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Gastric Cancer: 10-Year Survival after Surgery

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Abstract

Objective: 10-Year survival (10YS) after radical surgery for gastric cancer (GC) pa¬tients (GCP) (T1-4N0-2M0) was analyzed.

Methods: We analyzed data of 796 consecutive GCP (age=57.1±9.4 years; tumor size=5.4±3.1 cm) radically operated (R0) and monitored in 1975-2021 (m=556, f=240; distal gastrectomies-G=461, proximal G=165, total G=170, D2 lymph node dissection=551; combined G with resection of 1-7 adjacent organs (pancreas, liver, diaphragm, esophagus, colon transversum, splenectomy, small intestine, kidney, adrenal gland, etc.)=245; D3-4 lymph node dissection=245; only surgery-S=623, adjuvant chemoimmunotherapy-AT=173: 5FU+thymalin/taktivin; T1=237, T2=220, T3=182, T4=157; N0=435, N1=109, N2=252, M0=796; G1=222, G2=164, G3=410; early GC=164, invasive GC=632; Variables selected for 10YS study were input levels of 45 blood parameters, sex, age, TNMG, cell type, tumor size. Survival curves were estimated by the Kaplan-Meier method. Differences in curves between groups of GCP were evaluated using a log-rank test. Multivariate Cox modeling, discriminant analysis, clustering, SEPATH, Monte Carlo, bootstrap and neural networks computing were used to determine any significant dependence.

Results: Overall life span (LS) was 2130.8±2304.3 days and cumulative 5-year survival (5YS) reached 58.4%, 10 years – 52.4%, 20 years – 40.4%. 316 GCP lived more than 5 years (LS=4316.1±2292.9 days), 169 GCP – more than 10 years (LS=5919.5±2020 days). 294 GCP died because of GC (LS=640.6±347.1 days). AT significantly improved 10YS (62.3% vs. 50.5%) (P=0.0228 by log-rank test) for GCP. Cox modeling displayed that 10YS of LCP significantly depended on: phase transition (PT) early-invasive GC in terms of synergetics, PT N0—N12, cell ratio factors (ratio between cancer cells- CC and blood cells subpopulations), G1-3, AT, blood cell circuit, prothrombin index, hemorrhage time, residual nitrogen, age, sex, procedure type (P=0.000-0.039). Neural networks, genetic algorithm selection and bootstrap simulation revealed relationships between 10YS and healthy cells/CC (rank=1), PT early-invasive GC (rank=2), PT N0—N12(rank=3), erythrocytes/CC (4), thrombocytes/CC (5), monocytes/CC (6), segmented neutrophils/CC (7), eosinophils/CC (8), leucocytes/CC (9), lymphocytes/CC (10), stick neutrophils/CC (11). Correct prediction of 5YS was 100% by neural networks computing (area under ROC curve=1.0; error=0.0).

Conclusions: 10-Year survival of GCP after radical procedures significantly depended on: 1) PT early-invasive cancer; 2) PT N0--N12; 3) cell ratio factors; 4) blood cell circuit; 5) biochemical factors; 6) hemostasis system; 7) AT; 8) GC characteristics; 9) anthropometric data; 10) surgery type. Optimal diagnosis and treatment strategies for GC are: 1) screening and early detection of GC; 2) availability of experienced abdominal surgeons because of complexity of radical procedures; 3) aggressive en block surgery and adequate lymph node dissection for completeness; 4) precise prediction; 5) adjuvant chemoimmunotherapy for GCP with unfavorable prognosis.

Keywords: Gastric cancer; 10-Year Survival; Surgery; Prognosis.

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1. Introduction

Gastric cancer (GC) is the number two killer in the world in the structure of mortality from malignant neoplasms. Nevertheless, there is practically no analysis of 10-year survival of GC patients (GCP) in the literature. But information on the 10-year survival rate is extremely important in optimizing the treatment and diagnostic process in oncology and especially for extremely aggressive cancer –GC. The high mortality rate associated with GC is primarily due to the high incidence of late stage and the lack of curative management for the majority of GCP. Up to 70-90% of GCP present with stage III-IV disease. The role of adjuvant chemotherapy or chemoimmunotherapy after complete gastrectomies in GCP with stage II-IV remains controversial [1]. Moreover, the optimal treatment plan in general and optimal approach for adjuvant chemotherapy in particular has not been defined and long-term prognosis of GCP especially with stage III-IV remains poor, because of local relapse and distant metastases, with the real 5-year survival rate after radical procedures only 30-35% [2]. One of the approaches developed involves aggressive en-block surgery and complete lymphadenectomy. Another of the modern approaches developed to enhance the efficacy of surgery is the combination of chemotherapy and immunotherapy or gene therapy which offers the advantage of exposing GC cell population for drugs and immune factors thus obviating cancer cell-cycle cytotoxic and host-immunoprotective effects [3-4]. Nevertheless, very few studies have demonstrated convincing clinical results. We developed optimal treatment strategies that incorporate bolus chemotherapy and immunotherapy after radical, aggressive en-block surgery.

2. Patients and Methods

We conducted this study from 1975 to 2021. 796 consecutive GCP (male – 556, female – 240; age=57.1±9.4 years, tumor size=5.4±3.1 cm) (mean±standard deviation) entered this trial. All GCP were white Europeans. Patients were not considered eligible if they had stage IV, previous treatment with chemotherapy, immunotherapy or radiotherapy or if there were two primary tumors of the time of diagnosis. Patients after non-radical procedures, postoperative died GCP were excluded to provide a homogeneous patient group. The preoperative staging protocol included clinical history, physical examination, complete blood count with differentials, biochemistry and electrolyte panel, chest X-rays, roentgenoesophagogastroscopy, abdominal ultrasound, fibroesophagogastroscopy, electrocardiogram. Computed tomography scan of upper abdomen, liver and bone radionucle scan were performed whenever needed. All GCP were diagnosed with histologically confirmed GC. All had measurable tumor and ECOG performance status 0 or 1. Before any treatment each patient was carefully examined by medical panel composed of surgeon and chemotherapeutist to confirm the stage of disease. All patients signed a written informed consent form approved by the local Institutional Review Board.

