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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებში.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи.** Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html. В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებო!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე, დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემავსებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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PD-L1 EXPRESSION AND SERUM CA125: CLINICOPATHOLOGICAL CORRELATIONS IN HIGH-GRADE SEROUS OVARIAN CARCINOMA

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Abstract.

Introduction: Programmed death-ligand 1 (PD-L1) has emerged as an important immune checkpoint biomarker in ovarian cancer. However, its relationship with serum cancer antigen 125 (CA125), a routinely used biomarker for disease monitoring, remains insufficiently investigated, particularly in patients with high-grade serous ovarian carcinoma (HGSC).

Aim: To evaluate the association between PD-L1 expression and serum CA125 levels in patients with high-grade serous ovarian carcinoma and to investigate the relationships of PD-L1 expression with age and FIGO stage.

Materials and Methods: This retrospective case-control study included 69 women treated for ovarian tumors between 2018 and 2025, comprising 42 patients with histologically confirmed HGSC and 27 patients with benign epithelial ovarian tumors serving as controls. PD-L1 expression was assessed immunohistochemically using the VENTANA PD-L1 (SP263) assay and evaluated by the Tumor Proportion Score (TPS), with positivity defined as TPS $\geq 1\%$. Serum CA125 levels were categorized as ≤ 35 U/mL or > 35 U/mL. Statistical analyses included Pearson's chi-square test, Fisher's exact test, and odds ratios (ORs) with 95% confidence intervals (CIs), with statistical significance defined as $p < 0.05$.

Results: PD-L1 expression was detected in 17 (24.6%) of the 69 patients, including 16/42 (38.1%) patients with HGSC and 1/27 (3.7%) controls. PD-L1 positivity was significantly more frequent in HGSC than in benign tumors (OR=16.0; 95% CI 1.97–129.64; $p=0.0012$). Within the HGSC cohort, CA125 > 35 U/mL was observed in 13/16 (81.3%) PD-L1-positive and 22/26 (84.6%) PD-L1-negative patients. No significant association was identified between CA125 category and PD-L1 expression (OR=0.79; 95% CI 0.15–4.09; Fisher's exact $p=1.000$). No statistically significant associations were observed between PD-L1 expression and age ($p=0.454$) or FIGO stage ($p=0.978$).

Conclusion: PD-L1 expression was significantly more frequent in HGSC than in benign epithelial ovarian tumors. However, the initially observed association between PD-L1 expression and elevated serum CA125 was not confirmed when the analysis was restricted to the 42-patient HGSC cohort. Larger studies are needed to clarify the relationship between PD-L1 and CA125 within HGSC.

Key words. High-grade serous ovarian carcinoma, PD-L1, CA125.

Introduction.

Ovarian cancer remains one of the most lethal gynecological malignancies worldwide and is among the leading causes of cancer-related death in women. The high mortality rate is largely attributable to the absence of effective screening

methods, nonspecific early symptoms, and the fact that most patients are diagnosed at an advanced stage of disease [1-4]. Among epithelial ovarian cancers, high-grade serous carcinoma (HGSC) is the predominant histological subtype, accounting for approximately 70–80% of ovarian cancer-related deaths [2,3]. Despite advances in cytoreductive surgery and platinum-based chemotherapy, the prognosis of HGSC remains poor because of frequent recurrence, development of chemoresistance, and disease progression [2,3].

In recent years, increasing attention has been directed toward the interaction between ovarian cancer cells and the tumor immune microenvironment. One of the key mechanisms by which tumor cells evade immune surveillance involves PD-L1, an immune checkpoint molecule expressed on tumor cells and various immune cells within the tumor microenvironment. Binding of PD-L1 to programmed death 1 suppresses T-cell activation and proliferation, thereby facilitating immune escape and tumor progression [5-7]. Consequently, PD-L1 has emerged as both a potential prognostic biomarker and a predictive marker for response to immune checkpoint inhibitors in several solid malignancies [5,7].

The prognostic significance of PD-L1 expression in ovarian cancer remains controversial. While several studies have reported that increased expression is associated with advanced disease, poor survival, and resistance to chemotherapy, others have demonstrated no significant association or even favorable clinical outcomes [8,9]. These conflicting findings may be explained by differences in study populations, histological subtypes, antibodies used for immunohistochemical staining, scoring systems, and positivity thresholds. Therefore, further investigations focusing on homogeneous patient populations, particularly HGSC, are warranted.

