

TRENDS IN INCIDENCE AND MORTALITY OF OVARIAN CANCER IN THE REPUBLIC OF TAJIKISTAN: ANALYSIS BASED ON THE CLINICAL MATERIAL OF PATIENTS WITH PERITONEAL CARCINOMATOSIS WHO RECEIVED PIPAC

<https://doi.org/10.5281/zenodo.19275614>

Muzaffarzoda Matluba Muzafar

Deputy Director for Clinical Affairs, Candidate of Medical Sciences, Scientific Cancer Center of the Republic of Tajikistan. Republic of Tajikistsn. Tel: 992 918752100

Маълумот дар бораи муаллиф: Музаффарзода Матлуба Музафар - номзади илмҳои тиб, муовини директор оид ба корҳои таъбабатӣ, Маркази илмии саратоншиносии Ҷумҳурии Тоҷикистон. Ҷумҳурии Тоҷикистон. Тел: +992 918 75 21 00

Abstract

This article examines contemporary issues related to the epidemiology, pathogenesis, diagnosis, and treatment strategy of ovarian cancer. Based on an analysis of high-level international sources (CA Cancer J Clin, The Lancet, NCCN, ESMO) and modern clinical experience, the main trends in disease incidence and mortality, as well as the specific features of peritoneal carcinomatosis spread, are considered.

Special attention is paid to the evaluation of innovative treatment methods, including pressurized intraperitoneal aerosol chemotherapy (PIPAC), hyperthermic intraperitoneal chemotherapy (HIPEC), and the use of targeted therapy and PARP inhibitors.

The results of the analysis show that the integration of multimodal approaches (surgery + systemic + local therapy), together with precise patient stratification (using PCI, CRS, and PRGS), may contribute to improved survival outcomes and disease control.

Keywords

ovarian cancer; peritoneal carcinomatosis; PIPAC; HIPEC; PARP inhibitors; epidemiology; PCI; CRS; PRGS; targeted therapy; survival; oncology.

Аннотатсия

Мақолаи мазкур ба таҳқиқи муосири масъалаҳои эпидемиология, патогенез, тахҳис ва тактикаи муолиҷаи саратони тухмдон таҳқиқ шудааст. Дар заминаи таҳлили манбаъҳои байналмилалӣ сатҳи баланд (CA Cancer J Clin, The Lancet, NCCN, ESMO) ва таҷрибаи клиникӣ муосир, равандҳои асосӣ тағйирёбии нишондиҳандаҳои беморӣ ва ғавт, инчунин хусусиятҳои паҳншавии карсиноматози перитонеалӣ баррасӣ гардидаанд.

Таваччуҳи махсус ба арзёбии усулҳои инноватсионии муолиҷа, аз ҷумла химиотерапияи дохилишикамии аэрозолӣ зери фишор (PIPAC), гипертермияи дохилишикамӣ (HIPEC), инчунин истифодаи терапияи ҳадафнок ва PARP-ингибиторҳо равона шудааст.

Натиҷаҳои таҳлил нишон медиҳанд, ки ҳамгироии равишҳои мультимодалӣ (ҷарроҳӣ + системӣ + локалӣ) дар якҷоягӣ бо стратификацияи дақиқи беморон (бо истифода аз PCI, CRS, PRGS) метавонад ба беҳбудии нишондиҳандаҳои зиндамонӣ ва назорати беморӣ мусоидат намояд.

Калидвожаҳо

саратони тухмдон; карсиноматози перитонеалӣ; PIPAC; HIPEC; PARP-ингибиторҳо; эпидемиология; PCI; CRS; PRGS; терапияи ҳадафнок; зиндамонӣ; oncology.

Аннотация

Настоящая статья посвящена современному исследованию вопросов эпидемиологии, патогенеза, диагностики и тактики лечения рака яичников. На основе анализа высокорейтинговых международных источников (CA Cancer Journal for Clinicians, *The Lancet*, рекомендации NCCN и ESMO), а также современных клинических данных, рассмотрены основные тенденции изменения показателей заболеваемости и смертности, а также особенности распространения перитонеального карциноматоза.

Особое внимание уделено оценке инновационных методов лечения, включая внутрибрюшинную аэрозольную химиотерапию под давлением (PIPAC), гипертермическую внутрибрюшинную химиотерапию (HIPEC), а также применению таргетной терапии и ингибиторов PARP.

Результаты анализа показывают, что интеграция мультимодальных подходов (хирургическое + системное + локальное лечение) в сочетании с точной стратификацией пациентов (с использованием PCI, CRS, PRGS) способствует улучшению показателей выживаемости и контроля заболевания.

Ключевые Слова

рак яичников; перитонеальный карциноматоз; PIPAC; HIPEC; ингибиторы PARP; эпидемиология; PCI; CRS; PRGS; таргетная терапия; выживаемость; онкология.

Research Methodology: The study was conducted on the basis of the paradigm of evidence-based medicine (EBM) and a systematic analysis of the scientific literature.

Main methods:

bibliographic analysis of Q1 sources (PubMed, Scopus)

meta-analysis and comparison of clinical outcomes
analysis of international guidelines (NCCN, ESMO)
biostatistical methods (OS, PFS, response rate)
stratification analysis (PCI, ECOG, CRS)

Study design:

analytical review

elements of comparative clinical evaluation

Scientific Novelty

The main novelty of the study is expressed in the following aspects:

Comparative evaluation of the effectiveness of PIPAC and HIPEC as locoregional treatment strategies.

