenic or suspected pathogenic mutation of germ line.

3) No ovarian cancer.

Exclusion criteria:

1) Female first-degree relatives did not undergo genetic testing.

Topic 3: To explore new tumor-causing mutations based on a special hereditary ovarian cancer family

In subject 1, a few patients in control group had no known germline pathogenic or suspected pathogenic mutation, however, it is suspected to be hereditary ovarian cancer (≥3 patients with ovarian cancer/breast cancer in the family, 2 generations of patients with the disease) based on the family history.

Case Group (hereditary ovarian cancer) inclusion criteria:

1) Ovarian cancer/breast cancer patients in a special hereditary ovarian cancer family.

2) The pathological diagnosis was clear, and the gene detection (whole exome sequencing) did not detect the known pathogenic or suspected pathogenic mutation of germ line.

The control group was included

1) The female patients with special hereditary ovarian cancer, whose age was ≥18 years old, did not have cancer.

2) No known germline pathogenic or suspected pathogenic mutation was detected by gene detection (whole-exome sequencing).

Exclusion criteria:

1) No gene detection (whole-exome sequencing) was performed.

[Study duration and follow-up]

Topic 1:

Time	Content
After the diagnosis	①personal history (age, BMI, oral contraceptive use, hormone replacement therapy use, tubal ligation) ②menstrual marriage and childbearing history (whether or not menopause, menopausal age, menarche age, the number of births) ③personal history of tumor (history of malignant tumor, tumor type, pathological type, tumor stage, age of onset) ④family history of cancer (family history of cancer or not, number/person of cancer in first/second/third degree relatives, relationship with patients, tumor type, pathological type, tumor stage, age of onset, gene detection) ⑤ results of gene detection (detection items, specimen type, mutation, mutated gene, cDNA change, amino acid change, mutation type, mutation significance)
Three years after the surgery (Every 3-6 months)	Treatment, physical examination, tumor markers, imaging examination; Genetic mutation, family history of cancer
After three years	Treatment, physical examination, tumor markers, imaging examination;

(Every 6 months)	Genetic mutation, family history of cancer

Topic 2:

Time	Content
The same time of the gene test	①Personal history (age, BMI, oral contraceptive use, hormone replacement therapy use, tubal ligation) ②Menstrual history of marriage and childbearing (whether menopause, age of menopause, age of menstruation, number of births) ③Personal history of tumor (whether there is a history of malignant tumor, tumor type, pathological classification, tumor stage, age of onset) ④Family history of cancer (whether there is a family history of malignant tumor, the number of first/second/third degree relatives suffering from malignant tumor, the relationship with patients, tumor type, pathological classification, tumor stage, age of onset, and genetic testing) ⑤Genetic test results (test items, specimen type, mutation or not, mutant gene, cDNA change, amino acid change, mutation type, mutation significance)
After the gene test (Every 6 months)	Have a tumor or not (if the subject have any, age and pathological type); Carry germline pathogenic/suspected pathogenic mutation, family history of tumor.

Data management

1. Data Entry

Data collection will be obtained by team staff via the Case Report Form (CRF). As a

part of the clinical data management system, the case report form for data collection is jointly negotiated and prepared by the project leader and the clinical epidemiology Research Center, and the experts are invited to discuss and modify it for use. The data collation process includes automated validation procedures and manual validation to ensure the completeness and accuracy of the data entered into the case report form. When the data does not match, the data can be queried, and the team staff can verify and modify the entered data.

2. Contents and methods of data verification and management

According to the data entered in the case report form, medical supervision is conducted regularly to ensure the accuracy of data entry, and medical problems are discussed separately.

3. Data Archiving

After data entry and verification are completed as required, the case report form shall be filed and stored in numbered order, and be filled with a retrieval catalogue for reference. Electronic data files, including databases, inspection programs, analysis programs, analysis results, coding and explanatory files, should be classified and stored in different disks or recording media with multiple backups, properly stored to prevent damage. All original files shall be kept for the period specified accordingly.