CA125 is the most widely used serum biomarker in ovarian cancer and plays a pivotal role in clinical practice. Although it lacks sufficient specificity for early diagnosis, it remains an indispensable marker for evaluating disease burden, monitoring treatment response, and detecting recurrence [10-14]. Elevated serum CA125 levels generally reflect greater tumor burden and advanced disease; however, the relationship between CA125 and immune checkpoint molecules such as PD-L1 has not yet been fully elucidated.

The association between PD-L1 expression and serum CA125 levels may provide valuable insights into the biological behavior of HGSC. If a significant relationship exists, combined assessment of these biomarkers could improve risk stratification, identify patients with a more aggressive disease phenotype, and potentially aid in selecting candidates for immunotherapy. Moreover, understanding the interplay between systemic tumor burden, represented by CA125, and immune

evasion mechanisms, represented by PD-L1, may contribute to the development of more personalized therapeutic strategies [5,8,9,11,14-16].

Although numerous studies have investigated PD-L1 expression in epithelial ovarian cancer, relatively few have specifically examined its relationship with serum CA125 levels in patients with HGSC. This lack of evidence highlights the need for additional studies exploring the clinical significance of these biomarkers in a homogeneous histological subtype.

Aim. To investigate the association between PD-L1 expression and serum CA125 levels in patients with HGSC and to evaluate the relationships of PD-L1 expression with age and FIGO stage.

Materials and Methods.

This retrospective study was conducted at the Oncologic Clinic of Azerbaijan Medical University and the National Center of Oncology. Patients who underwent surgical treatment for ovarian tumors between 2018 and 2025 and had available clinicopathological and immunohistochemical data were included.

A total of 69 patients were enrolled, including 42 patients with histologically confirmed high-grade serous ovarian carcinoma and 27 patients with benign epithelial ovarian tumors, who served as the control group. Histopathological diagnoses were established according to the 2020 World Health Organization Classification of Female Genital Tumours. The benign control group comprised 11 serous cystadenomas, 8 serous cystadenofibromas, 6 mucinous cystadenomas, and 2 mucinous cystadenofibromas.

Demographic and clinicopathological characteristics, including age, FIGO stage, serum CA125 level, and PD-L1 expression, were obtained from medical records and pathology reports. Serum CA125 concentrations were measured preoperatively using a standard electrochemiluminescence immunoassay and categorized as 35 U/mL or lower or above 35 U/mL. Tumor staging was determined according to the International Federation of Gynecology and Obstetrics staging system.

Immunohistochemical staining for PD-L1 was performed on 4-μm-thick formalin-fixed paraffin-embedded tissue sections

using the VENTANA BenchMark ULTRA automated staining platform. PD-L1 expression was assessed using the VENTANA PD-L1 SP263 rabbit monoclonal antibody according to the manufacturer's recommended protocol. Tumor cell staining was evaluated using the tumor proportion score, defined as the percentage of viable tumor cells showing partial or complete membranous staining at any intensity. Expression was considered positive when the TPS was at least 1% and negative when it was below 1%. All immunohistochemical slides were independently evaluated by an experienced pathologist blinded to the clinical and laboratory findings.

Statistical analyses were performed using IBM SPSS Statistics version 26.0. Categorical variables are presented as frequencies and percentages. Comparisons between groups were performed using the Pearson chi-square test, while Fisher's exact test was applied when the expected cell frequency was less than five. The strength of associations was evaluated using odds ratios with exact 95% confidence intervals. For the primary analysis, the association between PD-L1 expression and serum CA125 category was specifically re-evaluated within the 42-patient HGSC cohort. A two-sided p-value below 0.05 was considered statistically significant.

Results and Discussion.

A total of 69 women were included, comprising 42 patients with HGSC and 27 women with benign epithelial ovarian tumors. The HGSC group represented 60.9% (42/69) of the study population, while the control group accounted for 39.1% (27/69). The mean age was 53.9±1.9 years, with a range of 14–83 years. The largest proportion of participants belonged to the 50–59-year age group (21/69, 30.4%), followed by the 60–69-year group (20/69, 29.0%). Nine patients (13.0%) were aged ≥70 years. The main clinicopathological characteristics are summarized in Table 1.

The benign control group consisted of 11 serous cystadenomas, 8 serous cystadenofibromas, 6 mucinous cystadenomas, and 2 mucinous cystadenofibromas.

PD-L1 expression was detected in 17/69 patients (24.6%), whereas 52/69 (75.4%) were negative. The distribution

Table 1. Clinicopathological characteristics of the study population.