Integration of morphological indicators (CRS, PRGS) into the clinical decision-making algorithm.

Proposal of an optimal multimodal therapy model for patients with peritoneal carcinomatosis.

Integrated analysis of the effect of targeted therapy and immunotherapy under conditions of drug resistance.

Adaptation of international approaches to the conditions of the national healthcare system.

Article Summary: The article analyzes ovarian cancer as one of the most challenging oncologic neoplasms, characterized by late diagnosis and a high mortality rate. Pathogenetic mechanisms, including the role of TP53 mutations, the tumor microenvironment, and peritoneal dissemination, are explained in detail.

In the clinical section, the effectiveness of conventional treatment (cytoreductive surgery + chemotherapy) is analyzed in comparison with newer methods (PIPAC, HIPEC, PARP inhibitors), and it is shown that innovative strategies may improve disease control in patients with a high PCI level.

In conclusion, the study substantiates the need to shift toward a personalized oncology model and the broad implementation of modern technologies in clinical practice.

Introduction

Ovarian cancer is one of the highly lethal neoplasms in the structure of gynecologic oncology and in most cases is diagnosed at advanced stages, with peritoneal carcinomatosis, ascites, and a high tumor burden [1, p. 209–249; 4, p. 284–296]. Therefore, the analysis of clinical trends, stage distribution, and follow-up outcomes in patients with this disease is of key importance for assessing the actual clinical situation.

At the same time, it should be emphasized methodologically that the presented material is not a national population-based registry, but rather a selected clinical database

of patients with ovarian cancer/peritoneal carcinomatosis in whom PIPAC was used. Therefore, the results below reflect not national trends in incidence and mortality, but rather referral trends, clinical structure, the level of disease progression, and intraco hort follow-up outcomes.

Ovarian cancer is one of the highly lethal neoplasms in the structure of gynecologic oncology and in most cases is diagnosed at advanced stages, with peritoneal carcinomatosis, ascites, and a high tumor burden. Therefore, the analysis of clinical trends, stage distribution, and follow-up outcomes in patients with this disease is of key importance for assessing the actual clinical situation.

At the same time, it should be emphasized methodologically that the presented material is not a national population-based registry, but rather a selected clinical database of patients with ovarian cancer/peritoneal carcinomatosis in whom PIPAC was used. Therefore, the results below reflect not national trends in incidence and mortality, but rather referral trends, clinical structure, the level of disease progression, and intraco hort follow-up outcomes.

1. Material and Method of Analysis

The analysis was carried out on the basis of the presented clinical table. According to the data of the main sheet, a total of 53 patients were included in the analysis. The following indicators were used for the study:

- date of first presentation;
- age;
- region of residence;
- ECOG and ASA;
- morphological characteristics;
- TNM staging;
- type of cytoreduction;
- number of PIPAC cycles;
- clinical and pathomorphological response;
- follow-up data: progression, date of last observation, vital status.

2. General Characteristics of the Cohort

According to the analysis, the age of patients ranged from 31 to 71 years, with a mean age of 55.3 years and a median age of 55 years. This indicates that most patients belonged to the perimenopausal and postmenopausal age groups, which is consistent with the general epidemiologic patterns of ovarian cancer [5, p. 1240-1253; 19, p. 287-299]. According to the analysis, the age of patients ranged from 31 to 71 years, with a mean age of 55.3 years and a median age of 55 years. This indicates that most patients belonged to the perimenopausal and postmenopausal age groups, which is consistent with the general epidemiologic patterns of ovarian cancer.

From the perspective of functional status, most patients were in a relatively acceptable condition for specific treatment:

ECOG 0 - 39 patients (73.6%);

ECOG 1 - 14 patients (26.4%).

This structure shows that even in the setting of advanced disease, the selection of patients for PIPAC was mainly carried out among those with a relatively preserved general condition.

3. Referral Trend and Patient Enrollment into the Cohort

According to the date of first presentation to the institution, a marked increase in the number of patients was observed in recent years:

2020 - 1 case;

2021 - 1 case;

2022 - 11 cases;

2023 - 14 cases;

2024 - 23 cases.

This trend may primarily be associated with three factors:

expansion of patient inclusion in intraperitoneal treatment protocols;

improved diagnosis of peritoneal-stage ovarian cancer;

increased referral of patients with recurrent or persistent disease to a specialized center.

From this, it can be concluded that this material demonstrates an upward trend in the clinical flow of patients to the center; however, this cannot be directly interpreted as an increase in national incidence.

4. Regional Structure of Patients

The distribution of patients by region was as follows:

Dushanbe - 18 patients;

districts of republican subordination - 17 patients;

Khatlon region - 14 patients;

Sughd region - 3 patients;

GBAO - 2 patients.

By living conditions, 25 patients were from rural areas and 20 from urban areas (data for the remaining cases are incomplete). This indicates that ovarian cancer with peritoneal carcinomatosis is not solely an urban issue, and access of rural patients to specialized centers has also gradually improved.

5. Morphological and Stage Characteristics

The analysis shows that the morphological structure of the cohort almost completely corresponds to the classical clinical pattern of advanced ovarian cancer [5, p. 1240-1253; 8,

p. 280-304]: the analysis showed that the morphological structure of the cohort almost completely corresponded to the classical clinical pattern of advanced ovarian cancer:

serous adenocarcinoma – 49 cases (92.5%);

mucinous adenocarcinoma – 1 case;

carcinosarcoma – 1 case;

in 2 cases, the data were not completely recorded.

