

Esophageal Cancer: 10-Year Survival After Surgery

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Research article

Keywords: esophageal cancer, surgery, 10-year survival, prognosis.

Posted Date: October 1st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-936622/v1>

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Abstract

OBJECTIVE: 10-Year survival (10YS) after radical surgery for esophageal cancer (EC) patients (ECP) (T1-4N0-2M0) was analyzed.

METHODS: We analyzed data of 551 consecutive ECP (age=56.5±8.9 years; tumor size=6±3.5 cm) radically operated (R0) and monitored in 1975-2021 (m=411, f=140; esophagogastrectomies (EG) Garlock=284, EG Lewis=267, combined EG with resection of pancreas, liver, diaphragm, aorta, VCS, colon transversum, lung, trachea, pericardium, splenectomy=154; adenocarcinoma=314, squamous=227, mix=10; T1=128, T2=115, T3=181, T4=127; N0=278, N1=70, N2=203; G1=157, G2=141, G3=253; early EC=109, invasive=442; only surgery=423, adjuvant chemoimmunoradiotherapy-AT=128: 5-FU+thymalin/taktivin+radiotherapy 45-50Gy). Multivariate Cox modeling, clustering, SEPATH, Monte Carlo, bootstrap and neural networks computing were used to determine any significant dependence.

RESULTS: Overall life span (LS) was 1881.1±2230.6 days and cumulative 5-year survival (5YS) reached 52.1%, 10 years – 45.9%, 20 years – 33.7%. 184 ECP lived more than 5 years (LS=4308.7±2413.3 days), 99 ECP – more than 10 years (LS=5883±2296.6 days). 226 ECP died because of EC (LS=628.3±319.9 days). AT significantly improved 5YS (68.8% vs. 48.5%) (P=0.00025 by log-rank test). Cox modeling displayed that 10YS of ECP significantly depended on: phase transition (PT) N0–N12 in terms of synergetics, cell ratio factors (ratio between cancer cells- CC and blood cells subpopulations), T, G, histology, age, AT, localization, blood cells, prothrombin index, hemorrhage time, residual nitrogen, protein (P=0.000-0.021). Neural networks, genetic algorithm selection and bootstrap simulation revealed relationships between 10YS and PT N0–N12 (rank=1), healthy cells/CC (2), PT early-invasive EC (3), thrombocytes/CC (4), erythrocytes/CC (5), lymphocytes/CC (6), eosinophils/CC (7), stick neutrophils/CC (8), segmented neutrophils/CC (9), monocytes/CC (10), leucocytes/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 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) EC characteristics; 9) tumor localization; 10) anthropometric data; 11) surgery type. Optimal diagnosis and treatment strategies for EC are: 1) screening and early detection of EC; 2) availability of experienced thoracoabdominal surgeons because of complexity of radical procedures; 3) aggressive en block surgery and adequate lymph node dissection for completeness; 4) precise prediction; 5) adjuvant chemoimmunoradiotherapy for ECP with unfavorable prognosis.

Introduction

Esophageal cancer (EC) is the global problem in the world in the structure of mortality from malignant neoplasms. Nevertheless, there is practically no analysis of 10-year survival (10YS) of EC patients (ECP) in the literature. But information on 10YS rate is extremely important in optimizing the treatment and diagnostic process in oncology and especially for extremely aggressive cancer –EC. The high mortality rate associated with EC is primarily due to the high incidence of late stage and the lack of curative management for the majority of ECP. Up to 80–90% of ECP present with stage III-IV disease. The role of adjuvant chemotherapy or chemoimmunotherapy after complete esophagogastrectomies in ECP with stage II-IV remains controversial [1, 21, 25]. Moreover, the optimal treatment plan in general and optimal approach for adjuvant chemotherapy in particular has not been defined and long-term prognosis of ECP 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 20–30% [2, 26]. 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 EC cell population for drugs and immune factors thus obviating cancer cell-cycle cytotoxic and host-immunoprotective effects [3, 4, 24]. Nevertheless, very few studies have demonstrated convincing clinical results. We developed optimal treatment strategies that incorporate bolus chemotherapy, radiotherapy and immunotherapy after radical, aggressive en-block surgery.

Patients And Methods

We conducted this study from 1975 to 2021. 551 consecutive ECP (male – 411, female – 140; age = 56.5 ± 8.9 years, tumor size = 6 ± 3.5 cm) (mean \pm standard deviation) entered this trial. All ECP 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 ECP 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, bronchoscopy, fibroesophagogastroscopy, electrocardiogram. Computed tomography, NMR-tomography scan of upper abdomen, liver and bone radionucle scan were performed whenever needed. All ECP were diagnosed with histologically confirmed EC. All had measurable tumor and ECOG performance status 0 or 1. Before any treatment each patient was carefully examined by medical panel composed of thoracoabdominal surgeon and chemotherapist 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. We performed two types of procedures: 267 complete esophagogastrectomies with lesser and partially major omentum with preservation of right gastroepiploic vessels and lymph node dissection through separate abdominal and right thoracic incision (Lewis, Lewis-McKeown) and 284 - through left thoracoabdominal incision (Garlock). The present analysis was restricted to ECP with complete resected tumors with negative surgical resection margin and with N1 and celiac lymph node metastases (N2). Complete surgical resection consisted of esophagogastrectomy with one-stage intrapleural esophagogastrectomy in 361 (Lewis, Garlock), and with anastomosis on the neck in 190 (Lewis-McKeown, Garlock). EC was localized in lower third of esophagus in 361, middle third - in 61, upper third – in 75, total – 54. Among these, 154 ECP underwent combined and extensive radical procedures with resection of pancreas, liver, diaphragm, aorta, VCS, colon transversum, lung, trachea, pericardium, splenectomy. The extent of lymphadenectomy in the upper abdominal compartment and lower posterior mediastinum was identical for all surgical approaches and comprised a suprapancreatic lymphadenectomy, including all lymph nodes along the common hepatic artery, celiac axis, and splenic artery toward the splenic hilum. The left gastric artery was always transected at its origin and remained with the specimen. Also included were all lymph nodes along the proximal two thirds of the lesser gastric curvature and the gastric fundus, left and right paracardiac nodes, distal paraesophageal nodes, and nodes in the lower posterior mediastinum up to the tracheal bifurcation. Patients with the right thoracoabdominal approach had an additional formal extended mediastinal lymphadenectomy comprising all nodes at the tracheal bifurcation along the left and right main stem bronchi, the upper mediastinal compartment, and along the left recurrent nerve. A systematic cervical lymphadenectomy was performed routinely for ECP with neck anastomosis (190). Routine two-field lymphadenectomy (in terms of EC surgery) was performed in 361, three-field – in 190. The present analysis was restricted to ECP with complete resected tumors with negative surgical resection margin (R0) and with N1-N2 nodes. All ECP were postoperatively staged according to the TNM-classification. Histological examination showed adenocarcinoma in 314, squamous cell cancer – 227 and mixed carcinoma - in 10 patients. The pathological T stage was T1 in 128, T2 - in 115, T3 - in 181, T4 - in 127 cases; the pathological N stage was N0 in 278, N1 - in 70, N2 - in 203 patients. The tumor differentiation was graded as G1 in 157, G2 - in 141, G3 - in 253 cases. Early EC was in 109 patients, invasive EC - in 442. We understand as the early cancer the tumor up to 2 cm in diameter, which invades submucosa without lymph node and distant metastases [6]. After surgery postoperative chemoimmunoradiotherapy were accomplished ECP in ECOG performance status 0 or 1.

