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ABSTRACT

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METASTATIC OVARIAN CANCER: BIBLIOGRAPHIC ANALYSIS

Introduction. Ovarian cancer is an oncogynecological disease with high mortality. High mortality caused by this pathology is associated with diagnosis at the III–IV stage of the disease. This stage of the disease is characterized by metastasis and reflected in the 5-year survival rate, decreasing to 30.2 %. At the same time, when diagnosed at the I–II stage, this indicator is 92.6%.

The aim of the work is bibliometric analysis and generalization of data from scientific sources on the study of ovarian cancer metastasis.

Materials and methods. Information was searched on electronic resources of the Scopus, Web of Science, PubMed, and Google Scholar databases using the keywords "ovarian cancer" and "metastases." An online platform for monitoring and analyzing scientific sources was used for bibliometric analysis. We used several VOSviewer bibliometric network visualization system tools and SciVal (Scopus) modern citation requirements.

Results. It has been established that metastasis of ovarian cancer can occur in several ways and depends on the conditions of the tumor microenvironment. The influence of E-cadherin, MMP-2, and transglutaminase-2 on metastasis processes was evaluated. Also, the role of cytokines in the invasiveness of the tumor process and metastasis was established. The results of bibliometric analysis of scientific sources showed that over the past 20 years, the number of publications on ovarian cancer metastasis has increased significantly, and the most widely given topic is studied in the USA and China.

Conclusions. Metastasis of ovarian cancer can occur in several ways and depends on the conditions of the tumor microenvironment. It was found that among the analyzed 496 publications, the most relevant directions are molecular-biological and signaling pathways, which are described in many ways in scientific sources on ovarian

cancer metastasis. The calcification of peritoneal metastases and their formation mechanism are currently not investigated, and there is no thorough explanation that may become a perspective for further research.

Keywords: ovarian cancer, metastasis, bibliometric analysis, calcification.

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МЕТАСТАТИЧНИЙ РАК ЯЄЧНИКІВ: БІБЛІОГРАФІЧНИЙ АНАЛІЗ

Вступ. Рак яєчників – це онкогінекологічне захворювання з високою смертністю. Висока смертність спричинена даною патологією пов'язана із діагностуванням на пізніх (III–IV) стадіях захворювання. III–IV стадії захворювання характеризуються процесами метастазування, що має своє відображення на 5-ти річній виживаності, знижуючись до 30,2 %. В той же час, при діагностуванні на I–II стадіях даний показник складає 92,6 %.

Метою роботи є бібліометричний аналіз та узагальнення даних наукових джерел щодо вивчення метастазування раку яєчників. Було проведено пошук інформації на електронних ресурсах бази даних Scopus, Web of Science, PubMed та Google Scholar за ключовими словами «рак яєчників», «метастазування». Для бібліометричного аналізу була застосована онлайн платформа щодо моніторингу та аналізу наукових джерел з використанням ряду інструментів системи побудови візуалізації бібліометричних мереж VOSviewer та сучасних вимог цитування SciVal (Scopus).

Результати. Встановлено, що метастазування раку яєчників може відбуватись декількома шляхами та залежить від умов пухлинного мікрооточення. Оцінено вплив на процеси метастазування E-кадгерину, MMP-2, трансглутамінази-2. А також, встановлено роль цитокінів в інвазивності пухлинного процесу та метастазування. Результати бібліометричного аналізу наукових джерел продемонстрували, що за останні 20 років помітно зростає кількість публікацій про метастазування раку яєчників та найбільш широко дана тематика вивчається у США та Китаї.

Висновок. Метастазування раку яєчників може відбуватись декількома шляхами та залежить від умов пухлинного мікрооточення. Виявлено, що серед проаналізованих 496 публікацій найбільш актуальними напрямками є молекулярно-біологічний та сигнальні шляхи, що досить багатогранно описується в наукових джерелах щодо метастазування раку яєчників. Кальцифікація перитонеальних метастазів та її механізм утворення є наразі не досліджений та немає ґрунтового пояснення, що може стати перспективою в подальших досліджень.

Ключові слова: рак яєчників, метастазування, бібліометричний аналіз, кальцифікація.

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INTRODUCTION / ВСТУП

Ovarian cancer is one of the leading causes of mortality among the female population in gynecological diseases. Since no effective ovarian cancer screening program has been developed to date, this pathology, in most cases, is manifested by metastatic spread [1, 2]. In 15.7% of cases, ovarian cancer is diagnosed at the I–II stage of the disease, and in 60–70% of patients at the III–IV stage, that is, the stage of metastasis, where the 5-year survival rate drops to 30.2%, at the same time with I–II is 92.6% [3]. About 80% of women with III–IV stages of ovarian cancer experience progression or recurrence of the tumor process. This leads to a decrease in indicators of working capacity and quality of life of the female population, which constitutes a medical and social problem on a global scale. Typical for the metastatic process of ovarian cancer is intra-abdominal spread, which is manifested by peritoneal carcinomatosis [3, 4]. The most common sites of distant metastases of ovarian cancer are the pleura, lungs, heart, and lymph nodes [5, 6].