From the point of view of stage distribution, a clear predominance of advanced local-peritoneal forms was observed:

T3c - 35 cases;

T3b - 11 cases;

T3a - 2 cases.

Thus, the majority of patients belonged to the group with a high tumor burden and extensive peritoneal dissemination. This explains why mortality and progression in such a cohort usually remain relatively high.

6. Treatment Characteristics and Cytoreduction

According to the type of cytoreduction, the following results were obtained [9, p. 377-382; 12, p. 230-240]: according to the type of cytoreduction, the following results were obtained:

optimal cytoreduction – 22 cases;

suboptimal cytoreduction – 22 cases;

non-optimal cytoreduction – 8 cases.

This indicates that only in a proportion of patients was optimal tumor volume reduction achievable, whereas in a substantial proportion residual tumor burden remained. From the perspective of surgical oncology, such a structure is fully consistent with the high prevalence of T3c disease and peritoneal carcinomatosis.

7. PIPAC Indicators and Peritoneal Tumor Burden

Among patients with complete data, the total number of PIPAC sessions was as follows [20, p. 107250; 21, p. 1845-1856]: among patients with complete data, the total number of PIPAC sessions was as follows:

3 PIPAC - 35 patients;

2 PIPAC - 13 patients.

The median number of PIPAC procedures was approximately 3.

The initial peritoneal carcinomatosis index (PCI) was high:

mean - 37.4;

median - 38.5.

This level indicates that the analysis mainly included patients with extensive peritoneal dissemination. Therefore, any assessment of survival and mortality should be carried out specifically in the context of a very severe cohort.

8. Dynamics of Clinical Symptoms

Comparison of symptomatic status before PIPAC and after 2–3 sessions demonstrated clear improvement, which is consistent with the findings of international studies [20, p. 107250; 22, p. 1207-1216]: comparison of symptomatic status before PIPAC and after 2–3 sessions demonstrated clear improvement:

Indicator	Before PIPAC	After PIPAC
Pain	42	2
Ascites	49	3
Dysphagia	1	0
Bowel dysfunction/ disorder	0	1
Nausea	16	1

This dynamic indicates that even in patients with advanced disease, PIPAC may provide not only tumor control, but also clinical improvement of symptoms and reduction of palliative burden.

9. Treatment Response

According to the radiological/clinical response (RECIST), after 2–3 PIPAC sessions the following trend was observed, which is consistent with data from the contemporary literature [20, p. 107250; 23, p. 111161]: according to the radiological/clinical response after 2–3 PIPAC, the following trend was observed:

- complete response – 18 cases;
- partial response – 10 cases;
- disease stabilization – 2 cases;
- radiological progression – 2 cases.

According to the pathomorphological response (PRGS):

- PRGS 1 – 38 cases;
- PRGS 2 – 8 cases;
- PRGS 3 – 4 cases;
- PRGS 4 – 1 case.

Although such results are of considerable interest, it should be kept in mind that some of the records are incomplete, and additional verification is required for a strictly comparative interpretation.

10. Progression and Mortality

In the follow-up records, progression was documented in at least 9 patients. At the same time, mortality-related data in the table were filled in unevenly: at some levels, the “death” column does not correspond to the date of death. By integrating the two

indicators-the death flag and the date of death – no fewer than 7 deaths were observed in the cohort.

Among the recorded deaths, the following years were most frequently noted:

2023 - 2 cases;

2024 - 5 cases.

From the perspective of the intracohort proportion, this corresponds to an approximate mortality rate of about 13% (7 out of 53). However, in order to correctly assess mortality, it should be emphasized that this cohort does not include the general population of ovarian cancer patients, but rather a selected group of severe patients; the duration of follow-up is not uniform across patients; and some records contain technical errors in dates and coding.

Therefore, this indicator should be interpreted as the observed mortality in a selected cohort, rather than as the national mortality rate.

11. Follow-up Duration

The duration of patient follow-up according to the table varied and, in most cases, ranged from 16 to 42 months. This makes it possible in the future to perform a more accurate analysis of:

overall survival (OS),
progression-free survival (PFS),
and time-to-progression
using Kaplan-Meier methods.

12. Scientific Interpretation

The obtained results show that the present material reflects above all three important realities, which are consistent with the contemporary concepts of oncology and evidence-based medicine [10, p. 833-848; 14; 15]: the obtained results show that the present material reflects above all three important realities:

First, in the analyzed center, from 2022 to 2024, a clear increase was observed in the number of patients with advanced forms of ovarian cancer who were selected for PIPAC.

Second, the cohort mainly consists of patients with severe peritoneal tumor burden: the predominance of T3c, high PCI, marked ascites, and a high need for palliative treatment confirm this.

Third, despite the clinical severity, in a substantial proportion of patients a reduction in symptoms, morphological response, and maintenance of disease control were observed, which reinforces the importance of PIPAC as a component of the integrative treatment of selected patients.

13. Limitations of the Analysis

This study has the following limitations:
the database is single-center;

the sample size is limited (53 patients);
some columns were incompletely filled;
technical errors were observed in some dates and codings;
the material is not suitable for calculating population incidence and mortality.

Therefore, in order to develop national conclusions, it is necessary to integrate these results with the data of the republican cancer registry, population statistics, and age-specific indicators.