The initial treatment was started with radical procedures (complete gastrectomies with lesser and major omentum and lymph node dissection). The present analysis was restricted to GCP with complete resected tumors with negative surgical resection margin (R0) and with N1-N2 nodes. Surgical complete resection consisted of total gastrectomy in 170, distal gastrectomy in 461, proximal gastrectomy in 165. Among these, 245 GCP underwent combined and extensive radical procedures with resection of 1-7 adjacent organs (esophagus, duodenum, diaphragm, mesocolon, colon transversum, liver, splenectomy, left hemipancreatectomy, etc.). 551 patients underwent routine lymph nodal D2-dissection. Extensive lymph nodal D3-4-dissection was performed in 245 GCP. All GCP were postoperatively staged according to the TNM-classification. Histological examination showed intestinal adenocarcinoma in 457, diffuse adenocarcinoma - in 320 and mixed adenocarcinoma - in 19 patients. The pathological TNM stage was I in 108, II – in 160, III - in 453 patients; the pathological T stage was T1 in 237, T2 - in 220, T3 - in 182, T4 - in 157 cases; the pathological N stage was N0 in 435, N1 - in 109, N2 - in 252 patients. The tumor differentiation was graded as G1 in 222, G2 - in 164, G3 - in 410 cases. The pathological P stage was P1 in 117, P2 – in 78 P3 – in 142 and P4 – in 459 patients. After surgery postoperative chemoimmunotherapy were accomplished GCP in ECOG performance status 0 or 1.

All patients (408 GCP) were divided between the two protocol treatment: 1) surgery and adjuvant chemoimmunotherapy (173 GCP – group A); 2) surgery alone without any adjuvant treatment (623 GCP – group B) – the control group.

All 173 patients completed adjuvant chemoimmunotherapy (group A): 1 cycle of bolus chemotherapy was initiated 10-14 days after complete resections and consisted of fluorouracil (5-FU) 500 mg/m^2 intravenously (IV) for 5 days. Immunotherapy consisted thymalin or taktivin 20 mg intramuscularly on days 1, 2, 3, 4 and 5. These immunomodulators produced by Pharmaceutics of Russian Federation (Novosibirsk) and approved by Ministry of Health of Russian Federation. Thymalin and taktivin are preparations from calf thymus, which stimulate proliferation of blood T-cell and B-cell subpopulations and their response [10]. The importance must be stressed of using immunotherapy in combination with chemotherapy, because immune dysfunctions of the cell-mediated and humoral

response were induced by tumor, surgical trauma and chemotherapy [6]. Such immune deficiency induced generalization of GC and compromised the long-term therapeutic result. In this sense immunotherapy shielded human organism from side and adverse effects of basic treatment. 4-5 courses of adjuvant chemoimmunotherapy were repeated every 28-day. During chemoimmunotherapy antiemetics were administered. Gastrointestinal side effects, particularly nausea and vomiting, were mild, and chemoimmunotherapy was generally well tolerated. Severe leukopenia, neutropenia, anemia and trombocytopenia occurred infrequently. There were no treatment-related deaths.

A follow-up examination was, generally, done every 3 month for the first 2 years, every 6 month after that and yearly after 5 years, including a physical examination, a complete blood count, blood chemistry, chest roentgenography. Endoscopy and abdominal ultrasound were done every 6-month for the first 3 years and yearly after that. Zero time was the data of surgical procedures. No one was lost during the follow-up period and we regarded the outcome as death through personal knowledge, physician's reports, and autopsy or death certificates. Survival time (days) was measured from the date of surgery until death or the most-recent date of follow-up for surviving patients.

Variables selected for 10-year survival and life span study were sex, age, TNM, cell type, tumor size. Survival curves were estimated by the Kaplan-Meier method. Differences in curves between groups of GCP were evaluated using a log-rank test. Multivariate proportional hazard Cox regression, structural equation modeling (SEPATH), Monte Carlo simulation and neural networks computing were used to determine any significant dependence [11-15]. Neural networks computing, system, biometric and statistical analyses were conducted using CLASS-MASTER program (Stat Dialog, Inc., Moscow, Russia), SANI program (Stat Dialog, Inc., Moscow, Russia), STATISTICA and STATISTICA Neural Networks program (Stat Soft, Inc., Tulsa, OK, the USA), DEDUCTOR program (BaseGroup Labs, Inc., Riazan, Russia), SPSS (SPSS Inc., Chicago, IL, USA), Table Curve3D (Systat Software Inc., San Hose, CA, USA). All tests were considered significant when the resulting P value was less than 0.05.

3. Results

For the entire sample of 796 patients overall life span (mean±standard error) was 2130.8±2304.3 days (95% CI, 21196.4-2423.5; median=1089.5) and cumulative 5-year survival reached 58.4%, 10-year survival – 52.4%, 20-year survival – 40.4% (Fig.1). 316 GCP (life span=4316.1±2292.9 days) lived more than 5 years and 169 (life span=5919.5±2020 days) – more than 10 years without any features of GC progressing. 294 GCP (life span=640.6±347.1 days) died due to the cancer generalization within the first 5 years after complete gastrectomies.