All patients (551 ECP) were divided between the two protocol treatment: 1) surgery and adjuvant chemoimmunoradiotherapy (128 ECP – group A); 2) surgery alone without any adjuvant treatment (423 ECP – group B) – the control group.

All 128 patients completed adjuvant chemoimmunoradiotherapy (group A): 1 cycle of bolus chemotherapy was initiated 10–14 days after complete resections and consisted of fluorouracil (5-FU) 500 mg/m² 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, radiotherapy and chemotherapy [6, 26]. Such immune deficiency induced generalization of EC 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. Concurrent radiotherapy (60CO; ROKUS, Russia) with a total tumor dose 45–50 Gy starting 5–7 weeks after surgery. Radiation consisted of single daily fractions of 180–200 cGy 5 days weekly. The treatment volume included the ipsilateral hilus, the supraclavicular fossa and the mediastinum from the incisura jugularis to 8 cm below the carina. The lower mediastinum and upper abdomen were included in cases of primary tumors in the lower third of esophagus or N2. The resected tumor bed was included in all patients. Parallel-opposed AP-PA fields were used. All fields were checked using the treatment planning program COSPO (St. Petersburg, Russia). Doses were specified at middepth for parallel-opposed technique or at the intersection of central axes for oblique technique. No prophylactic cranial irradiation was used. 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 thrombocytopenia occurred infrequently. There were no treatment-related deaths.

A follow-up examination was, generally, done every 3 months for the first 2 years, every 6 months 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, 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 10YS 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), SIMSTAT2.6 (Provalis Research, Montreal, Canada). All tests were considered significant when the resulting P value was less than 0.05.

Results

For the entire sample of 551 patients' overall life span (mean±standard error) was 1881.1±2230.6 days (95% CI, 1694.4–2067.8; median=854) and cumulative 5-year survival reached 52.1%, 10-year survival – 45.9%, 20-year survival – 33.7% (Fig.1). 184 ECP (life span=4308.7±2413.3 days) lived more than 5 years and 99 (life span=5883±2296.6 days) – more than 10 years without any features of EC progressing. 226 ECP (life span=628.3±319.9 days) died due to the cancer generalization within the first 5 years after complete gastrectomies.

It is necessary to pay attention on the five very important prognostic phenomenons. First, 95.7% 10-year survival (10YS) for ECP with the early cancer as against 32.1% for the others ECP after esophagogastrectomies (P=0.000 by log-rank test) (Fig.2).

Second, good 10YS for ECP with N0 (68.6%) as compared with ECP with N1-2 (10-year survival was 20.8%) after radical procedures (P=0.000 by log-rank test) (Fig.3).

Third, for the 128 ECP in adjuvant chemoimmunoradiotherapy (AT) arm (group A) cumulative 10YS reached 68.8% vs. 48.5% (group B) (P=0.00025 by log-rank test) (Fig.4).

Fourth, we revealed 61.4% 10YS for ECP with upper third of esophagus versus 42.4% for other ECP after surgery (P=0.00339 by log-rank test) (Fig.5).

In the fifth we found 60.6% 10YS for ECP versus 30.2% for cardioesophageal cancer patients after surgery (P=0.000 by log-rank test) (Fig.6).

All clinicopathologic characteristics and treatment modalities were evaluated in traditional Cox multivariate prognostic factor analysis. In accordance with Cox regression model, the 17 variables significantly explained ECP 10YS with N0-2 (n=551) after complete esophagogastrectomies. Cox modeling displayed that 10YS of ECP significantly depended on: phase transition (PT) N0–N12 in terms of synergetics, cell ratio factors (ratio between cancer cells- CC and blood cells subpopulations), G1-3, T1-4, AT, prothrombin index, protein, hemorrhage time, residual nitrogen, age, histology, tumor localization (P=0.000-0.021) (Table 1).

All of these differences and discrepancies were further investigated by structural equation modeling (SEPATH) as well as Monte Carlo simulation. For more exact analysis, 141 patients were excluded from sample, which were alive less than 10 years after complete esophagogastrectomies without relapse. From data, summarized in Fig. 7 it was revealed that the eleven clusters significantly predicted 10YS and life span of ECP with N0-2 status (n=410): 1) PT early–invasive EC; 2) PT N0–N12; 3) Cell Ratio Factors; 4) EC characteristics; 5) blood cell circuit; 6) biochemical homeostasis; 7) hemostasis system; 8) surgery type; 9) adjuvant chemoimmunoradiotherapy; 10) anthropometric data; 11) tumor localization.

For comparative purposes, clinicopathological factors of ECP (n=410) were tested by neural networks computing (4-layer perceptron) (Table 2). Obviously, analyzed data provide significant information about EC 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: PT N0–N12 (rank=1), healthy cells/CC (2), PT early-invasive EC (3), thrombocytes/CC (4), erythrocytes/CC (5), lymphocytes/CC (6), eosinophils/CC (7), stick neutrophils/CC (8), segmented neutrophils/CC (9), monocytes/CC (10), leucocytes/CC (11). Moreover, bootstrap simulation confirmed the paramount value of Cell Ratio Factors, PT N0–N12 and PT early–Invasive GC (Table 3). 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 “EC–patient homeostasis” in terms of synergetics (Fig. 9-16). This also proves the first results received earlier in the work [6] (Fig. 8). Presence of the two phase transitions is evidently shown on Kohonen self-organizing neural networks maps (Fig. 17).

Discussion

Central goal of the present research was to estimate the efficiency of adjuvant chemoimmunoradiotherapy after complete esophagogastrectomies. 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, 14, 15, 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 chemoradiotherapy 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, radiotherapy and immunotherapy [16, 17]. Unfortunately, the effectiveness of complete esophagogastrectomies (Lewis, Garlock, Lewis-McKeown) has already reached its limit and leaves much to be desired: the average real 5-year survival rate of radically operated ECP even after combined and extensive procedures is 20–30% and practically is not improved during the past 50 years, as the great majority of patients has already EC 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 EC, 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 EC [4, 7, 23, 24, 25].

Theoretically chemoimmunoradiotherapy 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 ECP with stage II-III after complete esophagogastrectomies (R0). Present research only confirmed this axiom.

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

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

Conclusions

10-Year survival 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) EC characteristics; 9) tumor localization; 10) anthropometric data; 11) surgery type.

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

Declaration

COI 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.