Characteristic	n	%
Total study population	69	100.0
HGSC	42	60.9
Benign epithelial ovarian tumors	27	39.1
PD-L1 positive	17	24.6
PD-L1 negative	52	75.4
Age <40 years	13	18.8
Age 40–49 years	6	8.7
Age 50–59 years	21	30.4
Age 60–69 years	20	29.0
Age ≥70 years	9	13.0

Table 2. Distribution of serum CA125 according to PD-L1 expression in the HGSC cohort.

PD-L1 status	CA125 ≤35 U/mL, n (%)	CA125 >35 U/mL, n (%)	Total, n
Positive	3 (18.8)	13 (81.3)	16
Negative	4 (15.4)	22 (84.6)	26
Total	7 (16.7)	35 (83.3)	42

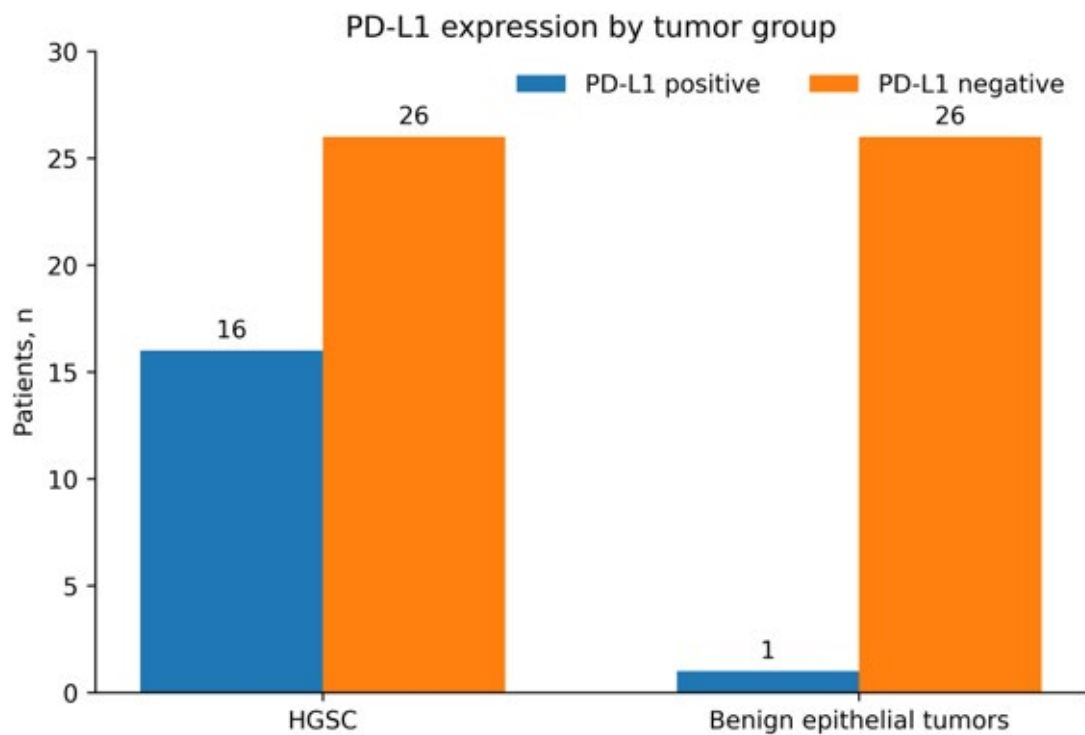


Figure 1. Programmed death ligand 1 expression according to tumor group.