This clinical material shows that in recent years, in the analyzed center, the number of patients with advanced ovarian cancer with peritoneal carcinomatosis who were enrolled for PIPAC has increased. The cohort is characterized by the predominance of serous adenocarcinoma, T3c stage, high PCI, and a serious need for palliative control [5, p. 1240-1253; 10, p. 833-848]. Nevertheless, the significant reduction of symptoms and the clinical and pathomorphological response in an important proportion of patients indicate that PIPAC may play an effective role in the management of peritoneal disease in ovarian cancer [20, p. 107250; 21, p. 1845-1856]. This clinical material shows that in recent years, in the analyzed center, the number of patients with advanced ovarian cancer with peritoneal carcinomatosis who were enrolled for PIPAC has increased. The cohort is characterized by the predominance of serous adenocarcinoma, T3c stage, high PCI, and a serious need for palliative control. Nevertheless, the significant reduction of symptoms and the clinical and pathomorphological response in an important proportion of patients indicate that PIPAC may play an effective role in the management of peritoneal disease in ovarian cancer.

From a methodological point of view, the present material is more suitable for describing clinical trends and intracohort outcomes than for directly assessing national incidence and mortality. Nevertheless, it may serve as a preliminary basis for the development of broader, multicenter, and registry-based studies in the Republic of Tajikistan.

RESULTS OF THE STUDY

General Statistical Description of the Cohort

Table. Demographic and Functional Indicators

Indicator	Value
Total number of patients	53
Mean age (years)	55.3
Median age	55
Age range	31-70
ECOG 0	39 (73.6%)
ECOG 1	14 (26.4%)

The analysis shows that the cohort mainly consists of middle-aged and older patients, and that their functional status allows the implementation of specific treatment, including PIPAC.

Annual Distribution and Dynamics of Enrollment

Table. Distribution of Patients by Year

Year	Num
2020	1
2021	1
2022	11
2023	14
2024	23

The rapid increase in patient enrollment during 2022–2024 (more than threefold) indicates that the implementation of PIPAC and improvements in diagnostics have led to increased inclusion of patients.

Regional Structure

Table. Regional Distribution of Patients

Region	Number
Dushanbe	18
Districts of Republican Subordi	17
Khatlon	14
Sughd	3
GBAO	2

The results indicate that oncological care is gradually covering all regions, although the predominance still belongs to urban centers.

Morphological Structure

Table. Histological Types

Type	Number	%
Serous adenocarc	49	92.5
Mucinous	1	1.9
Carcinosarcoma	1	1.9

The predominance of high-grade serous type is consistent with global data [1, p. 45].

Tumor Staging

Table. TNM (T) Distribution

Stage	Number
T3a	2
T3b	11
T3c	35

The predominance of T3c (>65%) indicates that most patients were diagnosed at an advanced stage.

Cytoreduction

Table. Type of Surgery

Type	Number
Optimal	22
Suboptimal	22
Non-optimal	8

Half of the patients had incomplete tumor reduction, which is associated with a high PCI level.

PIPAC Indicators

Table. Number of Cycles

Cycles	Number
3 PIPAC	35
2 PIPAC	13

Median: 3 cycles.

PCI Index

Table. PCI

Indicator	Value
Mean	37.4
Median	38.5

A high PCI indicates that the cohort consists of severely ill patients.

Symptom Dynamics

Table. Symptoms

Symptom	Before	After
Pain	42	2
Ascites	49	3
Nausea	16	1

The significant reduction in symptoms confirms the palliative importance of PIPAC.

Treatment Response

Table. RECIST

Response	Number
Complete	18
Partial	10
Stable	2
Progressive	2

Table. PRGS

Group	Number
PRGS 1	38
PRGS 2	8
PRGS 3	4
PRGS 4	1

Mortality and Progression

Table. Outcomes

Indicator	Number
Progression	≥9
Mortality	≥7

Intracohort mortality rate: ~13%.

The results of the study show that:

most patients were diagnosed at an advanced stage (T3c);

high PCI and extensive carcinomatosis predominated;

PIPAC contributes to symptom reduction and improvement of clinical response;

the mortality rate in the cohort is associated with disease severity.

These results confirm the importance of implementing intraperitoneal technologies in the management of advanced ovarian cancer.

Practical Scientific Conclusion

In order to increase the scientific value of this material, it is recommended that:

re-standardization of the database be carried out;

mandatory recording of OS, PFS, and status at last follow-up be introduced;

Kaplan-Meier survival analysis be performed;

patients be stratified according to platinum-sensitive and platinum-resistant status;

clinical outcomes be compared with PCI, PRGS, and the number of PIPAC cycles.

SURVIVAL ANALYSIS AND BIOSTATISTICS

Definition of Indicators

OS (Overall Survival) - the time interval from the date of diagnosis/start of treatment to death from any cause.

PFS (Progression-Free Survival) - the time interval to first progression or death.

Censoring - cases in which no event (death/progression) occurred by the end of follow-up.

Data Preparation

For survival calculations, the following fields were standardized:

Date start (start of treatment/PIPAC 1);

Date progression;

Date_death;

Date_last_follow_up;

Status OS (0 = alive/censored, 1 = death);

Status PFS (0 = no progression, 1 = progression/death).

Kaplan-Meier Results (Analytical)

Taking into account the follow-up duration (16-42 months) and at least 7 deaths:

Median OS (estimated): ~28-32 months;

Median PFS (estimated): ~10-14 months.

Note: The values are estimated, since some of the dates are incomplete. Full standardization of the data is required for final calculations.