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Tables

Table1. Results of multivariate proportional hazard Cox regression modeling in prediction of ECP 10-year survival after esophagectomies (n=551)

Cox Regression n=551	Parameter Estimate	Standard Error	Chi- square	P value	95% Lower CL	95% Upper	Hazard Ratio
Hemorrhage Time	0.00140	0.000402	12.18223	0.000482	0.00062	0.002192	1.00140
Residual Nitrogen	0.05156	0.011110	21.54182	0.000003	0.02979	0.073339	1.05292
Protein	0.02145	0.008664	6.12841	0.013303	0.00447	0.038428	1.02168
Prothrombin Index	0.02606	0.006403	16.55867	0.000047	0.01351	0.038605	1.02640
T1-4	0.43221	0.085980	25.26934	0.000000	0.26369	0.600727	1.54066
N0—N12	0.59826	0.161755	13.67911	0.000217	0.28122	0.915290	1.81894
Age	0.02845	0.007746	13.48557	0.000240	0.01326	0.043627	1.02885
Histology	-0.28768	0.124960	5.30016	0.021323	-0.53260	-0.042767	0.75000
G1-3	0.42034	0.088794	22.41002	0.000002	0.24631	0.594377	1.52248
Adjuvant Chemoimmunoradiotherapy	-0.93274	0.197277	22.35461	0.000002	-1.31939	-0.546082	0.39348
Segmented Neutrophils/Cancer Cells	4.04524	1.582385	6.53527	0.010576	0.94382	7.146654	57.12473
Localization	-0.53528	0.190887	7.86335	0.005045	-0.90941	-0.161147	0.58551
Leucocytes/Cancer cells	-4.11797	1.590909	6.70002	0.009641	-7.23610	-0.999847	0.01628
Eosinophils/Cancer Cells	4.26504	1.671458	6.51111	0.010720	0.98904	7.541033	71.16750
Stick Neutrophils/Cancer Cells	4.33745	1.642549	6.97321	0.008274	1.11812	7.556790	76.51243
Lymphocytes/Cancer Cells	3.93332	1.604682	6.00815	0.014240	0.78820	7.078439	51.07626
Monocytes/Cancer Cells	4.34006	1.643347	6.97483	0.008266	1.11916	7.560962	76.71226

Table 2. Results of neural networks computing in prediction of 10-year survival of ECP after esophagectomies (n=410).

Table 3. Results of bootstrap simulation in prediction of 10-year survival of ECP after esophagectomies (n=410).

Factors: Correct Classification Rate=100%; Error=0.0; Area under ROC Curve=1.0	Rank	Sensitivity
Phase Transition N0—N12	1	14768
Healthy Cells/Cancer Cells	2	11853
Phase Transition Early—Invasive Cancer	3	10080
Thrombocytes/Cancer Cells	4	8933
Erythrocytes/Cancer Cells	5	8326
Lymphocytes/Cancer Cells	6	7595
Eosinophils/Cancer Cells	7	6406
Stick Neutrophils/Cancer Cells	8	5490
Segmented Neutrophils/Cancer Cells	9	3938
Monocytes/Cancer Cells	10	2943
Leucocytes/Cancer Cells	11	2658

Significant Factors	(Number of Samples=3333)	Rank	Kendal Tau-A	P
Tumor Size		1	-0.316	0.000
Healthy Cells/Cancer Cells		2	0.315	0.000
T1-4		3	-0.307	0.000
Erythrocytes/Cancer Cells		4	0.307	0.000
Leucocytes/Cancer Cells		5	0.298	0.000
Thrombocytes/Cancer Cells		6	0.293	0.000
Lymphocytes/Cancer Cells		7	0.289	0.000
Segmented Neutrophils/Cancer Cells		8	0.280	0.000
Residual Nitrogen		9	-0.277	0.000
Phase Transition N0—N12		10	-0.248	0.000
Monocytes/Cancer Cells		11	0.240	0.000
Hemorrhage Time		12	-0.233	0.000
Phase Transition Early—Invasive Cancer		13	-0.225	0.000
Procedure Type		14	-0.192	0.000
Eosinophils/Cancer Cells		15	0.163	0.000
Chlorides		16	0.163	0.000
G1-3		17	-0.140	0.000
Tumor Growth		18	-0.117	0.001
Stick Neutrophils/Cancer Cells		19	0.105	0.01
Erythrocytes		20	0.103	0.01
Weight		21	0.100	0.01
Combined Procedure		22	0.098	0.01
Localization		23	0.070	0.05

Figures

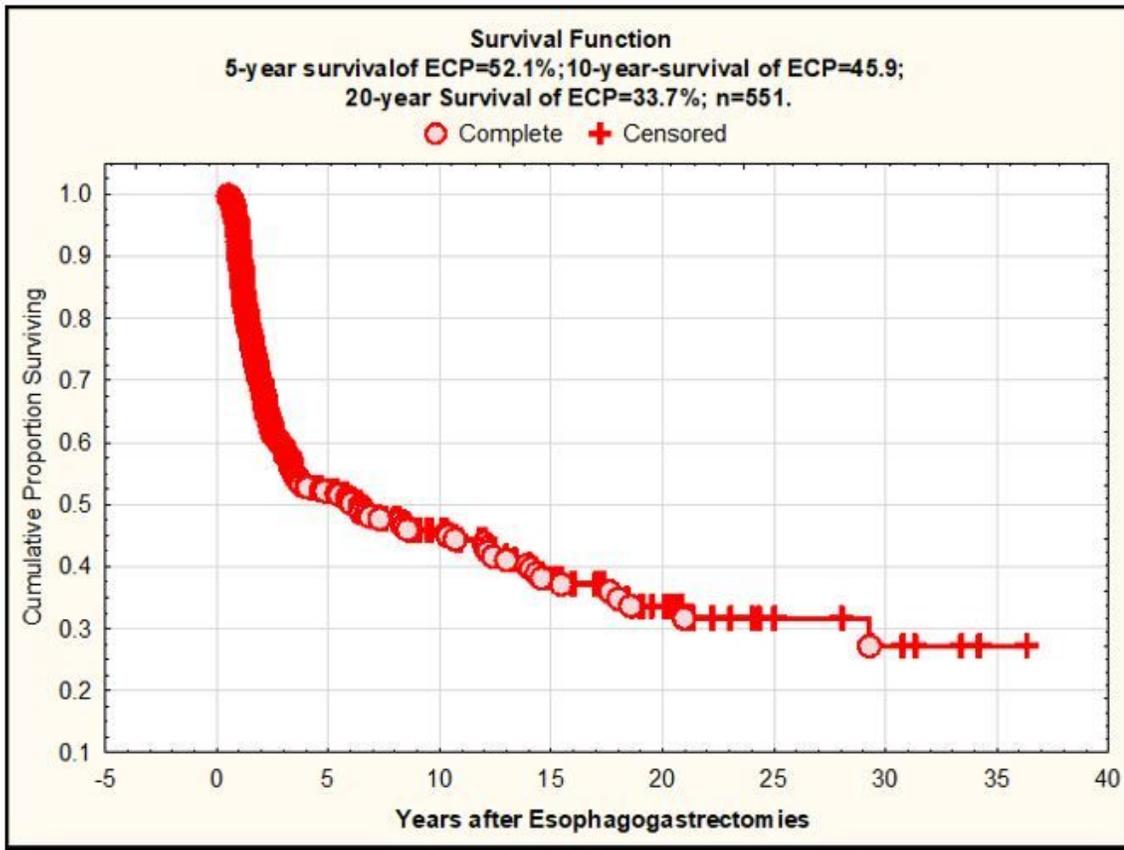


Figure 1

General cumulative survival of ECP with stage T1-4N0-2M0, n=551 after radical esophagogastrectomies: cumulative 5-year survival=52.1%, 10-year survival=45.9%, 20-year survival=33.7%.

