

Russian Cancer Research Center named after N. N. Blokhin

**Combined treatment of peritoneal pseudomixome:
practicability, forecasting factors**

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PSEUDOMIXOMA PERITONEUM

- - a rare disease characterized by ascites and carcinomatosis of the peritoneum as a cluster of "mucinous masses" [Moran B.J., 2003, Sugarbaker P.H., 2006].



PSEUDOMIXOMA PERITONEUM

- Disseminated peritoneal
Adenomucinosi - 84%
 - Peritoneal mucinous
Carcinomatosis - 6.7%
 - Intermediate group - 37.6%
- (p < 0.0001)

Ronnett B.M. in 1995



**Pseudomixoma is always a consequence,
the source of the disease can be benign tumors!**

PSEUDOMIXOMA PERITONEUM

How to treat?

- ❖ No treatment, symptomatic therapy
 - ❖ Systematic chemotherapy
 - ❖ Surgical treatment
- ❖ Surgical treatment + intraperitoneal chemotherapy
(HIPEC?)

PSEUDOMIXOMA PERITONEUM

Results of treatment with non-optimal tumor removal

Analysis of 174 observations

(Glehen, Sugarbaker Ann Surg 2004; 240: 278-85)

- 76 - EPIC, 61 - IPCH !!!
- Mortality: 0%; complication rate 33%
- Survival: 3-year-old = 34%, 5-year-old = 15%

Non-optimal surgical procedures are associated with poor prognosis!

Results of treatment

Author	Patients	Treatment	Survival (months)
GlehenM SugabakerP 2004	N=174	76 EPIC+CRS 61 IPCH+CRS	Median 20.5 3-year 34% 5-year 15%
Gough et all. (Mayo Cinic)1995	N=56	CRS CCR0 33%	5-year 53% Recurrence 97%
Miner et all.(Memorial SK) 2005	N=97	67 CRS 30 CRS+ IPCH CCR0 53%	10-year 21% Recurrence 88%
D. Elias, 2009	N=301	255 CRS+HIPEC CCR0 73%	5-year 75% 10-year 55%
Chua et al., 2012	N=2298	668 CRS+HIPEC+ EPIC 1382 CRS+HIPEC 44 CRS+ EPIC 203 CRS CCR0-1>80%	10-year 63% 15-year 59%
HUAN WANG et al. 2014	N=39	7 CRS+HIPEC 22 CRS+PIC 10 CRS	Median 37 5-year 89% 10-year 35%

Comment: CCR, completeness of cytoreduction; EPIC, early postoperative intraperitoneal chemotherapy; HIPEC, hyperthermic intraperitoneal chemotherapy; IPCH intraperitoneal chemotherapy; CRS cytoreduction surgeon; PIC, perioperative intraperitoneal chemotherapy.

PSEUDOMIXOMA PERITONEUM

Results of treatment with intraperitoneal hyperthermia chemotherapy

Chua et al., 2012.

Overall 5-year survival rate (n=2298):

85% at the index CC 0

80% - CC 1

24% - CC2-3

CC0-1 > 80% operations

Eric K., Nakakura: "The study reflects by a careful selection of patients, a good level of surgery or a combination of both factors"

PSEUDOMIXOMA PERITONEUM

«Peritonectomy»

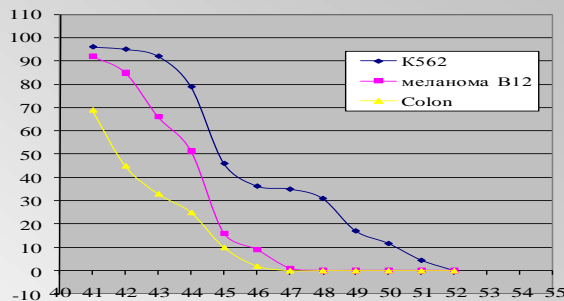
Sugarbaker P.H.

- Peritonectomy of the upper left quadrant of the abdominal cavity;
- Peritonectomy of the upper right quadrant of the abdominal cavity;
- Removal of the large omentum and spleen;
- Removal of the small omentum, peritoneum of the omentum bag and cholecystectomy;
- Removal of pelvic peritoneum with possible removal of sigmoid colon with mesentery and uterus with appendages in women;
- Removal of parietal peritoneum of lateral canals and anterior abdominal wall.