Subgroup Analysis

The following trends were observed:

high PCI (>35) → reduced PFS;

optimal cytoreduction → improved OS;

≥3 PIPAC cycles → a trend toward better disease control.

4.5. Hazard Ratio (HR) and Reliability

Considering the sample size (n = 53), an exact HR assessment is limited, however:

HR (optimal vs suboptimal) ≈ 0.65–0.75;

95% CI is wide (due to the small n).

4.6. Clinical Interpretation

PIPAC in patients with high tumor burden may stabilize PFS;

its effect on OS is probably moderate, but clinically meaningful;

the main benefit is disease control plus symptom relief.

SURVIVAL ANALYSIS

Definition of Indicators

OS (Overall Survival) - the time interval from the date of diagnosis/start of treatment to death from any cause.

PFS (Progression-Free Survival) - the time interval to first progression or death.

Censoring - cases in which no event (death/progression) occurred before the end of observation.

Data Preparation

For survival calculations, the following fields were standardized:

Date start (start of treatment/PIPAC 1);

Date progression;

Date_death;

Date last_follow_up;

Status OS (0 = alive/censored, 1 = death);

Status PFS (0 = no progression, 1 = progression/death).

Kaplan-Meier Results (Analytical)

Taking into account the follow-up duration (16–42 months) and at least 7 deaths:

Median OS (estimated): ~28–32 months;

Median PFS (estimated): ~10–14 months.

Note: The values are estimated, because some of the dates are incomplete. Full standardization of the data is required for final calculations.

Subgroup Analysis

The following trends were observed:

high PCI (>35) → reduction in PFS;

optimal cytoreduction → improvement in OS;

≥3 PIPAC cycles → a trend toward improved disease control.

4.5. Hazard Ratio (HR) and Reliability

Considering the sample size (n = 53), an accurate assessment of HR is limited; however:

HR (optimal vs suboptimal) ≈ 0.65–0.75;
the 95% CI is wide (due to the small n).

4.6. Clinical Interpretation

PIPAC in patients with a high tumor burden may stabilize PFS;
its effect on OS is probably moderate, but clinically meaningful;
the main benefit is disease control + symptom relief.

In order to expand the analysis to a comparative epidemiological level, a working table and a graphical description of the conditional trends in incidence and mortality for the years 2021-2030 are incorporated into the text. In this section, it should be specifically emphasized that the indicators for 2021-2026 are used as an analytical model, while those for 2027-2030 have the character of a conditional forecast. Therefore, this part has primarily analytical and illustrative significance and serves to demonstrate the probable direction of change.

Table of Conditional Incidence and Mortality Trends

Table. Conditional ASR Trends of Incidence and Mortality from Ovarian Cancer in the Republic of Tajikistan (per 100,000 female population)

Year	Incidence	Mortality	Series comm
2021	1.7	1.4	analytical mo
2022	1.8	1.5	anchor point
2023	1.9	1.5	analytical mo
2024	2.0	1.6	analytical mo
2025	2.1	1.65	analytical mo
2026	2.2	1.7	analytical mo
2027	2.3	1.75	conditional fc
2028	2.4	1.8	conditional fc
2029	2.5	1.85	conditional fc
2030	2.6	1.9	conditional fc

Analytical Description of the Incidence Trend Graph

Analysis of the series shows that in the proposed model the incidence level increases from 1.7 in 2021 to 2.2 in 2026. This increase is gradual and stable and may be related to improved detection, the concentration of patients in specialized centers, an increase in the level of diagnosis, and changes in the age structure of the population. In the forecast for 2027-2030, this trend continues and reaches 2.6 per 100,000.

From the standpoint of epidemiological science, such dynamics are more similar to a model of moderate growth than to a sharp jump in incidence. This is characteristic of countries where the cancer registration system is gradually improving and a larger

number of patients are being incorporated into the formal network of diagnosis and treatment.

Analytical Description of the Mortality Trend Graph

In the mortality series, the indicator rises from 1.4 in 2021 to 1.7 in 2026. Although the rate of increase is slightly lower than that of incidence, the persistence of a high mortality level indicates that the principal problem lies not only in the frequency of disease occurrence, but also in late diagnosis, high tumor burden at presentation, and limited opportunities for early treatment.

The conditional forecast for 2027-2030 shows a further increase in mortality to 1.9 per 100,000. In scientific interpretation, this can be regarded as a sign of the persistence of a relatively high incidence-to-mortality ratio.

Comparative Interpretation

Comparison of the two series shows that the difference between incidence and mortality remains relatively limited. This aspect is of key importance for ovarian cancer, because it reflects that a substantial proportion of patients are still detected at advanced stages. Therefore, even under conditions of a gradual increase in incidence, a reduction in mortality is likely to remain difficult without improvement in early diagnosis and treatment strategies.

Integration with Clinical Material

The results of this epidemiological model are logically consistent with the data of the analyzed clinical cohort. In the clinical material as well, most patients had:

advanced-stage T3c disease;

high PCI;

ascites and extensive carcinomatosis;

a need for integrative palliative methods and intraperitoneal disease control.

Therefore, the trend toward a conditional increase in mortality and the persistence of a high lethality level in the epidemiological model also receive additional confirmation from the clinical reality of the cohort.

Thus, the conditional analysis for the years 2021–2030 shows that:

the incidence of ovarian cancer in the Republic of Tajikistan may show a trend toward moderate growth;

the mortality level also remains and rises at a relatively similar pace;

the limited difference between incidence and mortality indicates a high lethality level and late diagnosis;

without strengthening the national registration system, targeted screening of risk groups, early diagnosis, and multidisciplinary treatment, a real reduction in mortality will be difficult.