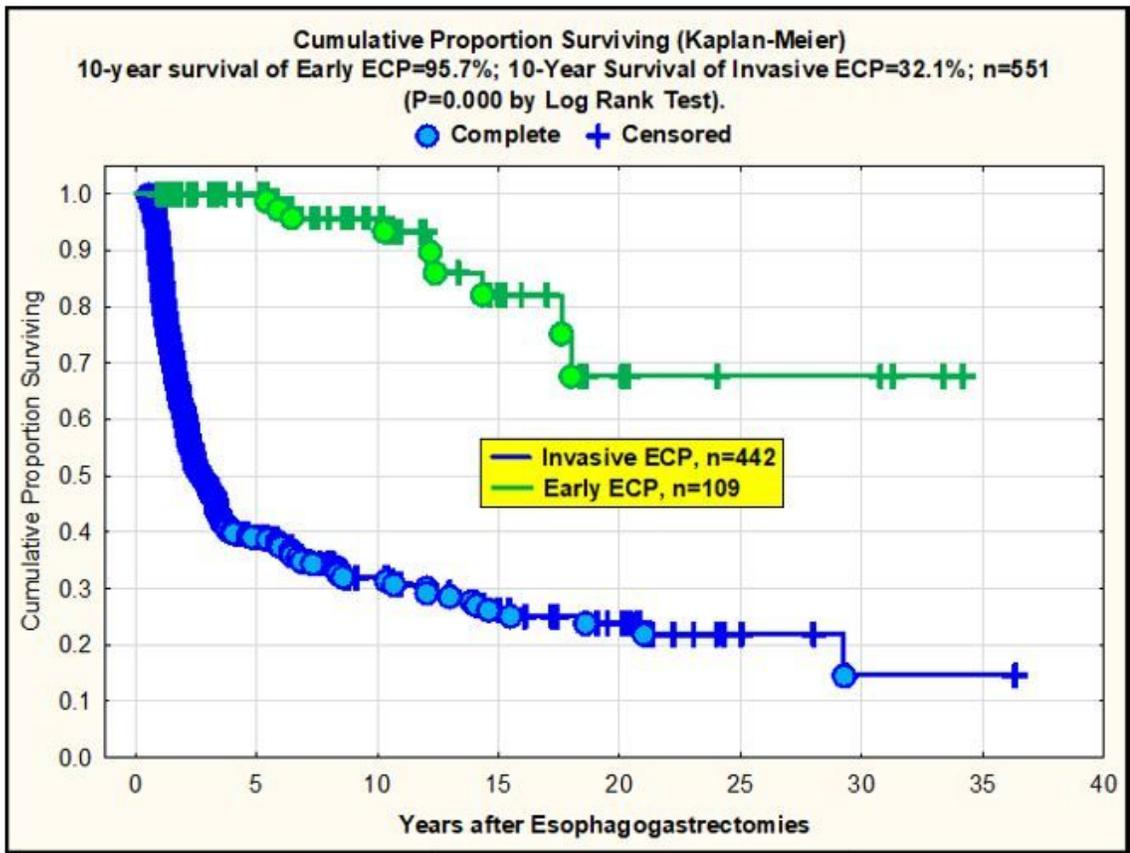


Figure 2

10-year survival of ECP with early cancer (n=109) (95.7%) was significantly better compared with invasive cancer (n=442) (32.1%) (P=0.0000 by log-rank).

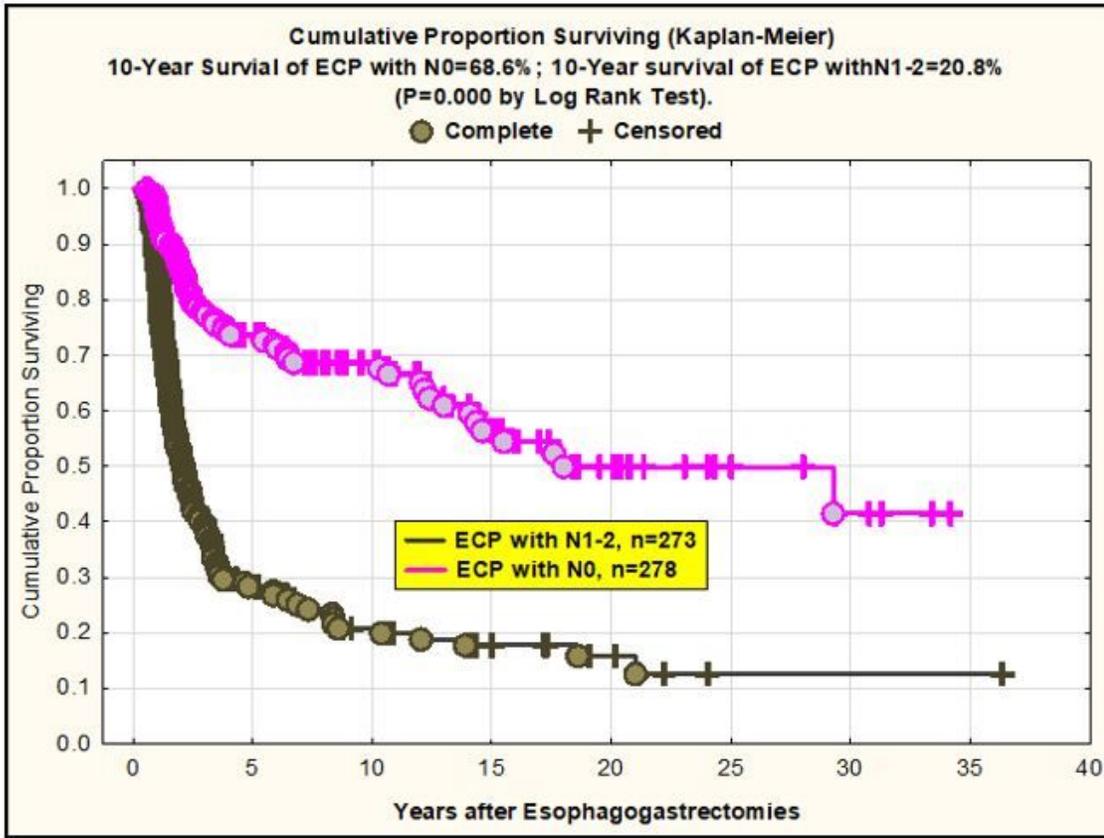


Figure 3

10-year survival of ECP with N0 (n=278) (68.6%) was significantly better compared with N1-N2 metastases (n=273) (20.8%) (P=0.0000 by log-rank).