It is necessary to pay attention on the three very important prognostic phenomenons. First, 88.4 % 10-year survival for GCP with the early cancer as against 41.7% for the others GCP after gastrectomies (P=0.000 by log-rank test) (Fig.2). We understand as the early cancer the tumor up to 2 cm in diameter, witch invades submucosa without lymph node and distant metastases [10].

Second, good 10-year survival for GCP with N0 (69.9%) as compared with GCP with N1-2 (10-year survival was 29.7%) after radical procedures (P=0.000 by log-rank test) (Fig.3).

Third, for the 173 GCP in adjuvant chemoimmunotherapy (AT) arm (group A) cumulative 10-year survival reached 62.3% vs. 50.5% (group B) (P=0.0228 by log-rank test) (Fig.4).

All clinicopathologic characteristics and treatment modalities were evaluated in traditional Cox multivariate prognostic factor analysis. In accordance with Cox regression model, the 18 variables significantly explained GCP 10-year survival with N0-2 (n=796) after complete gastrectomies: Cox modeling displayed that 10YS of GCP significantly depended on: phase transition (PT) early-invasive GC in terms of synergetics, PT N0—N12, cell ratio factors (ratio between cancer cells- CC and blood cells subpopulations), G1-3, AT, blood cell circuit, prothrombin index, hemorrhage time, residual nitrogen, age, sex, procedure type (P=0.000-0.039)(Table 1).

Table 1 Results of multivariate proportional hazard Cox regression modeling in prediction of GCP 10-year survival after esophagectomies (n=796)

Cox Proportional Hazards Results; N=796	Parameter Estimate	Standard Error	Chi-square	P value	95% Lower CL	95% Upper CL	Hazard Ratio	95% Hazard Ratio Lower CL	95% Hazard Ratio Upper CL
ESS	-0.013709	0.005071	7.30909	0.006861	-0.02365	-0.003771	0.986384	0.976629	0.996237
Hemorrhage Time	0.001264	0.000384	10.83952	0.000994	0.00051	0.002017	1.001265	1.000512	1.002019
Residual Nitrogen	0.048090	0.009213	27.24627	0.000000	0.03003	0.066147	1.049265	1.030488	1.068383
Prothrombin Index	0.019278	0.005025	14.71834	0.000125	0.00943	0.029126	1.019465	1.009474	1.029555
Phase Transition N0---N12	0.841424	0.129270	42.36770	0.000000	0.58806	1.094789	2.319668	1.800492	2.988551
Age	0.012906	0.006201	4.33143	0.037415	0.00075	0.025060	1.012989	1.000752	1.025376
Sex	0.345970	0.125315	7.62198	0.005766	0.10036	0.591583	1.413360	1.105565	1.806847
G1-3	0.155198	0.067288	5.31982	0.021084	0.02332	0.287080	1.167889	1.023590	1.332531
Procedure Type	0.178155	0.074898	5.65787	0.017377	0.03136	0.324953	1.195011	1.031854	1.383965
Adjuvant Chemoimmunotherapy	-0.586838	0.182073	10.38836	0.001268	-0.94369	-0.229982	0.556083	0.389188	0.794548
Phase Transition Early—Invasive Cancer	0.758099	0.297619	6.48829	0.010859	0.17478	1.341422	2.134216	1.190980	3.824479
Segmented Neutrophils/Cancer Cells	-0.077657	0.031421	6.10822	0.013455	-0.13924	-0.016073	0.925281	0.870017	0.984056
Leucocytes (tot)	-0.804807	0.345307	5.43216	0.019769	-1.48160	-0.128018	0.447174	0.227274	0.879838
Eosinophils (tot)	0.846919	0.349475	5.87288	0.015376	0.16196	1.531879	2.332450	1.175814	4.626860
Stick Neutrophils (tot)	0.727764	0.348207	4.36825	0.036615	0.04529	1.410236	2.070446	1.046333	4.096923
Segmented Neutrophils (tot)	0.824759	0.345890	5.68563	0.017104	0.14683	1.502690	2.281331	1.158154	4.493763
Lymphocytes (tot)	0.777852	0.345546	5.06736	0.024380	0.10059	1.455109	2.176791	1.105828	4.284951
Monocytes (tot}	0.883294	0.358395	6.07416	0.013717	0.18085	1.585736	2.418855	1.198238	4.882885

Table 2 Results of bootstrap simulation in prediction of 10-year survival of GCP after gastrectomies (n=611)

Bootstrap Simulation n=611 Significant Factors (Number of Samples=3333)	**Rank**	**Kendall'Tau-A**	**P<**
Healthy Cells/Cancer Cells	1	0.170	0.000
Lymphocytes/Cancer Cells	2	0.162	0.000
Leucocytes/Cancer Cells	3	0.159	0.000
Erythrocytes/Cancer Cells	4	0.158	0.000
Thrombocytes/Cancer Cells	5	0.158	0.000
Segmented Neutrophils/Cancer Cells	6	0.150	0.000
Coagulation Time	7	-0.142	0.000
Tumor Size	8	-0.120	0.000
Monocytes/Cancer Cells	9	0.118	0.000
PT N0---N12	10	-0.112	0.000
T1-4	11	-0.112	0.000
Residual Nitrogen	12	-0.109	0.000
Chlorides	13	0.105	0.000
PT Early---Invasive Cancer	14	-0.098	0.001
Procedures Type	15	-0.072	0.01
Localization	16	-0.068	0.05
Age	17	-0.067	0.05
Combined Procedures	18	0.065	0.05
Stick Neutrophils	19	-0.064	0.05
Prothrombin Index	20	-0.064	0.05
Stick Neutrophils abs	21	-0.062	0.05
Stick Neutrophils tot	22	-0.061	0.05