PSEUDOMIXOMA PERITONEUM

Hyperthermal intracavitary chemoperfusion

- *The creation of a high concentration of cytostatics in tumors,*
- *Reduction of systemic toxicity,*
- *Modification of the effect of cytotoxic drugs when using hyperthermia.*

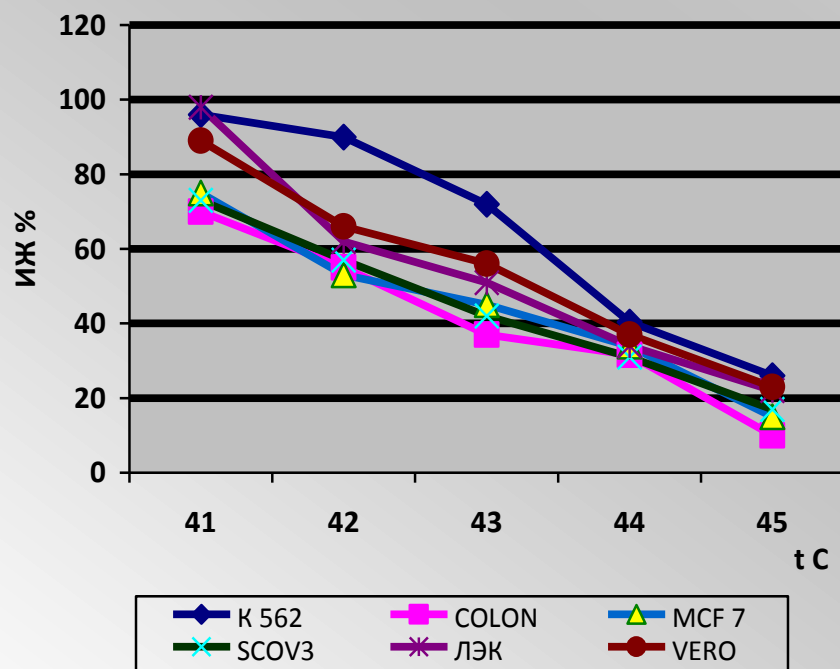


*Solution temperature > 45 ° C
within 2 hours!*

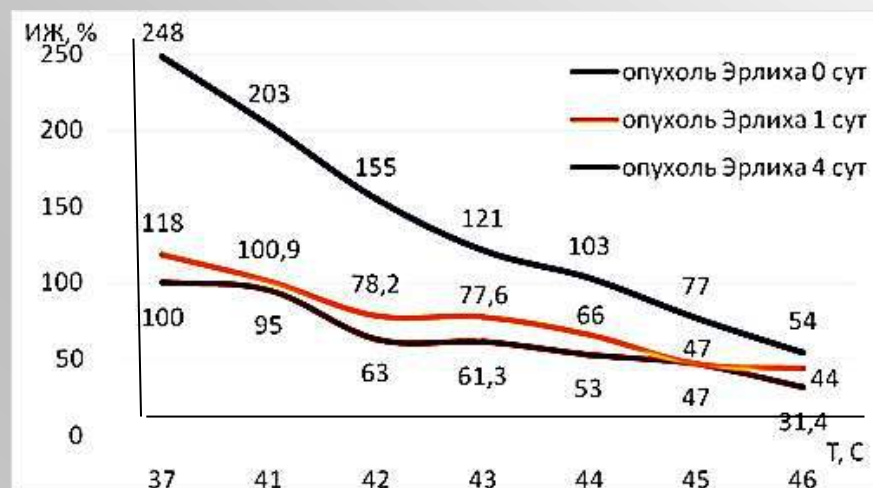
*The effect of hyperthermia on the physiological activity of the transfected lines of tumor and non-transformed cells in vitro. **Kisilevsky M. V.***

The effect of hyperthermia on the viability and proliferation of tumor and non-transformed cells in vitro