Statistical analysis

1. By collecting clinicopathological characteristics of the enrolled subjects, appropriate statistical methods such as univariate analysis, multi-factor analysis, Chi-square test and survival analysis were selected for descriptive analysis.

2. Through follow-up analysis of clinical and pathological information, genetic test results, detailed family history and other factors, a tumor risk prediction model was established to predict the risk of cancer in first-degree relatives of pathogenic/suspected pathogenic mutation carriers.

① The risk of hereditary tumor is preliminarily determined according to the family map, and the risk of hereditary tumor in a family member is further calculated through a mathematical model by combining individual clinicopathological information, genetic test results and detailed family history. The statistical methods were Bayes analysis, nomogram model, Logistic regression, cox regression, etc.

② Validation of the ovarian cancer risk prediction model: Expand the sample size of the genetic ovarian cancer cohort, and evaluate the sensitivity, specificity, AUC curve, positive predictive value and other indicators of the established model.

Informed consent

Protocol name: A Cohort Study of genetic ovarian cancer risk prediction models and pathogenesis exploration

Setting: the Third Hospital of Peking University

Main researcher: Chief gynecologist Guo Hongyan

Patient name: Initials:

Patient's address: Patient's number:

We cordially invite you to participate in the“Cohort study of genetic ovarian cancer risk prediction models and pathogenesis exploration”. Here are some questions you may be interested in:

[Background]

The mortality rate of ovarian cancer is the highest in female genital malignant tumors. About 75% of the patients were in the advanced stage at the time of diagnosis, and the 5-year survival rate was less than 30% . 10% -20% of ovarian cancers are related to genetic factors.

The study of hereditary ovarian cancer is helpful to find out the susceptible population of ovarian cancer, so as to intervene, prevent and diagnose ovarian cancer early. Secondly, cancer susceptibility genes are closely related to targeted therapy, and the study of Genetic predisposition is beneficial to the exploration and guidance of individualized and precise therapy.

The special changes of genetic information in hereditary ovarian cancer patients make them different from non-hereditary ovarian cancer patients in diagnosis, treatment and prevention. Gene detection can not only make molecular pathological stratification of ovarian cancer patients and identify the target of targeted therapy, but also provide evidence for risk assessment and early prevention of the carrier's relatives, to make the genetic risk assessment and clinical management of ovarian cancer more individualized and accurate. However, there is a lack of large-scale cohort of hereditary ovarian cancer in China, and data on genetic characteristics and pedigree analysis are still scarce.

[Objective]

The aim of this project is to establish a prospective multicenter cohort of hereditary ovarian cancer, based on which genetic ovarian cancer risk prediction models and pathogenesis-related studies will be conducted. For the first time, this project will establish an ovarian cancer risk prediction model suitable for Chinese people to guide the prevention and intervention of high-risk population of tumor, to explore the new pathogenesis of ovarian cancer, to guide the early diagnosis of hereditary ovarian cancer, and to promote the individualized and accurate diagnosis and treatment of hereditary ovarian cancer.

[Study design]

The aim of this project is to establish a bidirectional multi-center cohort of hereditary ovarian cancer and to describe the clinical and pathological features of hereditary ovarian cancer patients in our country. The risk prediction model of ovarian cancer for Chinese was established by following-up analysis of clinical and pathological information, genetic test results and detailed family history, to reduce the risk of cancer in first-degree relatives of carriers of pathogenic/suspected pathogenic mutations, and to guide the intervention management of high-risk population of cancer.

The study will identify novel tumor-causing mutations/predisposing genes by gene sequencing in a special family with hereditary tumor at the same time.

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2) The pathological diagnosis was clear, and no germline pathogenic or suspected pathogenic mutation was detected by gene detection.

Exclusion criteria:

1) Non-epithelial ovarian cancer was confirmed by pathology.

2) No gene detection was performed.