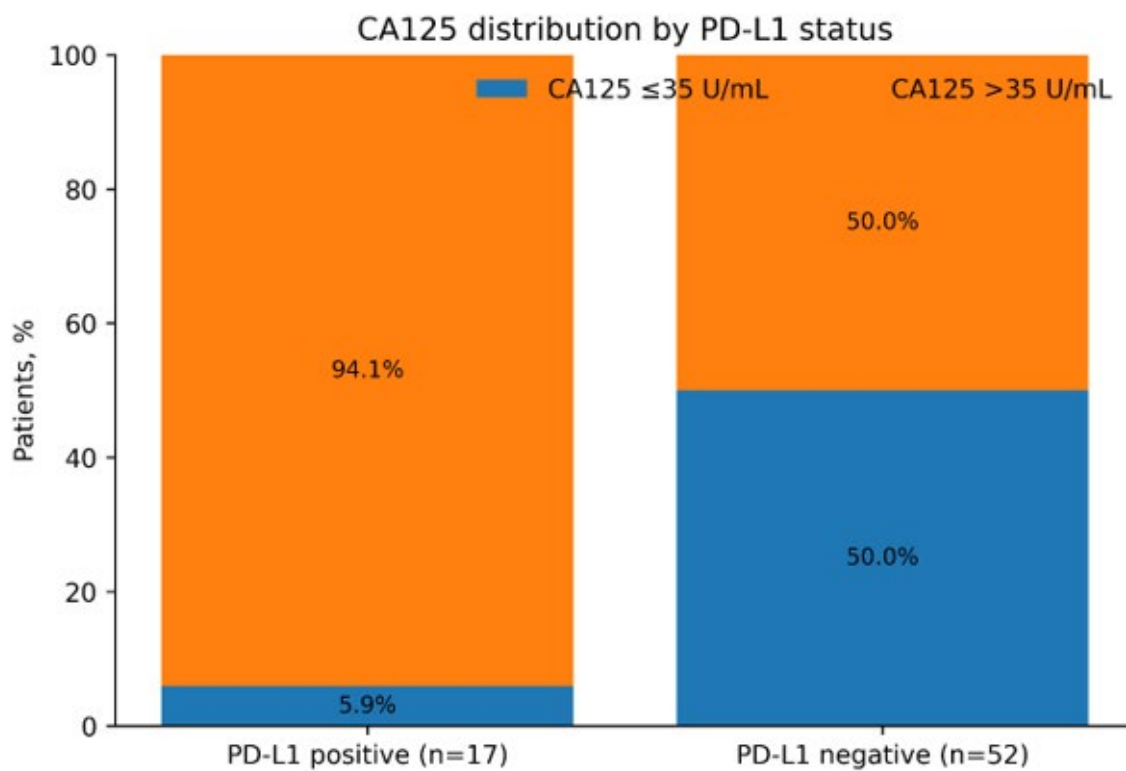


Figure 2. Distribution of serum CA125 categories according to PD-L1 status in HGSC.