Viability of tumor and non-transformed cells

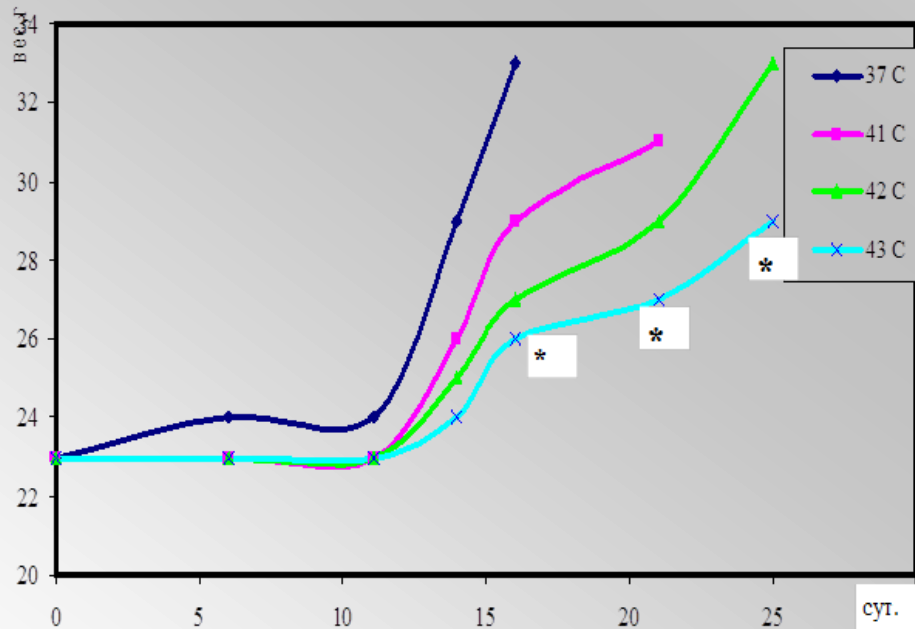


Viability and proliferative activity of Ehrlich ascitic tumor cells in mice

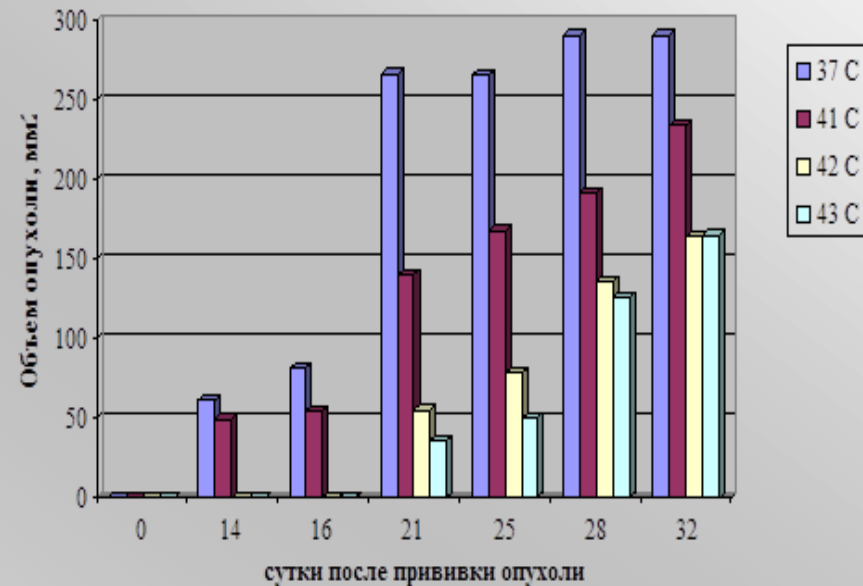


Dynamics of growth of Ehrlich's tumor after the temperature effect on the grafted cells