The work aims to conduct a bibliometric analysis and generalize data from scientific sources containing information on ovarian cancer metastasis.

Materials and methods

The literary data, which contained information on the ways of metastasis of ovarian cancer, were studied. We searched for information on ovarian cancer metastasis in electronic databases such as Scopus, Web of Science, PubMed, and Google Scholar using the keywords "ovarian cancer" and "metastasis". For bibliometric analysis, an online platform was established for monitoring and analyzing international scientific research using visualization tools and modern SciVal citation metrics. Also, several tools for building and visualizing bibliometric networks VOSviewer were used.

Results and discussion

We analyzed the scientific sources of the Scopus database, which included 496 publications. Electronic sources were formed into a database using the keywords "ovarian cancer" and "metastasis." According to the results of the bibliometric analysis, it was established that the number of publications on this topic over the past 20 years shows a growing trend, which indicates the relevance of this issue (Fig. 1).

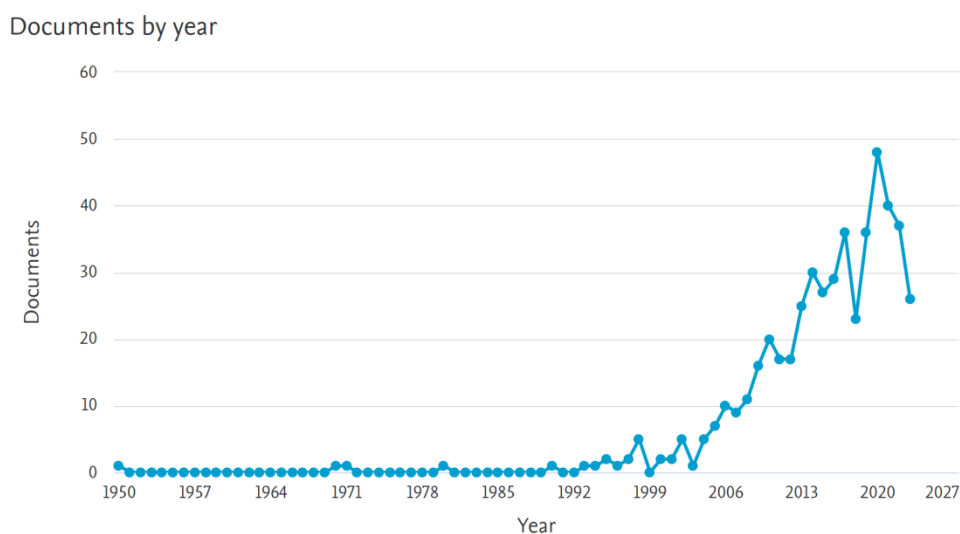


Figure 1 – Visualization of the number of publications from 1950 to 2023 using bibliometric analysis of the Scopus database

Every year, the incidence rate of ovarian cancer shows a growing trend. About 315,000 new cases of ovarian cancer are registered worldwide per year [7]. The highest incidence was found in Central and Eastern Europe, reaching 10.7 per 100,000 female population. In Northern Europe, the indicator was 8.8 per 100,000 female population [8]. At the same time, the incidence rate for North America and

Southeast Asia reached 8.1 per 100,000 population [9, 10]. This, in turn, is reflected in the interest of scientists in these countries in this issue. Therefore, based on bibliometric analysis, it was established that metastasis of ovarian cancer is widely studied in the United States of America and China. The slightest interest in this topic is observed in countries such as Italy and Hong Kong (Fig. 2).