All of these differences and discrepancies were further investigated by structural equation modeling (SEPATH) as well as Monte Carlo simulation. For more exact analysis 185 patients were excluded from sample, which were alive less than

10 years after complete gastrectomies without relapse. From data, summarized in Fig. 6 it was revealed that the ten clusters significantly predicted 10-year survival and life span of GCP with N0-2 status (n=611): 1) PT early--invasive GC 2)PT N0—N12; 3) Cell Ratio Factors; 4)GC characteristics; 5) biochemical homeostasis; 6) hemostasis system; 7) surgery type; 8) adjuvant chemoimmunotherapy; 9) anthropometric data; 10) tumor localization.

Table 3 Results of neural networks computing in prediction of 10-year survival of GCP after gastrectomies (n=611)

Neural Networks: n=611; Baseline Error=0.000; Area under ROC Curve=1.000; Correct Classification Rate=100%	**Rank**	**Sensitivity**
Healthy Cells/Cancer Cells	1	29567
Phase Transition Early--Invasive Cancer	2	27063
Phase Transition N0---N12	3	18552
Erythrocytes/Cancer Cells	4	26259
Thrombocytes/Cancer Cells	5	21247
Monocytes/Cancer Cells	6	14003
Segmented Neutrophils/Cancer Cells	7	10172
Eosinophils/Cancer Cells	8	9332
Leucocytes/Cancer Cells	9	8369
Lymphocytes/Cancer Cells	10	7665
Stick Neutrophils/Cancer Cells	11	7517

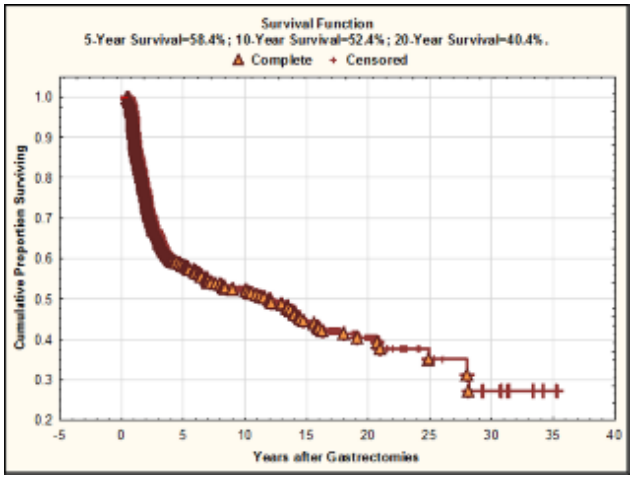

Figure 1 General cumulative survival of GCP with stage T1-4N0-2M0, n=796 after radical gastrectomies: cumulative 5-year survival=58.4%, 10-year survival=52.4%, 20-year survival=40.4%.

For comparative purposes, clinicopathological factors of GCP (n=611) were tested by neural networks computing (4-layer perceptron) (Table 3). Obviously, analyzed data provide significant information about GC prediction. High accuracy of classification (10-year survivors vs. losses) was achieved 100% (baseline error=0.000, area under ROC curve=1.0). In other words, it remains formally possible that at least 11 of these factors might predate neoplastic generalization: Healthy Cells/CC (rank=1), PT early---invasive GC (rank=2); PT N0---N12 (Rank=3); Erythrocytes/CC (4); Thrombocytes/CC (5); Monocytes/CC (6); Segmented Neutrophils (7); Eosinophils/CC (8); Leucocytes/CC (9); Lymphocytes/CC (10) Stick Neutrophils (11). Moreover, bootstrap simulation confirmed the paramount value of Cell Ratio Factors, PT N0---N12 and PT early---Invasive GC (Table 2).

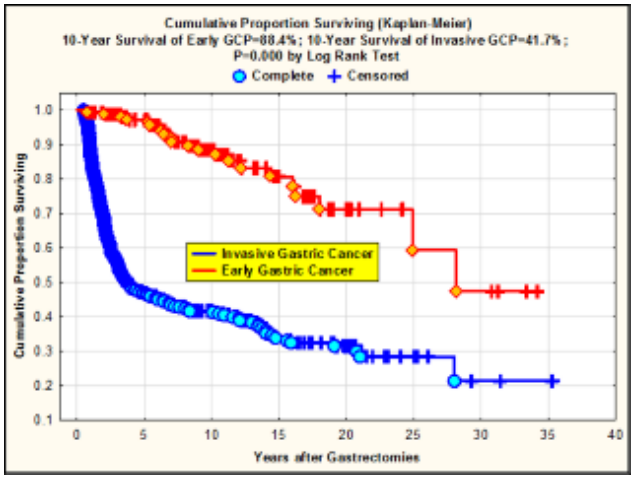

Figure 2 10-year survival of GCP with early cancer (n=164) (88.4%) was significantly better compared with invasive cancer (n=632) (41.7%) (P=0.0000 by log-rank)