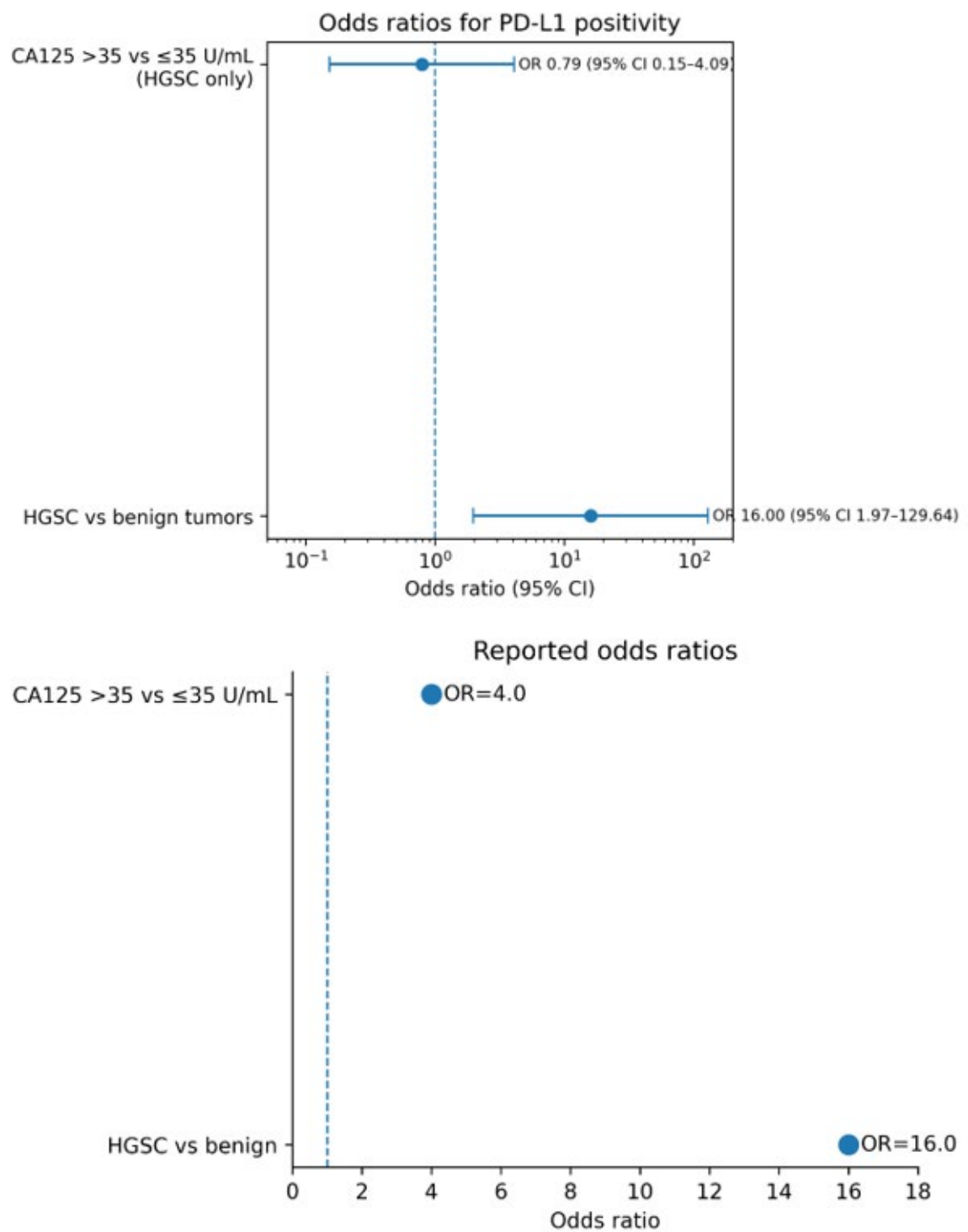


Figure 3. Odds ratios for PD-L1 positivity with 95% confidence intervals.

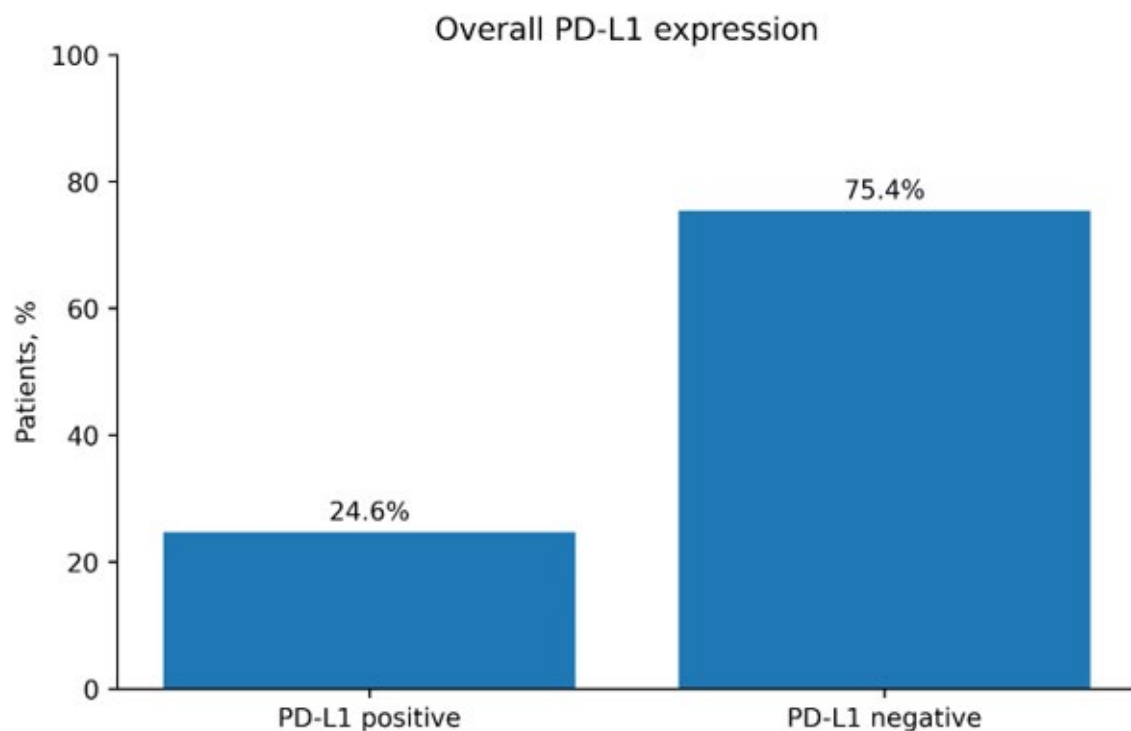


Figure 4. Overall distribution of PD-L1 expression: 17/69 (24.6%) positive and 52/69 (75.4%) negative.

according to age groups did not differ significantly ($\chi^2=3.658$, $p=0.454$). Although positivity was numerically more frequent among patients aged 60–69 years (41.2% of positive cases), no statistically significant association with age was identified.