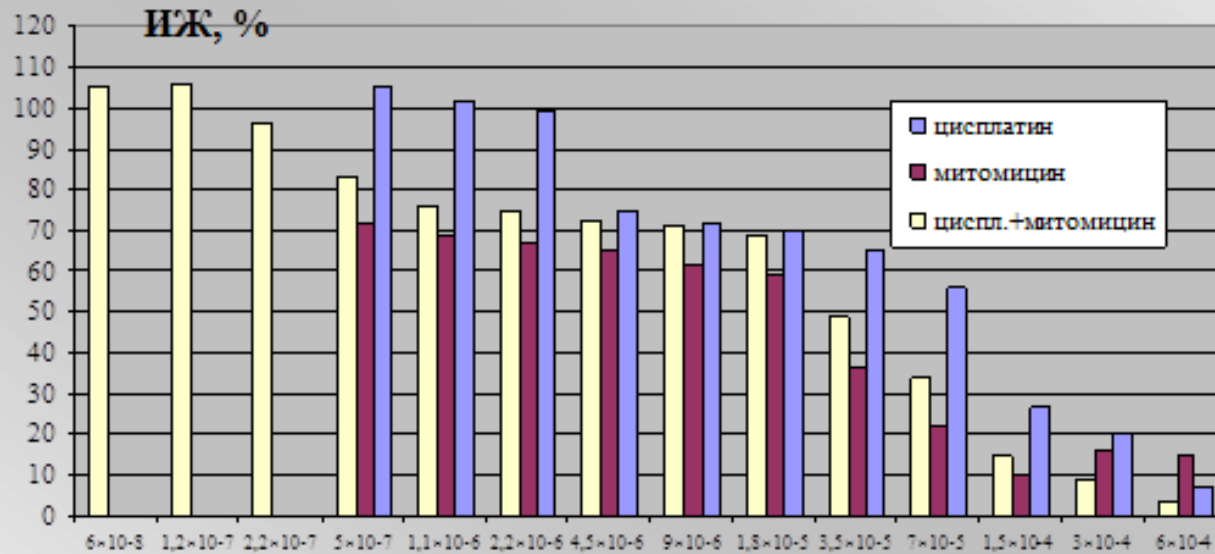
Intraperitoneal implantation of Ehrlich tumor cells



Subcutaneous implantation of Ehrlich tumor cells

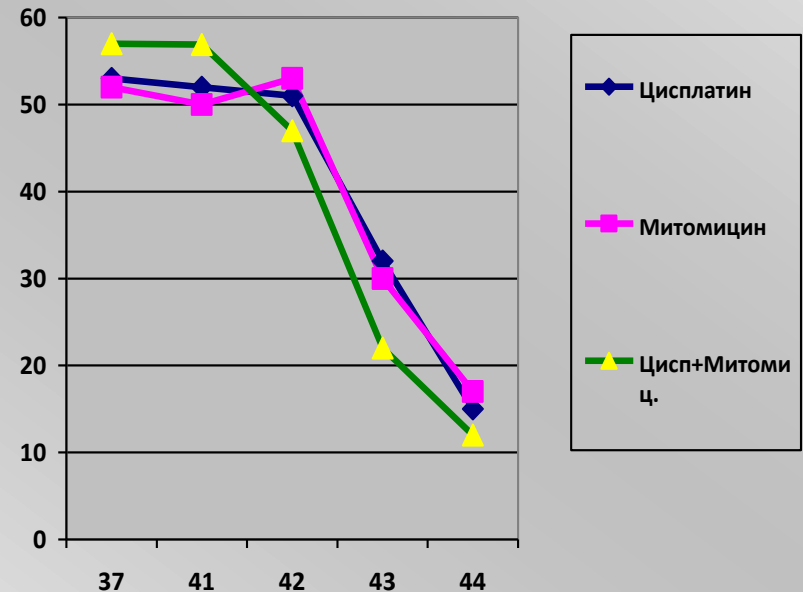


Combined effects of hyperthermia and cytostatics on the viability of the tumor cells of the COLON line



Cytotoxic activity of cisplatin, mitomycin, and combinations thereof

Combined effects of cytostatics and hyperthermia



PSEUDOMYXOMA PERITONEUM

FEATURE	Group	
	Examined n=43	Control n=26
Average age	48.5±15.6	46.8±9.5
Histological type: Low grade, DPAM High grade, PMCA	38 (88,4%) 5 (11,6%)	21 (80,8%) 5 (19,2%)
Degree of intraperitoneal dissemination:		
P1	6 (14%)	10 (39%)
P2	10 (23%)	5 (19%)
P3	27 (63%)	11 (42%)
Gender:		
Male	7 (16%)	6 (23%)
Female	36 (84%)	20 (77%)
<p>Note: DPAM — <i>Disseminated peritonea ladenomucinosi</i>, PMCA — <i>Peritoneal mucinous carcinomatosis</i>.</p>		

Examination



- *Histological confirmation of the disease*
- Blood tests: PЭA, CA-19.9, CA-125
- X-ray examination of the thoracic cavity organs
- *CT / MRI of the abdominal cavity and small pelvis with contrast, determination of the degree of carcinomatosis*
- Esophagogastroduodenoscopy
- In the presence of indications (massive tumor lesion of the pelvis and mesogastrium) - colonoscopy and cystoscopy with catheterization of the ureters on the eve of the operation.
- Laparoscopy?
- *Assessment of the functional status*