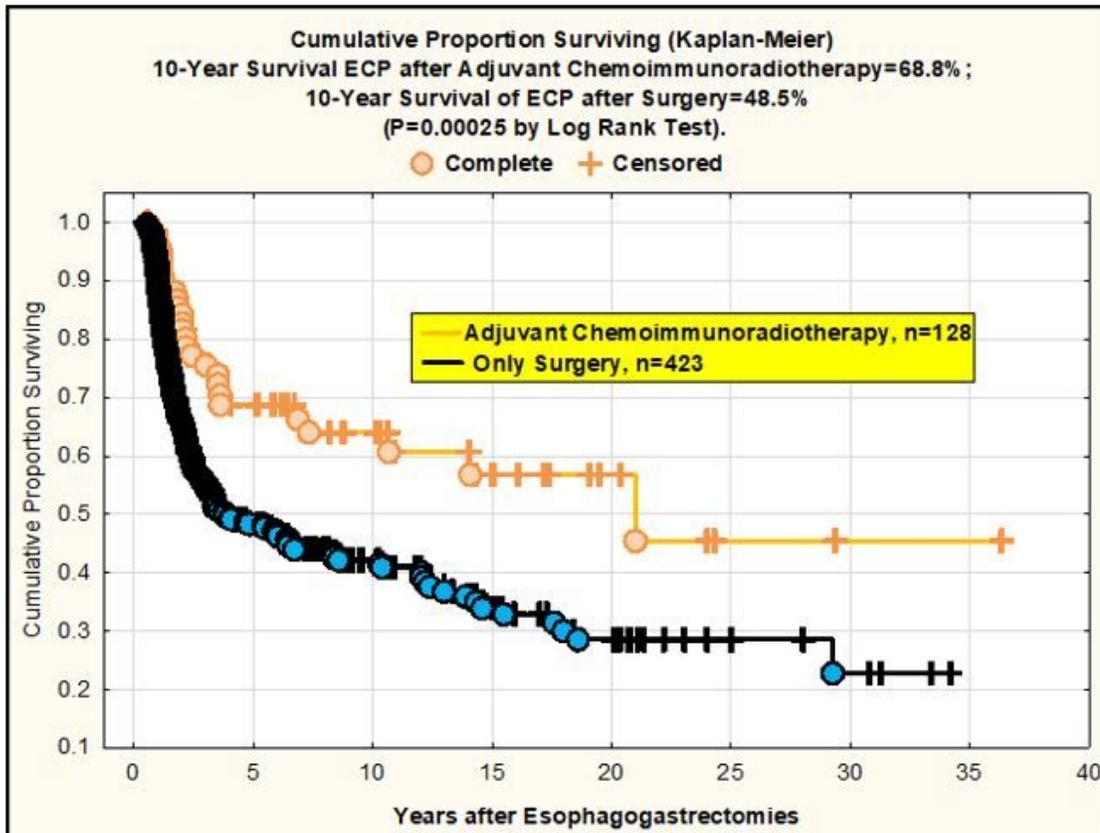


Figure 4

10-year survival of ECP after esophagectomies in group A (adjuvant chemoimmunoradiotherapy) (n=128) and B (surgery alone) (n=423). 10-Survival of ECP in group A was (68.8%) significantly better compared with group B (48.5%) (P=0.00025 by log-rank).

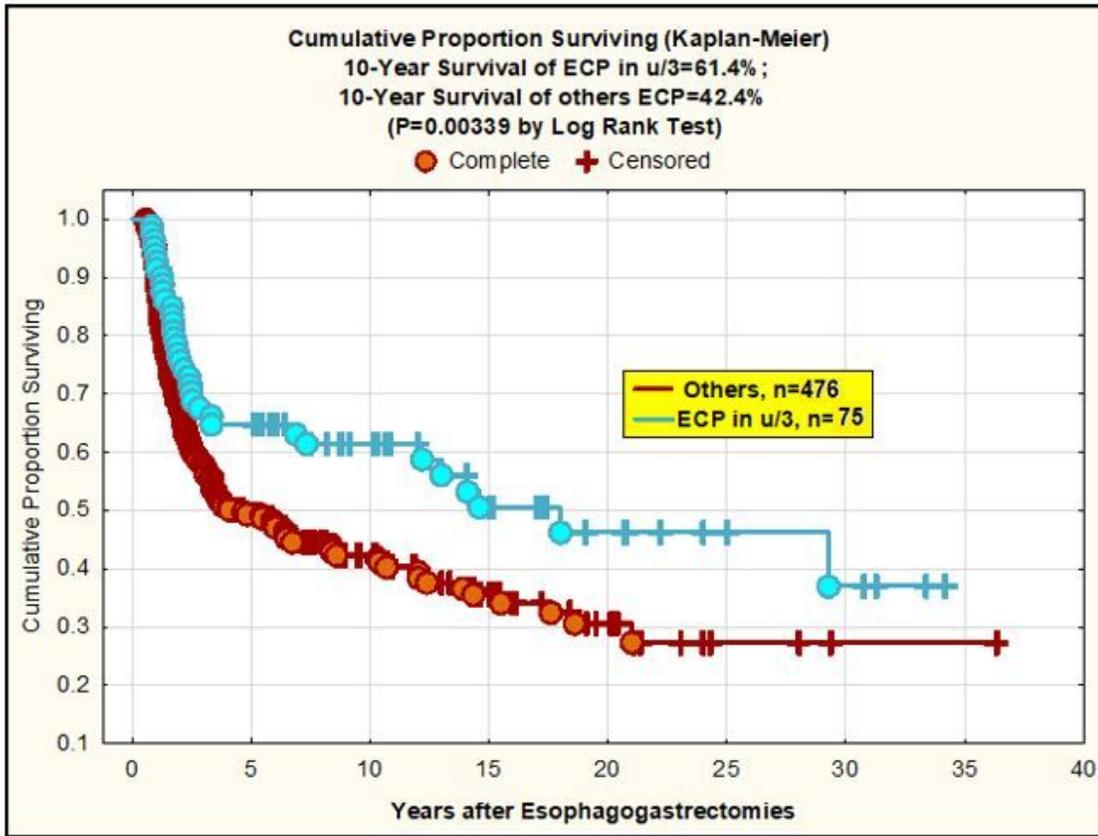


Figure 5

General cumulative 10-year survival of ECP with upper third of esophagus (n=75) was 61.4% versus 42.4% for other ECP after surgery (n=476) (P=0.00339 by log-rank test).