Within the HGSC cohort, most patients were diagnosed with FIGO stage III disease, representing 69.2% of PD-L1-negative cases and 68.7% of PD-L1-positive cases. No significant association was observed between PD-L1 expression and FIGO stage ($\chi^2=0.045$, $p=0.978$).

A statistically significant difference in PD-L1 expression was observed between the HGSC and control groups. Among the 17 positive cases, 16/17 (94.1%) belonged to the HGSC group and 1/17 (5.9%) to the control group. Among the 52 negative cases, 26/52 (50.0%) belonged to each group. The association was significant ($\chi^2=10.47$, $p=0.0012$), with an odds ratio of 16.0 (95% CI 1.97–129.64). Thus, patients with HGSC had substantially higher odds of PD-L1 positivity than patients with benign epithelial ovarian tumors.

Positive expression was observed in 16/42 (38.1%) patients with HGSC and 1/27 (3.7%) patients with benign epithelial ovarian tumors.

Within the HGSC cohort, the relationship between serum CA125 and PD-L1 expression was re-evaluated as requested. Elevated CA125 levels above 35 U/mL were observed in 13/16 (81.3%) PD-L1-positive patients and 22/26 (84.6%) PD-L1-negative patients. No statistically significant association was identified (Pearson $\chi^2=0.08$, $p=0.7763$; Fisher's exact $p=1.000$). The odds ratio for PD-L1 positivity comparing CA125 >35 U/mL with CA125 ≤35 U/mL was 0.79 (95% CI 0.15–4.09), indicating a wide confidence interval and substantial uncertainty around the estimate.

Pearson $\chi^2=0.08$, $p=0.7763$; Fisher's exact $p=1.000$; OR=0.79 (95% CI 0.15–4.09).

HGSC versus benign tumors, OR=16.0 (95% CI 1.97–129.64); CA125 >35 U/mL versus ≤35 U/mL within HGSC, OR=0.79 (95% CI 0.15–4.09).

The principal findings of the study were that PD-L1 expression was significantly more frequent in HGSC than in benign epithelial ovarian tumors, whereas the initially observed association between elevated serum CA125 and PD-L1 positivity was not confirmed when the analysis was restricted to the 42-patient HGSC cohort. No significant associations were observed with age or FIGO stage.

HGSC is characterized by marked genomic instability, aggressive biological behavior, and a highly immunogenic tumor microenvironment. Increasing evidence indicates that immune checkpoint molecules, particularly PD-L1, contribute to immune evasion and disease progression. In the present study, PD-L1 positivity was significantly more frequent in the HGSC group than in the control group, with an odds ratio of 16.0. This finding is consistent with previous reports indicating that PD-L1 expression is more common in malignant ovarian tumors than in benign ovarian lesions [17,18–20].

The primary analysis initially suggested an association between serum CA125 and PD-L1 expression when HGSC and benign tumors were considered together. However, this relationship was not maintained after restricting the analysis to the 42 patients with HGSC. Within HGSC, CA125 >35 U/mL was present in 81.3% of PD-L1-positive and 84.6% of PD-L1-negative patients, with OR=0.79 (95% CI 0.15–4.09; Fisher's exact $p=1.000$). The wide confidence interval reflects the limited sample size and indicates substantial uncertainty in the estimate. These findings suggest that the association observed

in the combined cohort was likely influenced by the difference in disease status between HGSC and benign controls rather than representing a clear relationship within HGSC itself.

The absence of a significant association within HGSC does not exclude a biological relationship between tumor burden and immune checkpoint activity, but the present data are insufficient to establish such a relationship. CA125 can also be elevated in benign gynecologic conditions, which further supports the importance of restricting biomarker analyses to clinically homogeneous populations.

No significant association was identified between PD-L1 expression and age ($p=0.454$). Likewise, no statistically significant relationship was observed with FIGO stage ($p=0.978$). Most patients in both PD-L1 groups presented with stage III disease, which may have limited the ability to identify differences across stages. Differences among studies may also be related to patient populations, antibodies, scoring systems, and positivity thresholds [17-20].

The study has several strengths. It focused on a homogeneous high-grade serous ovarian carcinoma population, used the SP263 antibody with a predefined TPS threshold, and included a benign epithelial ovarian tumor control group. The main limitations are the retrospective design, limited sample size, absence of survival, recurrence, and treatment-response analyses, and assessment of tumor-cell PD-L1 without evaluation of immune-cell expression or other components of the tumor microenvironment.