Examination

Source of pseudomixom formation						
				Study group	Control group	
Mucinous cystadenoma of the ovaries				3	6	
Mucinous cystadenoma of the appendix				10	2	
Adenocarcinoma of the appendix				19	3	
Source not defined				11	15	
Total				43	26	
Gender	Expression of markers,% of cells				PAX8, % of cores	Immuno- phenotype
	CK7	CK20	CDX-2	MUC2		
M	100	80	75	100	0	appendix
F	35	100	90	80	0	appendix
F	90	80	65	75	0	appendix
F	100	85	50	100	0	appendix
F	100	90	20	0	0	appendix
F	30	90	25	85	0	appendix
F	20	100	70	80	0	appendix
F	75	95	95	90	0	appendix
F	40	80	60	90	0	appendix
F	0	100	85	90	0	intestinal
F	0	90	75	90	0	intestinal

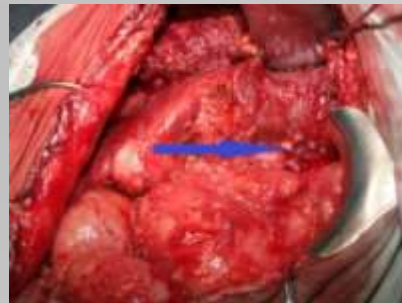
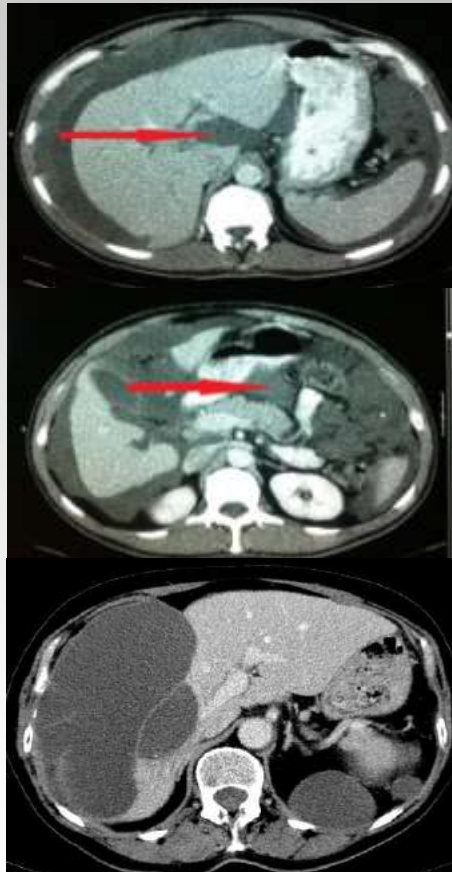
93% of cases of pseudomixoma has an intestinal immunophenotype

Examination



Determination of the degree of intraperitoneal dissemination

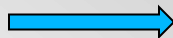
PCI (Peritoneal Cancer Index)