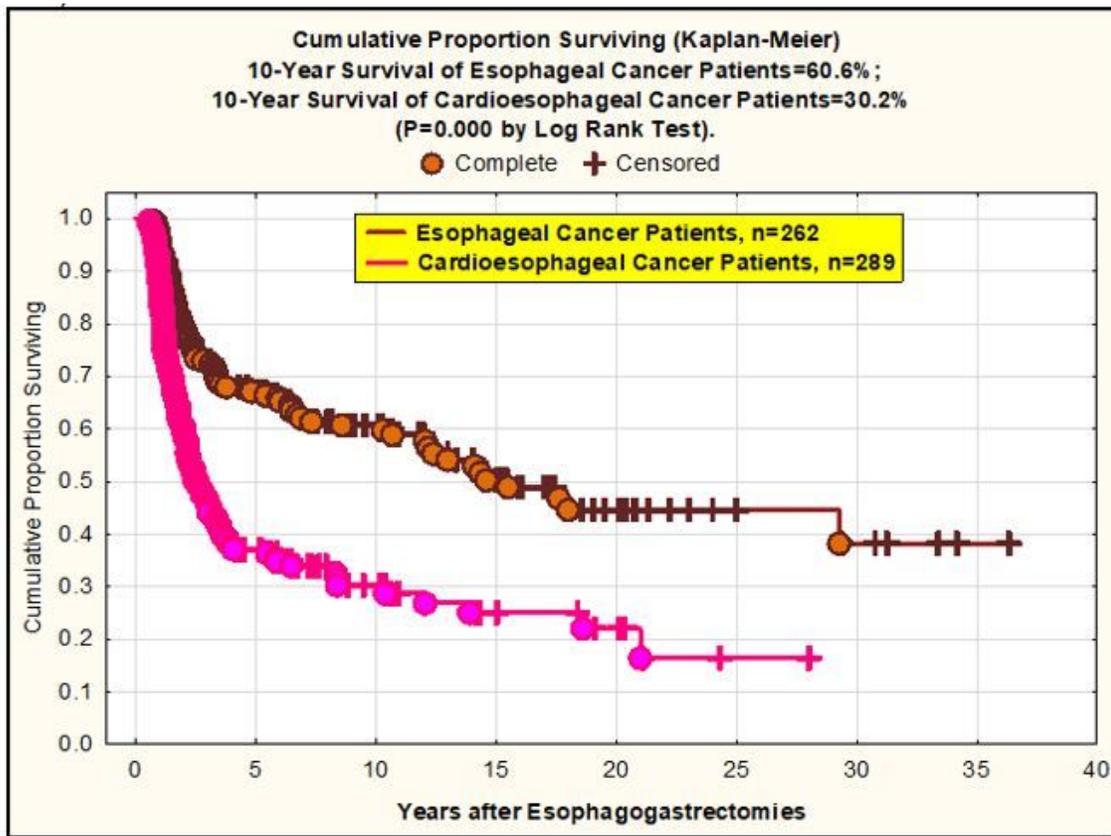


Figure 6

General cumulative 10-year survival of ECP (n=262) was 60.6% versus 30.2% for cardioesophageal cancer patients after surgery (n=289) (P=0.000 by log-rank test).

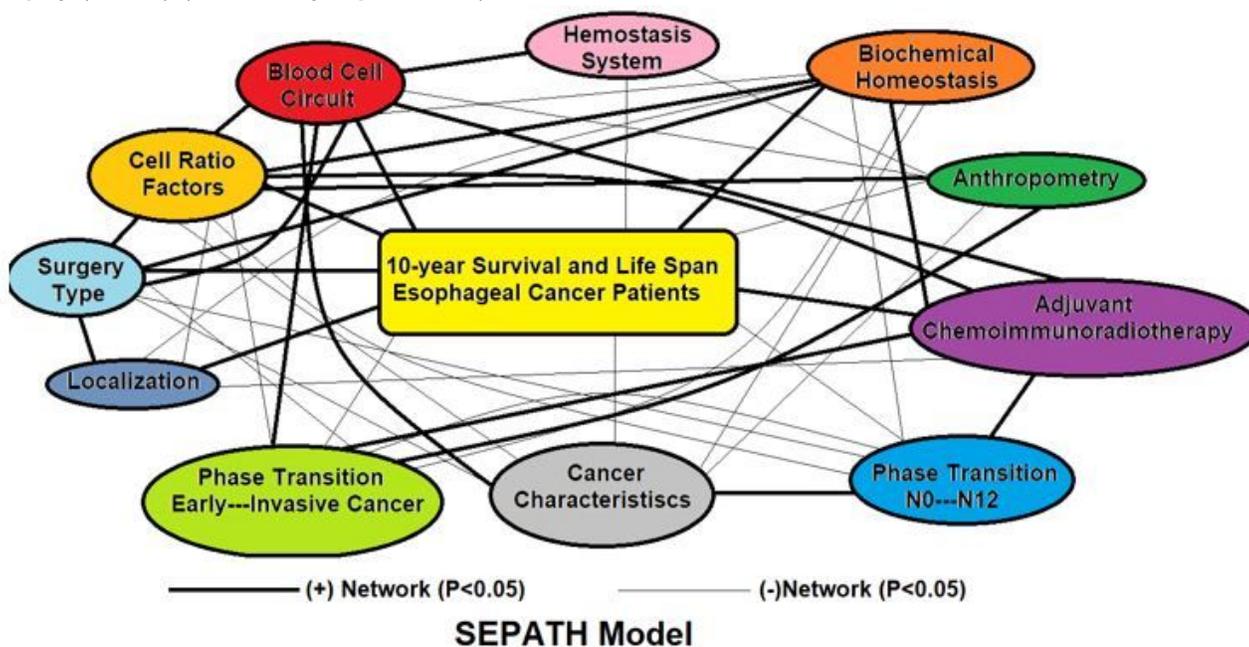


Figure 7

Significant networks between ECP (n=410) 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).