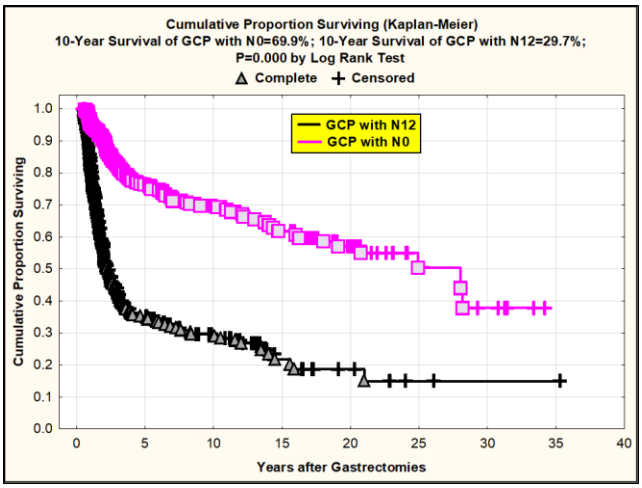

Figure 3 10-year survival of GCP with N0 (n=435) (69.9%) was significantly better compared with N1-N2 metastases (n=361) (29.7%) (P=0.0000 by log-rank)

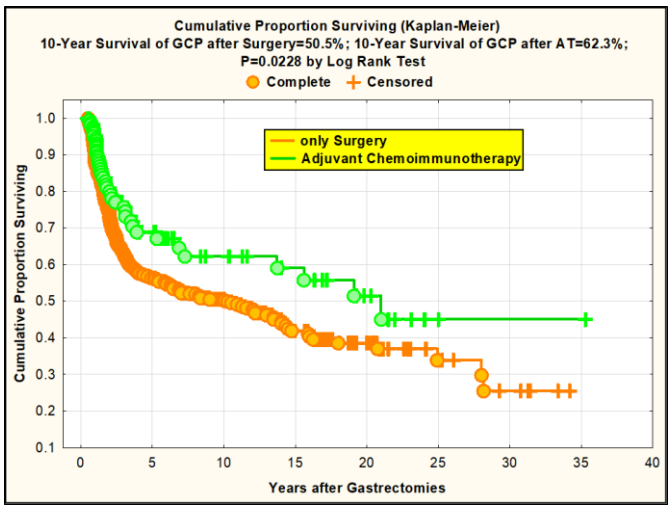

Figure 4 10-year survival of GCP after esophagectomies in group A (adjuvant chemoimmunotherapy) (n=173) and B (surgery alone) (n=623). 10-Survival of GCP in group A was (62.3%) significantly better compared with group B (50.5%) (P=0.0228 by log-rank)

It is necessary to note a very important law: both transitions of the early cancer into the invasive cancer, as well as the cancer with N0 into the cancer with N1-N2, have the phase character. These results testify by mathematical and imitating modeling of system "GC—patient homeostasis" in terms of synergetics (Fig. 7-16). This also proves the first results received earlier in the work [10] (Fig.5). Presence of the two phase transitions is evidently shown on Kohonen self-organizing neural networks maps (Figure 17).

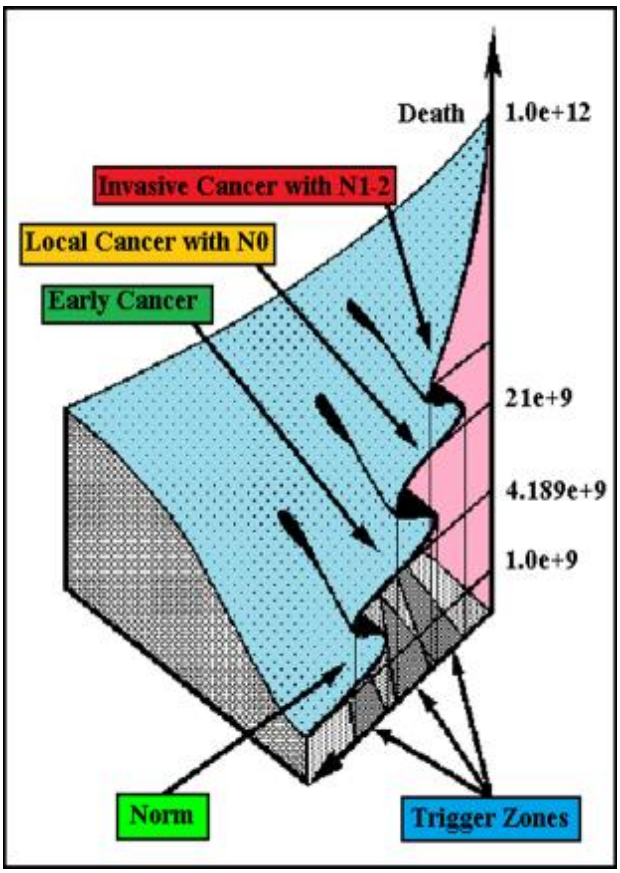

Figure 5 Gastric cancer cell dynamics: Presence of the two phase transitions "early cancer—invasive cancer" and "cancer with N0—cancer with N1-N2" in terms of synergetics

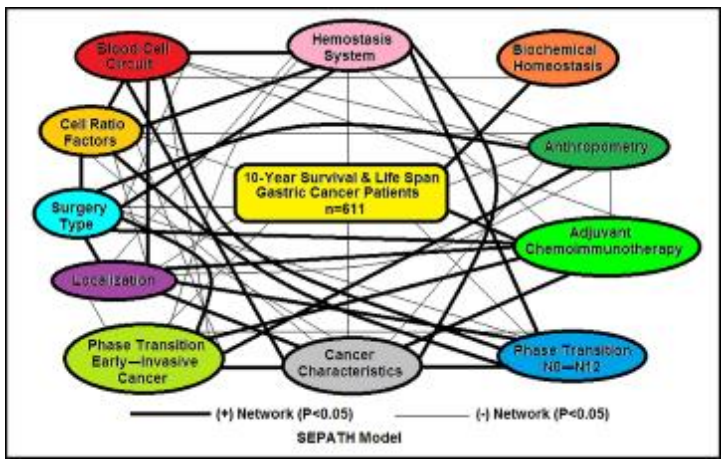

Figure 6 Significant networks between GCP (n=611) 10-year survival, life span, cancer characteristics, blood cell circuit, cell ratio factors, hemostasis system, biochemic and anthropometric data, phase transition "early cancer—invasive cancer", phase transition "cancer with N0—cancer with N1-N2" and treatment protocols (SEPATH network model)