Infiltration of the hepatoduodenal ligament, "usurization" of the liver capsule



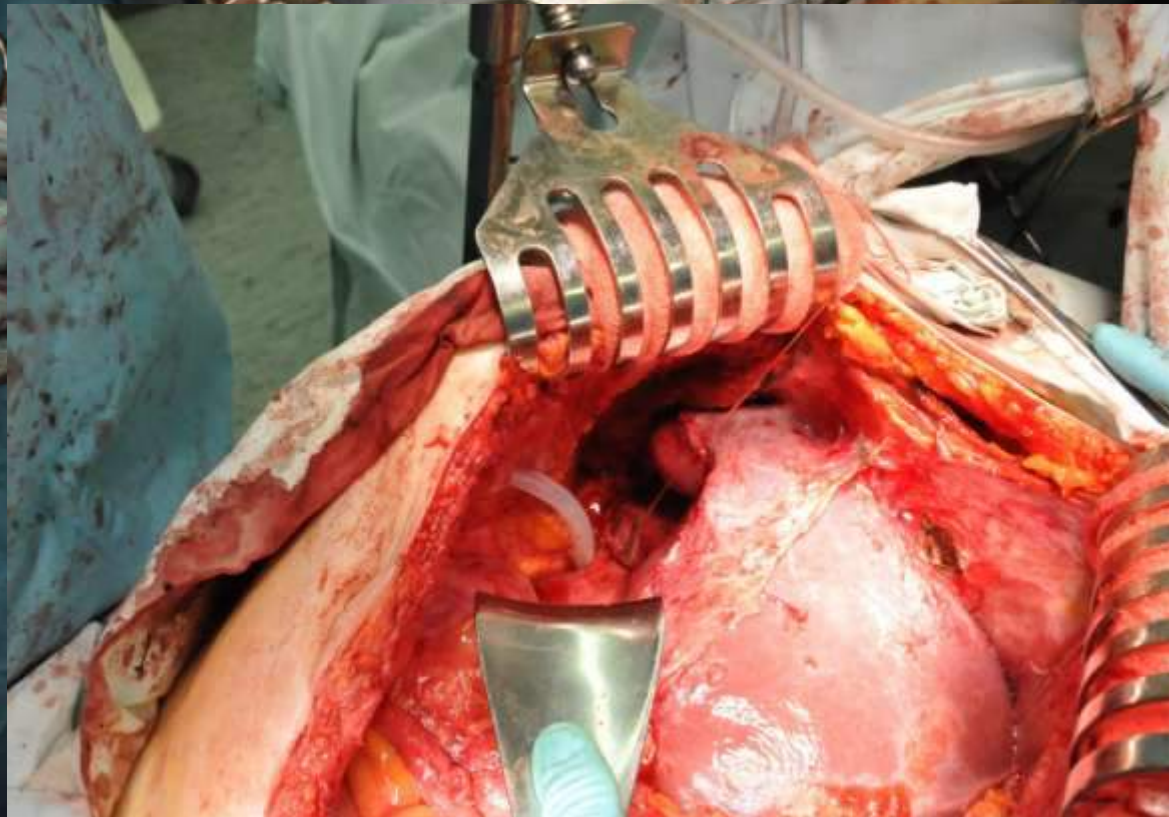
Tumor screenings in the area of the gland bag



For peritoneal adenomycinosis, PCI is not important!

PSEUDOMIXOMA PERITONEUM

Surgical stage
basic principles



Cytoreductive operations

Scope of surgical intervention

PERITONECTOMY, EXTREMATION OF LARGE GLAND	Hemicolectomy	15
	Splenectomy	27
	Small bowel resection	19
	Cholecystectomy	11
	Appendectomy	8
	Distal Pancreas Resection	4
	Extirpation of the uterus	24
	Diaphragm resection	8
	Resection of the sigmoid colon	5
	Resection of the ileo-cecal angle	11
	Resection of the transverse colon	3
	Abdominal resection of rectum	2
	Extirpation of the cervix stump	5
	Resection of the bladder	5
	Ureteral resection	2

Parameters of hyperthermic intraperitoneal chemotherapy

- Isotonic 0.9% NaCl solution (volume 3000-5000 ml)
- Average temperature of solution for perfusion – $43,6 \pm 0,5$ °C
- Duration of perfusion – 60-90 мин.
- Doses of cytostatics
- Cisplatinum 100 mg / m²
- Mitomycin C 10 mg / m²



*Change in perfusion parameters depending on
the development of possible toxicity!*

STRUCTURE OF POSTOPERATIVE COMPLICATIONS

Type of complication	Frequency
Surgical	12/43 (28 %)
Pulmonary	9/43 (23 %)
Due to chemotherapy	6/43 (14 %)

STRUCTURE OF POSTOPERATIVE COMPLICATIONS

The nature of surgical complications

Interintestinal abscess*	1
Suppuration of a postoperative wound	4
Pancreatitis	4
The inconsistency of sigmo-rectoanastomosis	1
Flotational phlebothrombosis	1
Partial intestinal obstruction	1
TOTAL	12/43
	(28%)