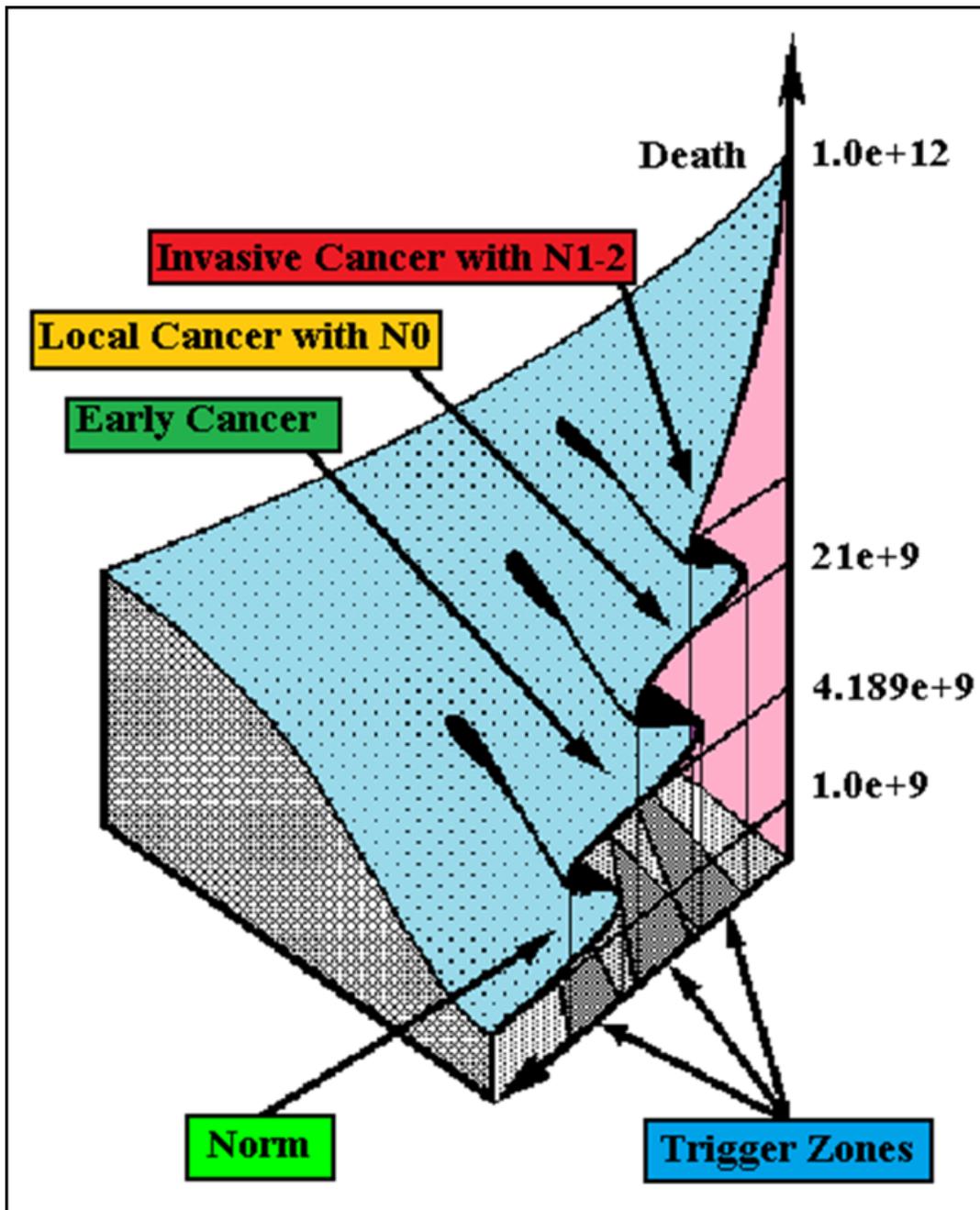


Figure 8

Esophageal 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.

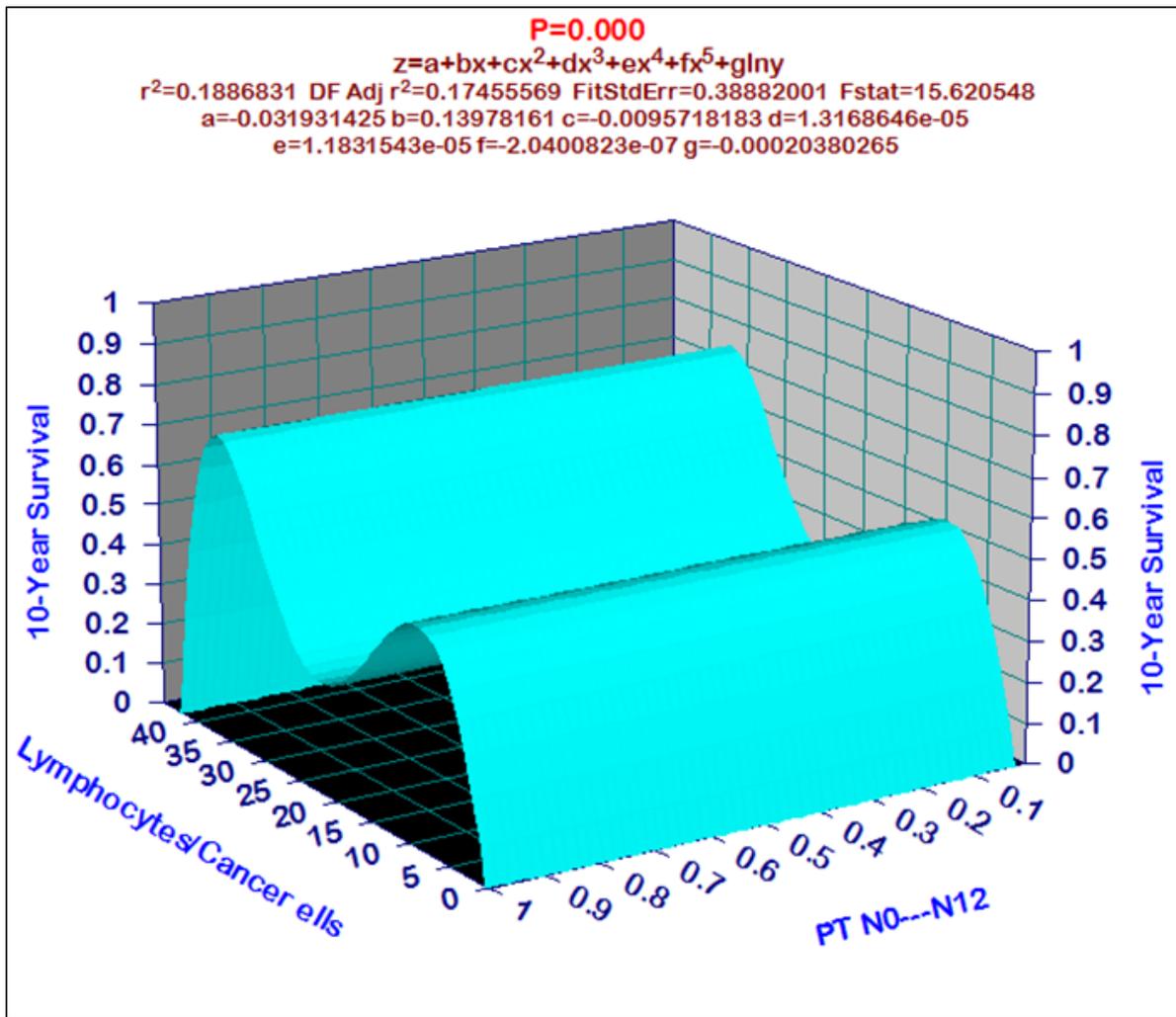


Figure 9

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), phase transition N0–N1-2 and blood Lymphocytes/Cancer cells (P=0.000).