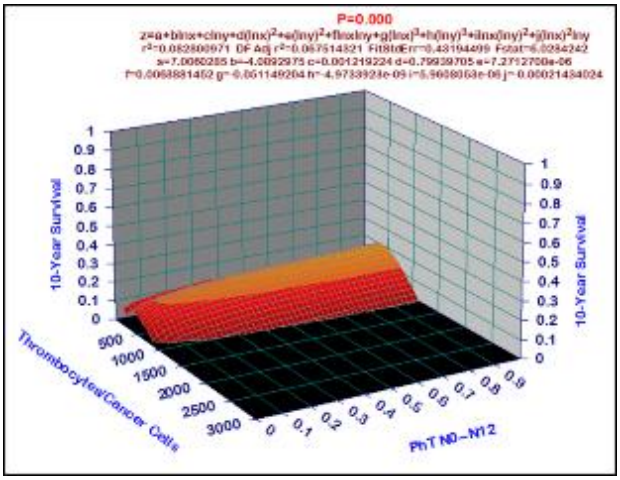

Figure 7 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition N0---N1-2 and blood Thrombocytes/Cancer cells (P=0.000)

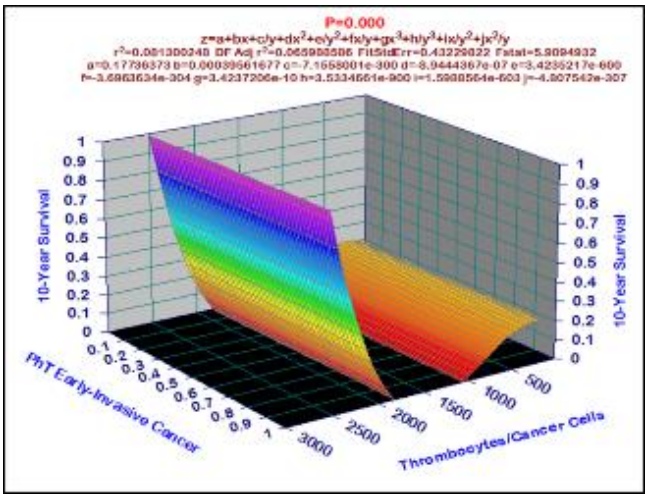

Figure 8 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition early---invasive cancer and blood Thrombocytes/Cancer cells (P=0.000)

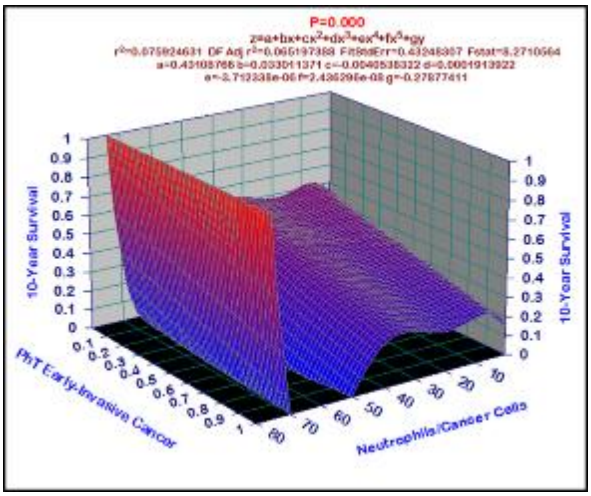

Figure 9 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition early---invasive cancer and blood Neutrophils/Cancer cells (P=0.000)

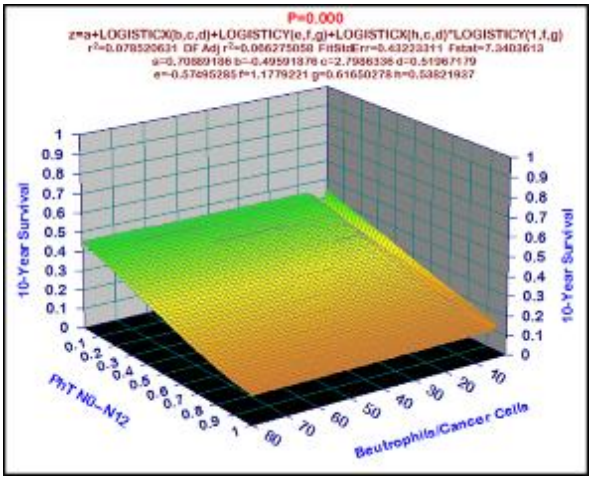

Figure 10 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition N0---N1-2 and blood Neutrophils/Cancer cells (P=0.000)

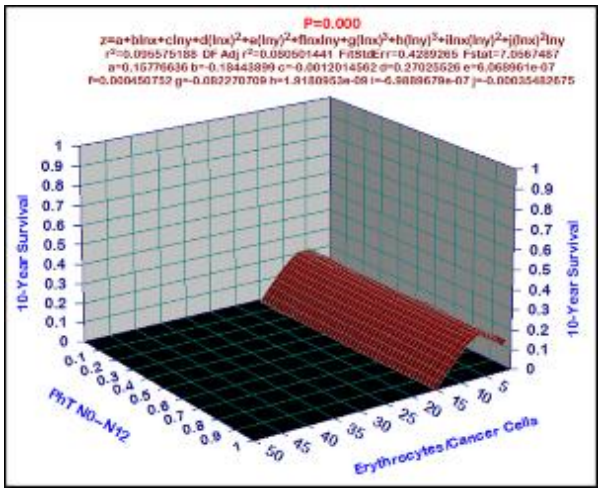

Figure 11 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition N0---N1-2 and blood Erythrocytes/Cancer cells (P=0.000)