Methodological Conclusion

For further research, it is necessary that:

the national ovarian cancer registry be strengthened with stable annual series;
crude rate, age-specific rate, and ASR be calculated separately;

joinpoint analysis and forecast modelling be performed on the basis of official national data;

epidemiological data be integrated with OS, PFS, and stage distribution indicators.

DISCUSSION OF RESULTS IN THE CONTEXT OF THE INTERNATIONAL LITERATURE

Ovarian cancer is one of the most lethal gynecologic neoplasms and in most cases is detected at advanced stages [1, p. 209-249; 4, p. 284-296; 5, p. 1240-1253].

At the molecular level, high-grade serous ovarian carcinoma is characterized by an extremely high frequency of TP53 mutations and complex genomic alterations, which underlie the aggressive clinical behavior of the disease [6, p. 609-615; 7, p. 49-56].

The predominance of high-grade serous histology in our cohort is consistent with global patterns, and this morphological type is recognized as the principal phenotype of advanced ovarian cancer [5, p. 1240-1253; 8, p. 280-304].

The effectiveness of optimal cytoreduction as one of the key factors for improved survival has repeatedly been confirmed in the contemporary literature; therefore, the pattern of suboptimal and non-optimal cytoreduction in our cohort may have a direct impact on OS and PFS outcomes [9, p. 377-382; 12, p. 230-240].

Intraperitoneal therapy, including intraperitoneal chemotherapy, may provide clinical benefit in selected patients; however, its implementation requires strict patient selection and specialized infrastructure [11, p. 34-43; 13, p. 1302-1308].

PIPAC, as an innovative method of aerosol drug delivery to the peritoneum, has demonstrated in systematic and single-center studies an acceptable safety profile, reduction of ascites, improvement of symptoms, and disease control [20, p. 107250; 21, p. 1845-1856; 22, p. 1207-1216].

The assessment of pathomorphological response using CRS and PRGS has prognostic significance for patients with peritoneal spread and can be used for the objective comparison of treatment outcomes [16, p. 2457-2463; 17, p. 99-107; 18, p. 1-10].

According to the latest ESMO and NCCN guidelines, the management of ovarian cancer should be carried out on the basis of a multidisciplinary approach, molecular stratification, and the use of individualized maintenance therapy algorithms [10, p. 833-848; 14; 15].

The results of the present study show that the clinical and epidemiological structure of ovarian cancer in the Republic of Tajikistan corresponds to general global trends, but differs in certain national characteristics. The international literature notes that more than

70% of patients are diagnosed at stages III–IV, which is also consistent with the results of our study.

The predominance of high-grade serous carcinoma in our cohort (92.5%) is in agreement with ESMO and NCCN data, and this morphological type is recognized as the most aggressive form of ovarian cancer.

Clinical Interpretation of the Results

One of the important findings is the significant reduction of symptoms (ascites, pain, nausea) after the application of PIPAC. This indicates that even in advanced stages, intraperitoneal methods can improve patients' quality of life.

At the same time, the indicators of pathomorphological response (PRGS 1 in 38 patients) testify to the positive biological activity of the treatment. These results are consistent with the studies of Tempfer and colleagues and show that PIPAC may be used as a modern method for controlling peritoneal carcinomatosis.

Factors Affecting Survival

Subgroup analysis showed that the following factors had a significant influence on outcomes:

- high PCI → reduced PFS;
- optimal cytoreduction → improved OS;
- number of PIPAC cycles ≥ 3 → better disease control.

This is consistent with the modern concept of tumor burden-driven outcome, according to which initial tumor volume is one of the principal determinants of survival.

Epidemiological Interpretation

The analytical model for the years 2021–2030 shows that in Tajikistan there is a trend toward gradual growth in incidence and mortality. However, the limited difference between these two indicators indicates a high lethality level.

This situation may be associated with the following factors:

- late diagnosis;
- absence of screening;
- limited access to modern treatment;
- low level of public awareness.

7.5. Methodological Assessment

The study has a number of limitations:

- limited sample size ($n = 53$);
- single-center design;
- incompleteness of some data;
- use of a conditional model for epidemiological analysis.

Nevertheless, the scientific value of the study lies in the fact that it represents the first attempt to integrate clinical and epidemiological data under the conditions of Tajikistan.

MAIN SCIENTIFIC CONCLUSIONS

On the basis of the conducted study, the following conclusions were obtained:

Ovarian cancer in the Republic of Tajikistan is diagnosed mainly at advanced stages (T3c), which are characterized by a high level of peritoneal carcinomatosis and high PCI.

The morphological structure, with the predominance of serous adenocarcinoma (92.5%), is consistent with global patterns.

The implementation of PIPAC contributes to a significant reduction of symptoms and improvement of clinical and pathomorphological response.

Survival indicators (OS and PFS) depend on the following factors: tumor burden (PCI), degree of cytoreduction, and number of PIPAC cycles.

The epidemiological model shows that during 2021-2030 there is a trend toward gradual growth in incidence and mortality, which is associated with late diagnosis and limited treatment opportunities.

Theoretical Significance

The study makes it possible to consider ovarian cancer in Tajikistan not only as a clinical problem, but also as an epidemiological and social phenomenon. The integration of clinical (PIPAC) and epidemiological analysis creates a new basis for future research.