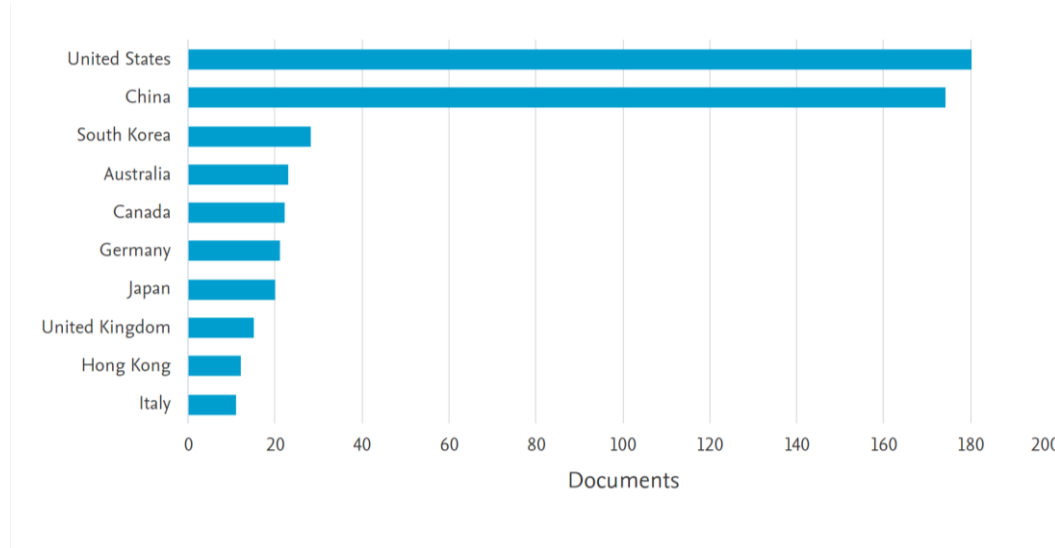


Figure 2 – The result of visualization of the number of scientific researches in Asia and Europe

A bibliometric analysis of publications in the Scopus database between 1950 and 2023 using the keywords "ovarian cancer" and "metastases" showed that the number of articles in this field has increased significantly over the past ten years, with the majority of studies conducted in the United States, China, and with a noticeable lag in the number, South Korea. These publications can be divided into 4 clusters, mainly devoted to molecular biological aspects (101), studies of signaling pathways and pharmacological perspectives of treatment (99), discussion of clinical and diagnostic data (92), and experimental studies in animal models (33) (Fig. 3).

Among the most exciting and widespread areas of publishing activity are the ways of metastasis of ovarian cancer because the process of metastasis in ovarian cancer differs from the model of hematogenous metastasis, which is characteristic of most cancers of other localizations [11]. The stages of intra- and extravasation characterize this model before the development of metastasis in one or another organ [12]. However, the metastatic process of ovarian cancer is somewhat more straightforward. After the tumor cells have separated from the primary tumor, they can be both single cells and their clusters, metastasizing according to the passive mechanism [13]. This mechanism is carried out by

the physiological movement of peritoneal fluid to the peritoneum and omentum.

Before ovarian cancer tumor cells detach and begin their metastatic journey, they undergo epithelial-mesenchymal transformation. This facilitates further attachment of epithelial cells to the basement membrane, weakening intercellular connections between tumor cells. An essential role in the adhesion of neighboring epithelial cells is played by E-cadherin, which is a membrane glycoprotein located at the junctions of cell adhesions [14]. E-cadherin binds to actin microfilaments in the cytoplasm via α - and β -catenin, thereby promoting attachment of epithelial cells to each other. In general, the loss of E-cadherin in ovarian cancer correlates with epithelial-mesenchymal transformation, contributing to invasion [15].

Based on clinical data, it is known that ovarian cancer spreads quite quickly inside the abdominal cavity but rarely metastasizes outside of it. An exciting feature of ovarian cancer is that tumor implants penetrate the layers of mesothelial cells but rarely reach the deep layers of the peritoneum [16]. Ovarian cancer tumor cells, attaching to mesothelial cells, increase the regulation of MMP-2, which further cleaves extracellular matrix proteins such as

as well as the formation of blood vessels and ascitic fluid, plays a vital role in the malignancy of the tumor process and metastasis. VEGF participates in the intraperitoneal spread of the tumor process, promoting neovascularization and permeability of vessels, which leads to the invasiveness of the procedure and the development of peritoneal carcinomatosis [26, 27].

A rather exciting phenomenon is the case described by Elhamady about the calcification of peritoneal metastases of ovarian cancer [28]. However, the mechanism of calcification of ovarian

cancer metastases has not been investigated, and there is no thorough explanation. However, the relationship between calcification and tumor metastasis is quite common [29]. Instead, calcification (pathological biomineralization) of ovarian cancer is one of the clinical and morphological signs of serous ovarian carcinomas in the early diagnosis of this pathology [30, 31].

Limitations of the study: This research include publications only in Scopus database from 1950 to 31.08.2023.

CONCLUSIONS / ВИСНОВКИ

Metastasis of ovarian cancer can occur in several ways and depends on the conditions of the tumor microenvironment. According to the results of the bibliometric analysis of 496 publications of the Scopus database using the tools of the SciVal service for the keywords "ovarian cancer" and "metastasis"

for the period 1950–2023, it was established that the majority of scientific publications are in the field of medicine. A total of 4 main clusters were identified, the most relevant directions are molecular-biological and signaling pathways, described in many ways in scientific sources on ovarian cancer metastasis, discussion of clinical and diagnostic data and experimental studies in animal models.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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None.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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