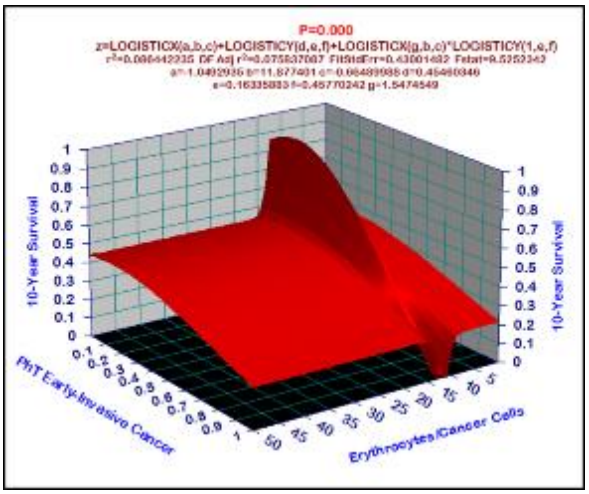

Figure 12 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition early---invasive cancer and blood Erythrocytes/Cancer cells (P=0.000)

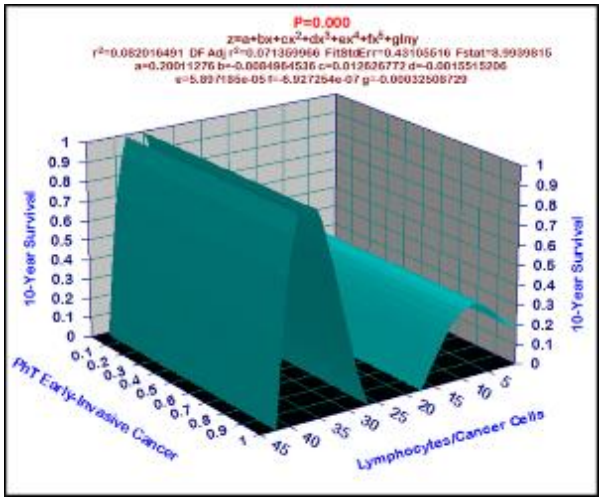

Figure 13 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition early---invasive cancer and blood Lymphocytes/Cancer cells (P=0.000)

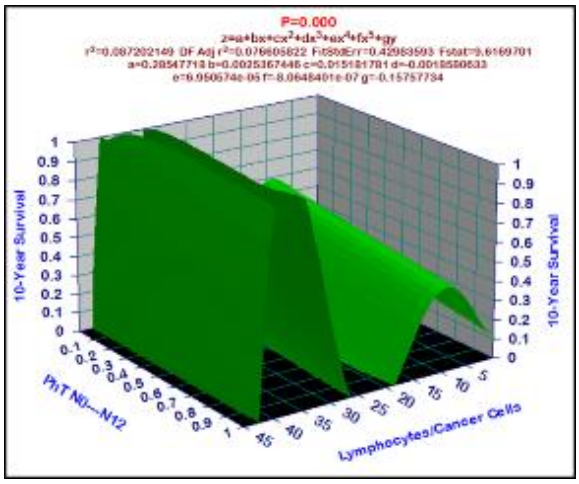

Figure 14 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition N0---N12 and blood Lymphocytes/Cancer cells (P=0.000)

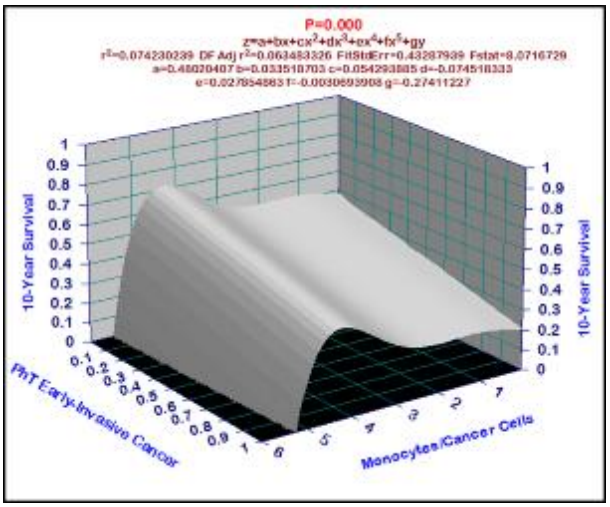

Figure 15 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition early---invasive cancer and blood Monocytes/Cancer cells (P=0.000)

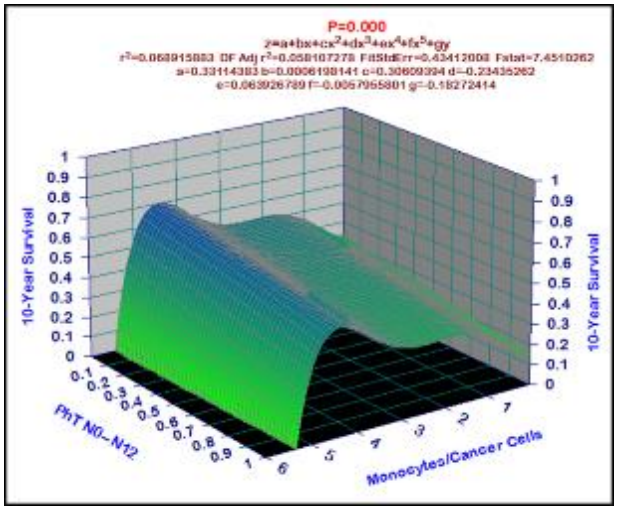

Figure 16 Prognostic equation model of 10-year survival of gastric cancer patients (n=611), phase transition N0---N12 and blood Monocytes/Cancer cells (P=0.000)