STRUCTURE OF POSTOPERATIVE COMPLICATIONS

The nature of pulmonary complications

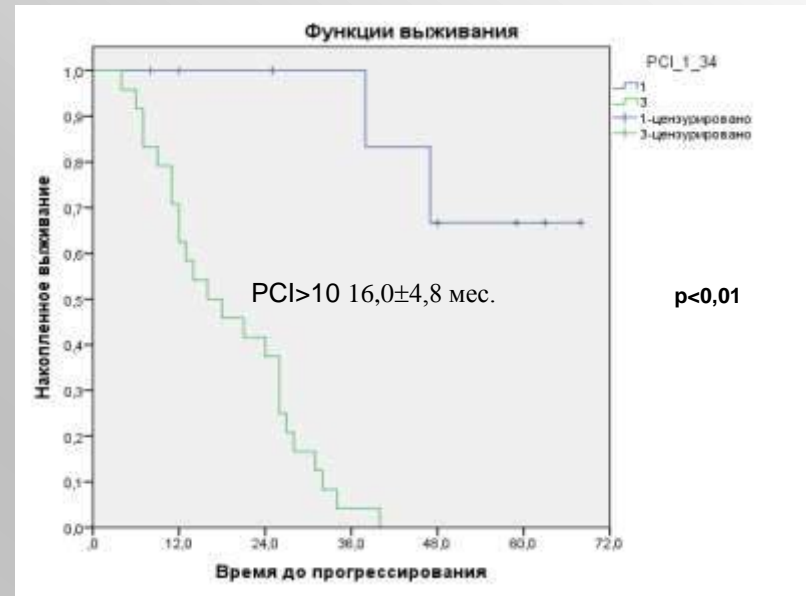
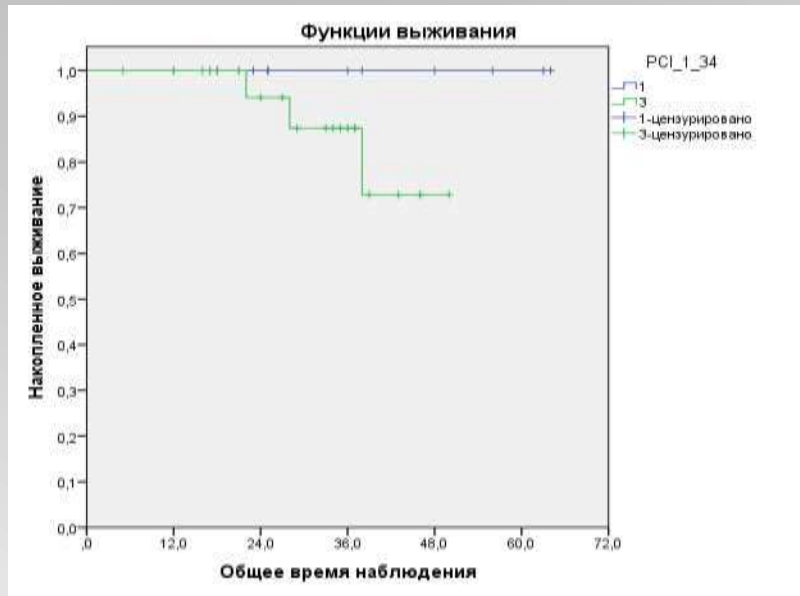
Complications	Number of patients (n=10/43), 23%
Hydrothorax	6
Combination of pneumo- and hydrothorax	2
Hydrothorax and left-sided pneumonia	1
Pulmonary embolism	1

Results of treatment

- Pseudomixome of peritoneum - study group (n=43)
- Pseudomixome of peritoneum – control group(n=26)
- ✓ Histological type of tumor *DPAM/PMCA*
 - ✓ Treatment in anamnesis
- ✓ The degree of carcinomatosis *P1-3/PCI*
- ✓ Completeness of cytoreduction performed *CCR0-3*