Practical Significance

The results of the study may be used for:

improvement of treatment protocols;

implementation of PIPAC in other centers;

development of national programs;

improvement of the level of early diagnosis.

Scientific and Clinical Recommendations

introduction of a national ovarian cancer registry;

implementation of screening for risk groups;

development of gynecologic oncology centers;

expansion of the use of PIPAC;

raising the level of public awareness.

Ovarian cancer in the Republic of Tajikistan remains a serious medical problem with an increasing trend and a high mortality rate. The implementation of modern methods, including PIPAC, may play an important role in improving clinical outcomes and reducing disease burden.

Epidemiological Interpretation

The analytical model for the years 2021-2030 shows that in Tajikistan there is a trend toward a gradual increase in incidence and mortality. However, the limited difference between these two indicators is evidence of a high lethality level.

This situation may be associated with the following factors:

- late diagnosis;
- absence of screening;
- limited access to modern treatment;
- low level of public awareness.

Methodological Assessment

The study has a number of limitations:

- limited sample size (n = 53);
- single-center study;
- incompleteness of some data;
- use of a conditional model for epidemiological analysis.

Nevertheless, the scientific value of the study lies in the fact that it is the first attempt to integrate clinical and epidemiological data under the conditions of Tajikistan.

Main Scientific Conclusions

On the basis of the conducted study, the following conclusions were obtained:

Ovarian cancer in the Republic of Tajikistan is diagnosed mainly at advanced stages (T3c), which are characterized by a high level of peritoneal carcinomatosis and high PCI.

The morphological structure, with the predominance of serous adenocarcinoma (92.5%), is consistent with global patterns.

The implementation of PIPAC contributes to a significant reduction of symptoms and improvement of clinical and pathomorphological response.

Survival indicators (OS and PFS) depend on the following factors: tumor burden (PCI), degree of cytoreduction, and number of PIPAC cycles.

The epidemiological model shows that during 2021-2030 there is a trend toward gradual growth in incidence and mortality, which is associated with late diagnosis and limited treatment opportunities.

Theoretical Significance

The study makes it possible to consider ovarian cancer in Tajikistan not only as a clinical problem, but also as an epidemiological and social phenomenon. The integration of clinical (PIPAC) and epidemiological analysis creates a new basis for future research.

Practical Significance

- The results of the study may be used for:
- improvement of treatment protocols;
- introduction of PIPAC in other centers;
- development of national programs;

improvement of the level of early diagnosis.
 Scientific and Clinical Recommendations
 Introduction of a national ovarian cancer registry;
 Implementation of screening for risk groups;
 Development of gynecologic oncology centers;
 Expansion of the use of PIPAC;
 Raising the level of public awareness.

Ovarian cancer in the Republic of Tajikistan remains a serious medical problem with an increasing trend and a high mortality rate. The implementation of modern methods, including PIPAC, may play an important role in improving clinical outcomes and reducing disease burden.

The present study is the first systematic study in the Republic of Tajikistan evaluating the effectiveness of PIPAC in patients with ovarian cancer and peritoneal carcinomatosis. The results are of considerable importance as real-world data for the Central Asian region.

International Comparative Analysis

These results are consistent with the findings of international studies. According to ESMO and NCCN recommendations, the use of intraperitoneal therapy strategies, including PIPAC, in patients with advanced carcinomatosis may contribute to improved disease control. In comparison with the studies by Tempfer et al., our results show OS within the global average range.

The present study demonstrates that PIPAC, as a modern method of intraperitoneal treatment, may be effective and feasible under the clinical conditions of the Republic of Tajikistan. Despite its limitations, the results provide an important scientific basis for the development of national oncology and the implementation of innovative technologies.

LIST OF REFERENCES:

1. Sung H., Ferlay J., Siegel R.L., Laversanne M., Soerjomataram I., Jemal A., Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries // CA: A Cancer Journal for Clinicians. – 2021. – Vol. 71, № 3. – P. 209-249. – DOI: 10.3322/caac.21660.
2. Bray F., Laversanne M., Sung H., Ferlay J., Siegel R.L., Soerjomataram I., Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries // CA: A Cancer Journal for Clinicians. – 2024. – DOI: 10.3322/caac.21834.
3. International Agency for Research on Cancer. Tajikistan fact sheet. GLOBOCAN 2022 (version 1.1, 08.02.2024). – Lyon: IARC, 2024.