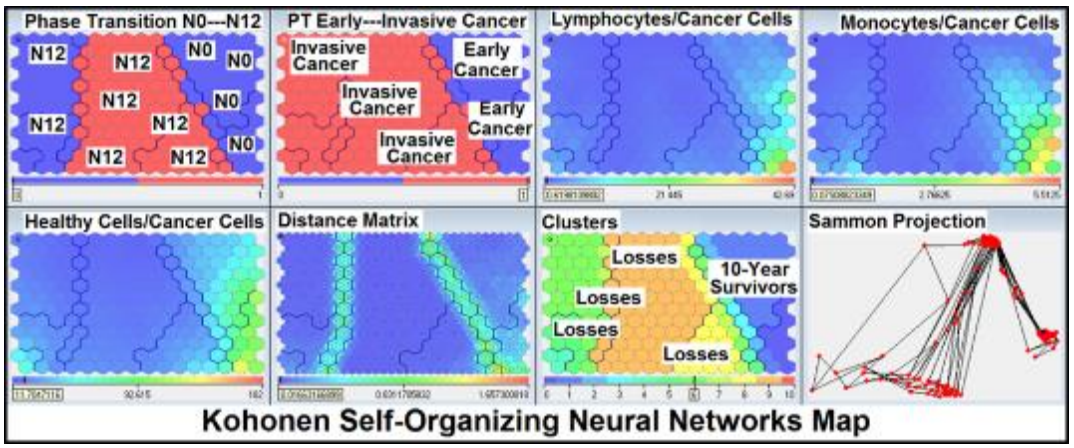

Figure 17 Results of Kohonen self-organizing neural networks computing in prediction of GCP 10-year survival after gastrectomies (n=611)

4. Discussion

Central goal of the present research was to estimate the efficiency of adjuvant chemoimmunotherapy after complete gastrectomies. The importance must be stressed of using complex system analysis, artificial intelligence (neural networks computing), statistical methods and simulations in combination, because the different approaches yield complementary pieces of prognostic information [6, 25].

Although there is no consensus on adjuvant treatment followed by radical procedures two of the most commonly employed strategies are surgery alone and adjuvant chemotherapy with or without immunotherapy.

Actually surgical removal of tumor and its metastases remains basic management of this very aggressive cancer giving the real chance for recovery in spite of quite intensive researches developed during the last 30 years in terms of chemotherapy and immunotherapy [16,17]. Unfortunately, the effectiveness of complete gastrectomies (total, distal and proximal) has already reached its limit and leaves much to be desired: the average real 5-year survival rate of radically operated GCP even after combined and extensive procedures is 30-35% and practically is not improved during the past 50 years, as the great majority of patients has already GC with stage II-III [5,18].

In the last 10-20 years a number of new drugs have been shown to have good activity against GC, including mitomycin C, UFT, epirubicin, etoposide, cisplatin, doxetacel, irinotecan, etc. [19,20-22]. On the other hand new immunomodulators, checkpoint inhibitors, new adoptive immunotherapeutic modalities with lymphokine-activated

killer cells, tumor-infiltrating lymphocytes and high-dose interleukins have been developed and antitumor effect have been successfully demonstrated in advanced malignancies, including GC [4,7,23-25].

Theoretically chemoimmunotherapy is most effective when used in patients with a relatively low residual malignant cell population (approximately 1 billion cancer cells per patient) in terms of hidden micrometastases [6]. This is typical clinical situation at GCP with stage II-III after complete gastrectomies (R0). Present research only confirmed this axiom.

In summary, when adjuvant chemoimmunotherapy is applied to complete gastrectomies for GC, the following benefits should be considered: 1) possibility of total elimination of residual hidden micrometastases; 2) surgery and chemotherapy can result immunosuppressive state, which can be improved by immunotherapy; 3) radical operated GCP with stage II-III are thought to be potentially good candidates for adjuvant chemoimmunotherapy as the majority of these patients would be expected to have GC progressing.

Further investigations will be required to determine efficiency, compatibility and tolerance of new drugs and immunomodulators, checkpoint inhibitors after gastrectomies. The results of the present research will offer guidance for the design of future studies.

5. Conclusion

10-Year survival of GCP after radical procedures significantly depended on: 1) PT early-invasive cancer; 2) PT N0--N12; 3) cell ratio factors; 4) blood cell circuit; 5) biochemical factors; 6) hemostasis system; 7) AT; 8) GC characteristics; 9) anthropometric data; 10) surgery type.

Optimal diagnosis and treatment strategies for GC are: 1) screening and early detection of GC; 2) availability of experienced abdominal surgeons because of complexity of radical procedures; 3) aggressive en block surgery and adequate lymph node dissection for completeness; 4) precise prediction; 5) adjuvant chemoimmunotherapy for GCP with unfavorable prognosis.

Compliance with ethical standards

Funding statement

I do not have any financial, commercial, legal, or professional relationship with other organizations, or with the people working with them, that could influence my research.

Statement of informed consent

All patients signed a written informed consent included in the study, approved by the local Institutional Review

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