Results of treatment

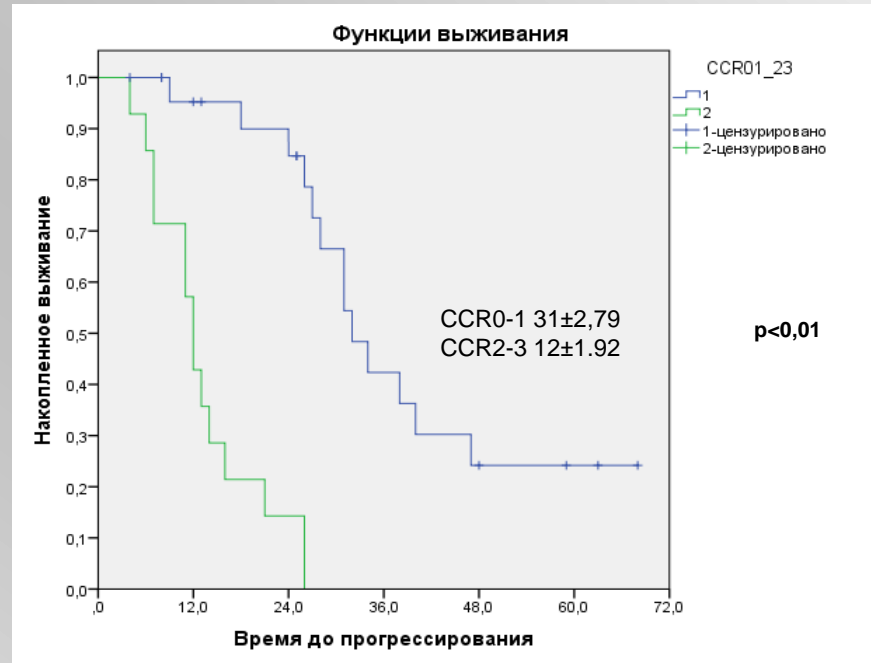
PSEVDOMIXOMA. STUDY GROUP



Effects of the degree of intraperitoneal dissemination (PCI) on total and disease-free survival in patients with peritoneal pseudomixoma in the study group

Results of treatment

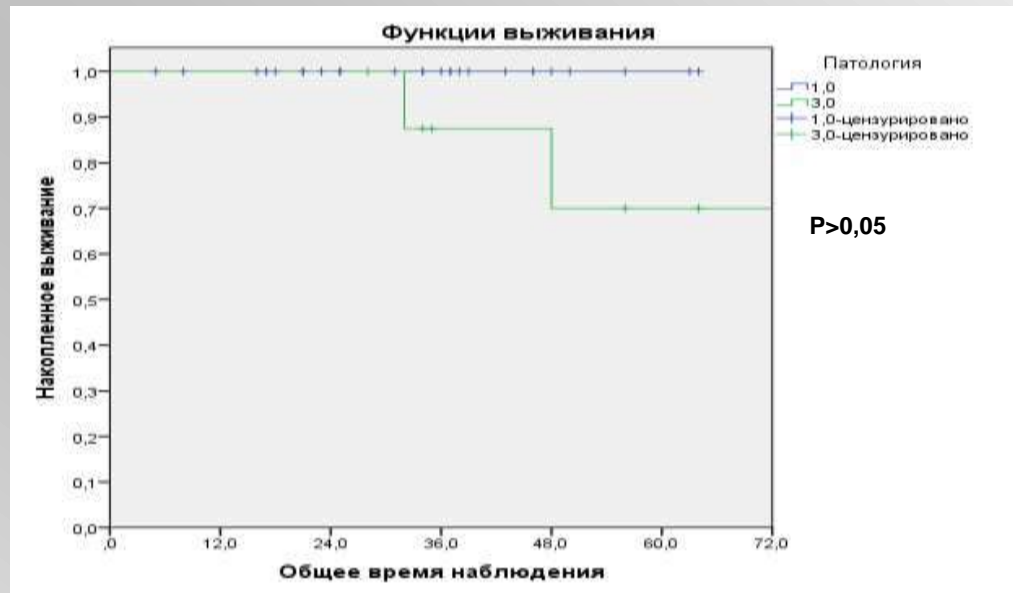
PSEVDOMIXOMA. STUDY GROUP



Comparison of the indices of disease-free survival at the optimal (CCR0-1) and non-optimal cytoreduction (CCR2-3) in patients with pseudomixome peritoneum in the study group

Results of treatment

PSEUDOMIXOMA STUDY AND CONTROL GROUPS



- After the optimal removal of the tumor !! There was no significant difference in overall survival in the two groups
- In multivariate analysis, the only reliable predictor in patients with pseudomixoma was the completeness of the performed cytoreduction!

PSEUDOMIXOMA PERITONEUM

Conclusion

- **Patients with pseudomixoma of the peritoneum are shown surgical treatment due to the lack of an alternative and the threat of complications of tumor growth**
- **The main criterion for survival rates improvement is the volume of the residual tumor after surgery**
- **Hyperthermal intraperitoneal chemo-perfusion in an independent version is not an effective therapeutic remedy and can be used under the condition of optimal cytoreductive operation**
- **It is necessary to search for the most effective regimens of intraperitoneal chemo-perfusion, possibly based on the molecular-biological features of the tumor**

**Thank you
for your attention!**