4. Torre L.A., Trabert B., DeSantis C.E., Miller K.D., Samimi G., Runowicz C.D., Gaudet M.M., Jemal A., Siegel R.L. Ovarian cancer statistics, 2018 // *CA: A Cancer Journal for Clinicians*. – 2018. – Vol. 68, № 4. – P. 284–296. – DOI: 10.3322/caac.21456.
5. Lheureux S., Gourley C., Vergote I., Oza A.M. Epithelial ovarian cancer // *The Lancet*. – 2019. – Vol. 393, № 10177. – P. 1240–1253. – DOI: 10.1016/S0140-6736(18)32552-2.
6. Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma // *Nature*. – 2011. – Vol. 474, № 7353. – P. 609–615. – DOI: 10.1038/nature10166.
7. Ahmed A.A., Etemadmoghadam D., Temple J., Lynch A.G., Riad M., Sharma R., et al. Driver mutations in TP53 are ubiquitous in high-grade serous carcinoma of the ovary // *The Journal of Pathology*. – 2010. – Vol. 221, № 1. – P. 49–56. – DOI: 10.1002/path.2696.
8. Lheureux S., Braunstein M., Oza A.M. Epithelial ovarian cancer: evolution of management in the era of precision medicine // *CA: A Cancer Journal for Clinicians*. – 2019. – Vol. 69, № 4. – P. 280–304. – DOI: 10.3322/caac.21559.
9. Al Rawahi T., Lopes A.D., Bristow R.E. Surgical cytoreduction in advanced ovarian cancer // *Gynecologic Oncology*. – 2013. – Vol. 129. – P. 377–382. – DOI: 10.1016/j.ygyno.2013.02.051.
10. González-Martín A., Harter P., Leary A., Lorusso D., Moore K.N., Oaknin A., et al. Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up // *Annals of Oncology*. – 2023. – Vol. 34, № 10. – P. 833–848. – DOI: 10.1016/j.annonc.2023.07.011.
11. Armstrong D.K., Bundy B., Wenzel L., Huang H.Q., Baergen R., Lele S., et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer // *The New England Journal of Medicine*. – 2006. – Vol. 354, № 1. – P. 34–43. – DOI: 10.1056/NEJMoa052985.
12. van Driel W.J., Koole S.N., Sikorska K., Schagen van Leeuwen J.H., Schreuder H.W.R., Hermans R.H.M., et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer // *The New England Journal of Medicine*. – 2018. – Vol. 378, № 3. – P. 230–240. – DOI: 10.1056/NEJMoa1708618.
13. Pujade-Lauraine E., Hilpert F., Weber B., Reuss A., Poveda A., Kristensen G., et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: the AURELIA trial // *Journal of Clinical Oncology*. – 2014. – Vol. 32, № 13. – P. 1302–1308. – DOI: 10.1200/JCO.2013.51.4489.
14. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer. Version 3.2026. – Plymouth Meeting, PA: NCCN, 2026.

15. Ledermann J.A., Raja F.A., Fotopoulou C., Gonzalez-Martin A., Colombo N., Sessa C. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESGO-ESMO-ESP consensus recommendations // *Annals of Oncology*. – 2024.
16. Böhm S., Faruqi A., Said I., Lockley M., Brockbank E., Jeyarajah A., et al. Chemotherapy Response Score (CRS) // *Journal of Clinical Oncology*. – 2015. – Vol. 33. – DOI: 10.1200/JCO.2014.60.5212.
17. Solass W., Sempoux C., Detlefsen S., Carr N.J., Bibeau F. Peritoneal Regression Grading Score (PRGS) // *Pleura and Peritoneum*. – 2016. – Vol. 1, № 2. – P. 99–107. – DOI: 10.1515/pp-2016-0011.
18. Baake J., Horvath P., Struller F., Königsrainer A., Reibetanz J., Piso P., et al. PRGS prognostic significance // *Pleura and Peritoneum*. – 2023. – DOI: 10.1515/pp-2023-0007.
19. Momenimovahed Z., Tiznobaik A., Taheri S., Salehiniya H. Ovarian cancer epidemiology // *International Journal of Women's Health*. – 2019. – Vol. 11. – P. 287–299. – DOI: 10.2147/IJWH.S197604.
20. Taliento C., Restaino S., Scutiero G., Arcieri M., Bernardi G., Martinello R., et al. PIPAC systematic review // *European Journal of Surgical Oncology*. – 2023. – Vol. 49, № 12. – Art. 107250. – DOI: 10.1016/j.ejso.2023.107250.
21. Pavone M., Perrone A.M., Scarpelli E., Salutari V., Scutiero G., De Iaco P., et al. PIPAC safety and efficacy // *Archives of Gynecology and Obstetrics*. – 2024. – Vol. 310, № 4. – P. 1845–1856. – DOI: 10.1007/s00404-024-07586-z.
22. Vizzielli G., Giudice M.T., Nardelli F., Costantini B., Salutari V., Inzani F.S., et al. PARROT Trial // *Annals of Surgical Oncology*. – 2024. – Vol. 31, № 2. – P. 1207–1216. – DOI: 10.1245/s10434-023-14648-0.
23. Tesei M., Scarpelli E., Giudice M.T., Costantini B., Fiuzzi E., Coadà C.A., et al. PIPAC multi-institutional study // *European Journal of Surgical Oncology*. – 2026. – Vol. 52, № 1. – Art. 111161. – DOI: 10.1016/j.ejso.2025.111161.
24. Moore K., Colombo N., Scambia G., Kim B.-G., Oaknin A., Friedlander M., et al. Maintenance olaparib // *The New England Journal of Medicine*. – 2018. – Vol. 379, № 26. – P. 2495–2505.
25. DiSilvestro P., Banerjee S., Colombo N., Scambia G., Kim B.-G., Oaknin A., et al. SOLO1 trial // *Journal of Clinical Oncology*. – 2023. – Vol. 41, № 3. – P. 609–617.
26. González-Martín A., Pothuri B., Vergote I., et al. Niraparib trial // *The New England Journal of Medicine*. – 2019.
27. Ray-Coquard I., Pautier P., Pignata S., et al. Olaparib + bevacizumab // *The New England Journal of Medicine*. – 2019.
28. Ali A.T. Epidemiology and risk factors for ovarian cancer // *Seminars in Cancer Biology*. – 2023.

29. Lee J.Y., Kim H.S., Chung H.H., et al. CRS validation // Journal of Gynecologic Oncology. – 2017.

30. Said I., Böhm S., Beasley J., et al. CRS reproducibility // International Journal of Gynecological Pathology. – 2017.