Taken together, the findings support the value of carefully stratified analyses when evaluating PD-L1 and serum CA125. Larger prospective studies with adequate statistical power are required to determine whether either biomarker provides independent prognostic or predictive information within HGSC.

Conclusion.

In conclusion, PD-L1 expression was significantly more frequent in patients with HGSC than in patients with benign epithelial ovarian tumors. However, the initially observed association between elevated serum CA125 and PD-L1 positivity was not confirmed when the analysis was restricted to the HGSC cohort. Within HGSC, CA125 >35 U/mL was not significantly associated with PD-L1 expression (OR=0.79; 95% CI 0.15–4.09; Fisher's exact $p=1.000$).

No significant associations were identified between PD-L1 expression and patient age or FIGO stage. These findings should be interpreted in the context of the retrospective design and limited sample size.

The results emphasize the importance of evaluating biomarker associations within homogeneous histological groups rather than allowing differences between malignant and benign tumors to drive the observed association. Further large-scale prospective studies are warranted to clarify the clinical and biological relationship between PD-L1 and CA125 in HGSC.

Further large-scale, prospective, multicenter studies are warranted to validate these findings and to determine whether combined PD-L1 and CA125 assessment has independent prognostic or predictive significance in high-grade serous ovarian carcinoma.

Conflict of Interest.

The authors have no conflicts of interest to declare.

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АННОТАЦИЯ

Введение: Лиганд программируемой клеточной смерти 1 (PD-L1) рассматривается как важный биомаркер иммунных контрольных точек при раке яичников. Однако взаимосвязь между экспрессией PD-L1 и уровнем сывороточного ракового антигена 125 (CA125), широко используемого для мониторинга заболевания, остается недостаточно изученной, особенно у пациенток с высокозлокачественной серозной карциномой яичника (HGSC).

Цель: Оценить взаимосвязь между экспрессией PD-L1 и уровнем сывороточного CA125 у пациенток с высокозлокачественной серозной карциномой яичника, а также изучить взаимосвязь экспрессии PD-L1 с возрастом пациенток и стадией заболевания по классификации FIGO.

Материалы и методы: В данное ретроспективное исследование типа «случай–контроль» были включены 69 женщин, проходивших лечение по поводу опухолей яичника в период с 2018 по 2025 год. Основную группу составили 42 пациентки с гистологически подтвержденной высокозлокачественной серозной карциномой яичника, контрольную группу — 27 пациенток с доброкачественными эпителиальными опухолями яичника. Экспрессия PD-L1 оценивалась иммуногистохимическим методом с использованием набора VENTANA PD-L1 (SP263) и определялась по показателю доли опухолевых клеток (Tumor Proportion Score, TPS); положительной считалась экспрессия при $TPS \geq 1\%$. Уровень сывороточного CA125 классифицировали как ≤ 35 Ед/мл или >35 Ед/мл. Статистический анализ включал критерий χ^2 Пирсона, точный критерий Фишера и отношение шансов (OR) с 95% доверительным интервалом (ДИ); статистически значимыми считались различия при $p < 0,05$.

Результаты: Экспрессия PD-L1 была выявлена у 17 (24,6%) из 69 пациенток, включая 16/42 (38,1%) пациенток с HGSC и 1/27 (3,7%) пациенток контрольной группы. PD-L1 значительно чаще выявлялся при HGSC, чем при доброкачественных опухолях (OR=16.0; 95% ДИ 1.97–129.64; $p=0,0012$). В пределах группы HGSC уровень CA125 >35 Ед/мл отмечался у 13/16 (81,3%) PD-L1-положительных и 22/26 (84,6%) PD-L1-отрицательных пациенток. Статистически значимой связи между категорией CA125 и экспрессией PD-L1 не выявлено (OR=0.79; 95% ДИ 0.15–4.09; точный критерий Фишера $p=1,000$). Статистически значимой взаимосвязи между экспрессией PD-L1 и возрастом ($p=0,454$) или стадией FIGO ($p=0,978$) не выявлено.

Заключение: Экспрессия PD-L1 значительно чаще выявлялась при HGSC, чем при доброкачественных эпителиальных опухолях яичника. Однако первоначально выявленная связь между экспрессией PD-L1 и повышенным уровнем CA125 не подтвердилась при анализе, ограниченном 42 пациентками с HGSC. Для уточнения взаимосвязи между PD-L1 и CA125 при HGSC необходимы более крупные исследования.

Ключевые слова: высокозлокачественная серозная карцинома яичника, PD-L1, CA125.