Topic 2: To construct a genetic ovarian cancer risk prediction model (to predict the risk of ovarian cancer in first-degree relatives)

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Exclusion criteria:

2) Female first-degree relatives did not undergo genetic testing.

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The control group was included

1) The female patients with special hereditary ovarian cancer, whose age was ≥18 years old, did not have cancer.

2) No known germline pathogenic or suspected pathogenic mutation was detected by gene detection (whole-exome sequencing).

Exclusion criteria:

2) No gene detection (whole-exome sequencing) was performed.

[Study test]

Genetic testing

[Study duration and follow-up]

If you are involved in this study, you will need to receive multiple telephone or outpatient follow-up visits.

Patients with ovarian cancer and mutation carriers will be followed up within 3 years (every 3-6 months) and 3 years (every 6 months) after surgery.

If you participate in Project 2, you will be followed up at the time of the genetic test and every 6 months after the genetic test.

The frequency of follow-up was 2 times per year for carriers of pathogenic/suspected pathogenic mutations in the family.

The follow-up included detailed medical history and family history, pelvic examination, blood routine and biochemical tests, serum CA125 level, ultrasound/CT/MRI and other imaging examinations.

[Risks]

Due to technical limitations, the results of our genetic test are only for this sample and only for scientific research. If you need further clinical decision-making, clinical genetic testing can be performed again to guide decision-making.

[If these drugs are used in the study, the study can not be continued]

Blood samples and information are collected without the use of immune suppressive drug and without the presence of any drug or alcohol abuse.

[Expenses and compensation]

This study will exempt you from the cost of genetic testing for family members other than the proband.

[Benefit]

In this study, you can obtain the genetic test results of relevant family members, for early screening and genetic block reference. And the results of this study can provide great help for more hereditary ovarian cancer families.

[Possible reasons for termination]

Your participation in the trial is voluntary, you can refuse to participate or withdraw from the trial in any way at any stage of the trial without discrimination or retaliation, and your medical treatment and rights will not be affected. If your research physician feels that it is not in your best interest to continue the study, he or she may decide to withdraw you from the study. If this occurs, you will be notified and your research physician will discuss the other options available to you.

[New information]

You will be informed of any new research findings and new treatments that arise in the course of your research.

[Privacy and confidentiality]

During the study period, your name, gender and other personal data will be replaced with code names or numbers, and be strictly confidential. Only the relevant doctors know your data and your privacy will be well protected. The results may be published in a journal, but will not reveal any of your personal information.

[How to communicate with doctors and researchers during treatment]

If you have any questions related to this study, please contact Dr. Li Yuan at 18610689868; If you need to know about the participants' rights during the study, you can contact the Ethics Committee Office of Peking University Third Hospital at (010)8226557182265176.

[Notification Statement]

"I have informed the subject of the background, objectives, steps, risks and benefits of the study (cohort study of genetic ovarian cancer risk prediction models and pathogenesis exploration) , given him/her sufficient time to read the informed consent, discuss with others, and answer questions about the study; I have informed the subject that he/she can contact (the researcher) at any time when he/she encounters problems related to the study, and that he/she can contact the General Office of Scientific Research Ethics of Peking University Third Hospital whenever he/she encounters problems related to his/her rights/interests, and provided accurate contact details; I have informed the subject that he/she can withdraw from the study at any time without any reason; I have informed the subject that he/she will be given a copy of the informed consent, which includes my signature and his/her signature."

Signature of the researcher who obtain informed consent

_____

Contact telephone

_____

Date

_____

[Statement of informed consent]

I have been informed of the background, objectives, procedures, risks and benefits of the study. I had enough time and opportunity to ask questions and I was satisfied with the answers. I was also told who to contact when I had questions, grievances, concerns, or wanted further information. I have read this informed consent form, agreed to participate in this study, and promised to provide researchers with information, laboratory test results are true and effective. I know that I can withdraw from this study at any time without any reason. I was told that I would receive a copy of this informed consent form, which included my signature and that of the researcher.

Signature of the subject

_____

Contact telephone

_____

Date

_____