რეზიუმე

დასკვნა: PD-L1-ის ექსპრესია მნიშვნელოვნად უფრო ხშირად გამოვლინდა HGSC-ის მქონე პაციენტებში, ვიდრე საკვერცხის კეთილთვისებიანი ეპითელური სიმსივნეების მქონე პაციენტებში. თუმცა PD-L1-ის ექსპრესიასა და შრატის CA125-ის მომატებულ დონეს შორის თავდაპირველად გამოვლენილი კავშირი არ დადასტურდა, როდესაც ანალიზი მხოლოდ HGSC-ის 42 პაციენტით შემოიფარგლა. HGSC-ის ფარგლებში PD-L1-სა და CA125-ს შორის კავშირის დასაზუსტებლად საჭიროა უფრო დიდი კვლევები.

შედეგები: PD-L1-ის ექსპრესია გამოვლინდა 69 პაციენტიდან 17-ში (24.6%), მათ შორის HGSC-ის 42 პაციენტიდან 16-ში (38.1%) და საკონტროლო ჯგუფის 27 პაციენტიდან 1-ში (3.7%). PD-L1-ის დადებითი ექსპრესია მნიშვნელოვნად უფრო ხშირად აღინიშნებოდა HGSC-ში, ვიდრე კეთილთვისებიან სიმსივნეებში (OR=16.0; 95% CI 1.97–129.64; $p=0.0012$). HGSC-ის ჯგუფში CA125 >35 U/mL PD-L1-დადებითი პაციენტების 13/16-ში (81.3%) და PD-L1-უარყოფითი პაციენტების 22/26-ში (84.6%) აღინიშნებოდა. CA125-ის კატეგორიასა და PD-L1-ის ექსპრესიას შორის სტატისტიკურად მნიშვნელოვანი კავშირი არ გამოვლენილა (OR=0.79; 95% CI 0.15–4.09; Fisher-ის ზუსტი ტესტი $p=1.000$). PD-L1-ის ექსპრესიასა და ასაკს ($p=0.454$) ან FIGO-ის სტადიას ($p=0.978$) შორის სტატისტიკურად მნიშვნელოვანი კავშირი არ გამოვლენილა.

მასალა და მეთოდები: რეტროსპექტულ შემთხვევა-კონტროლის კვლევაში ჩართული იყო საკვერცხის სიმსივნისგამო 2018–2025 წლებში მკურნალობაგავლილი 69 ქალი: ჰისტოლოგიურად დადასტურებული HGSC-ის მქონე 42 პაციენტი და კეთილთვისებიანი ეპითელური საკვერცხის სიმსივნის მქონე 27 პაციენტი, რომლებიც საკონტროლო ჯგუფს წარმოადგენდნენ. PD-L1-ის ექსპრესია შეფასდა იმუნოჰისტოქიმიურად VENTANA PD-L1 (SP263) ტესტის გამოყენებით და განისაზღვრა სიმსივნური უჯრედების წილის მაჩვენებლით (TPS); დადებითად ჩაითვა TPS $\geq 1\%$. შრატის CA125 კლასიფიცირდა ≤ 35 U/mL და >35 U/mL კატეგორიებად. სტატისტიკური ანალიზი მოიცავდა Pearson-ის χ^2 ტესტს, Fisher-ის ზუსტ ტესტს და 95%-იანი სანდოობის ინტერვალებით (CI) OR-ის გაანგარიშებას; სტატისტიკურად მნიშვნელოვნად ჩაითვა $p < 0.05$.

მიზანი: მაღალი ხარისხის სეროზული საკვერცხის კარცინომის მქონე პაციენტებში PD-L1-ის ექსპრესიასა და შრატის CA125-ის დონეს შორის კავშირის შეფასება და PD-L1-ის ექსპრესიის ასაკთან და FIGO სტადიასთან ურთიერთობის შესწავლა.

შესავალი: პროგრამირებული უჯრედული სიკვდილის ლიგანდი 1 (PD-L1) განიხილება როგორც მნიშვნელოვანი იმუნური საკონტროლო წერტილის ბიომარკერი საკვერცხის კიბოს დროს. თუმცა PD-L1-ის ექსპრესიასა და შრატის კიბოს ანტიგენ 125-ის (CA125) დონეს შორის ურთიერთკავშირი, განსაკუთრებით მაღალი ხარისხის სეროზული საკვერცხის კარცინომის (HGSC) მქონე პაციენტებში, არასაკმარისად არის შესწავლილი.

საკვანძო სიტყვები: მაღალი ხარისხის სეროზული საკვერცხის კარცინომა, PD-L1, CA125.