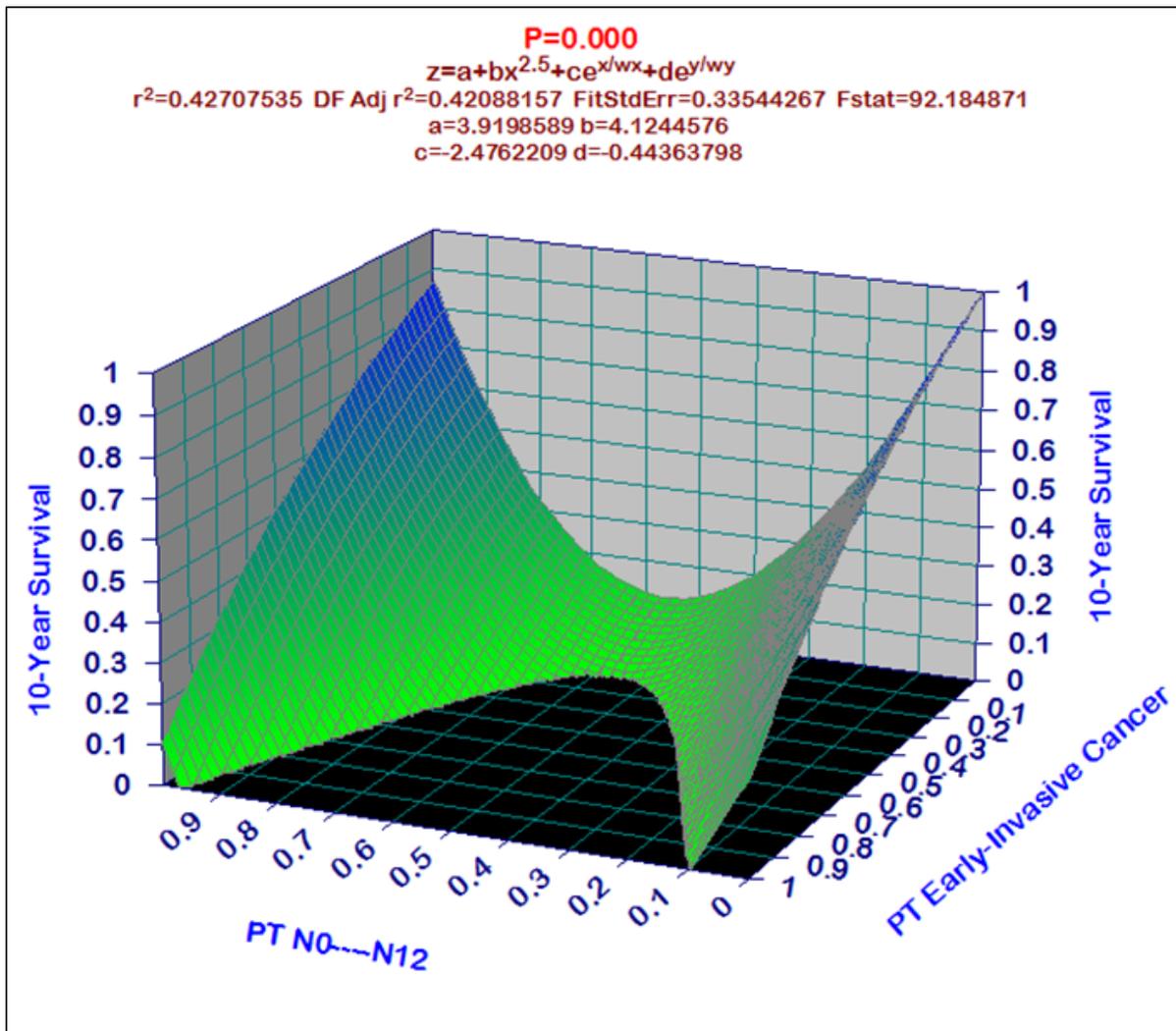


Figure 10

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), phase transition N0—N1-2 and phase transition “early—invasive cancer” (P=0.000).

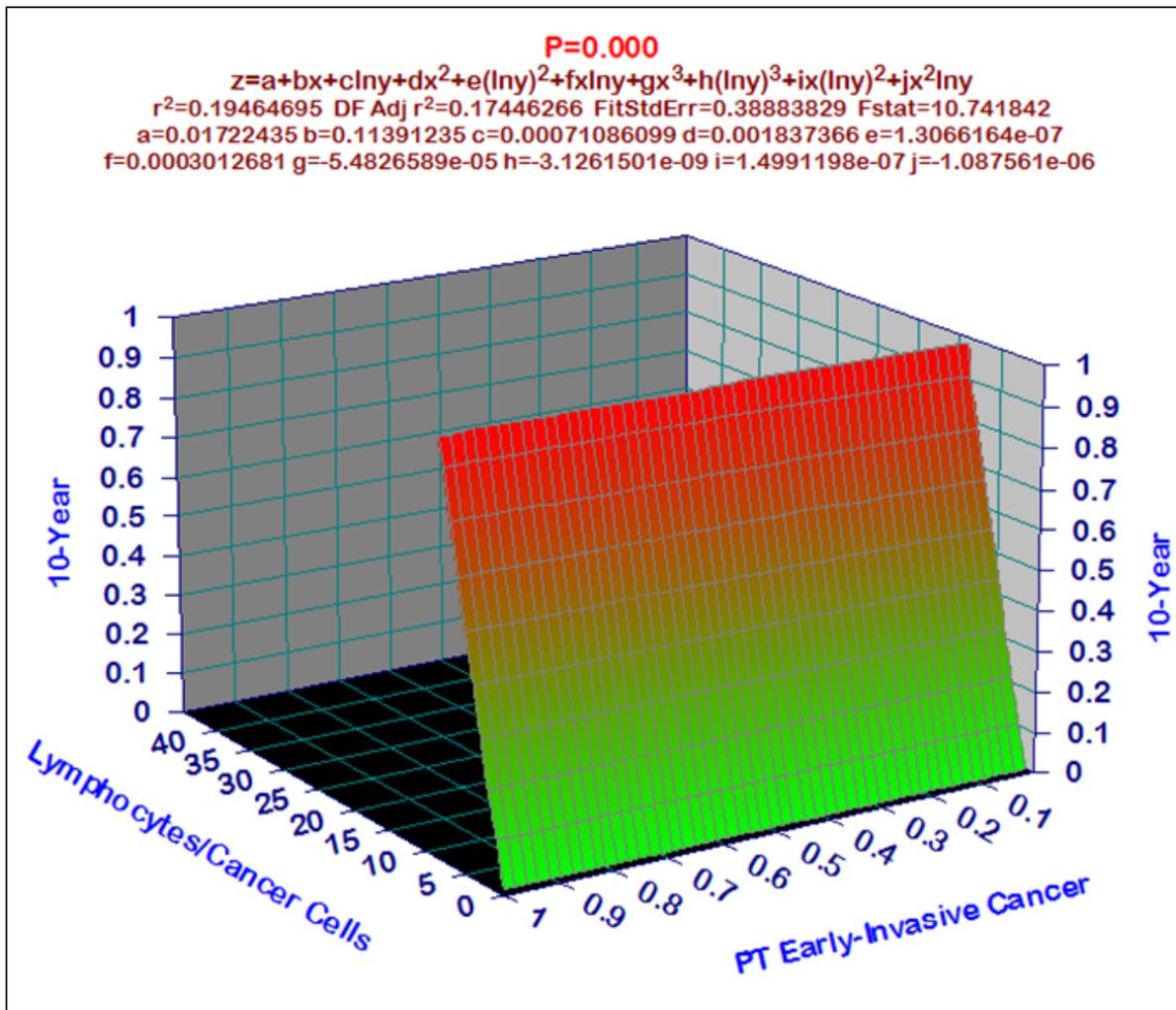


Figure 11

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), phase transition phase transition “early–invasive cancer” and Lymphocytes/Cancer cells (P=0.000).

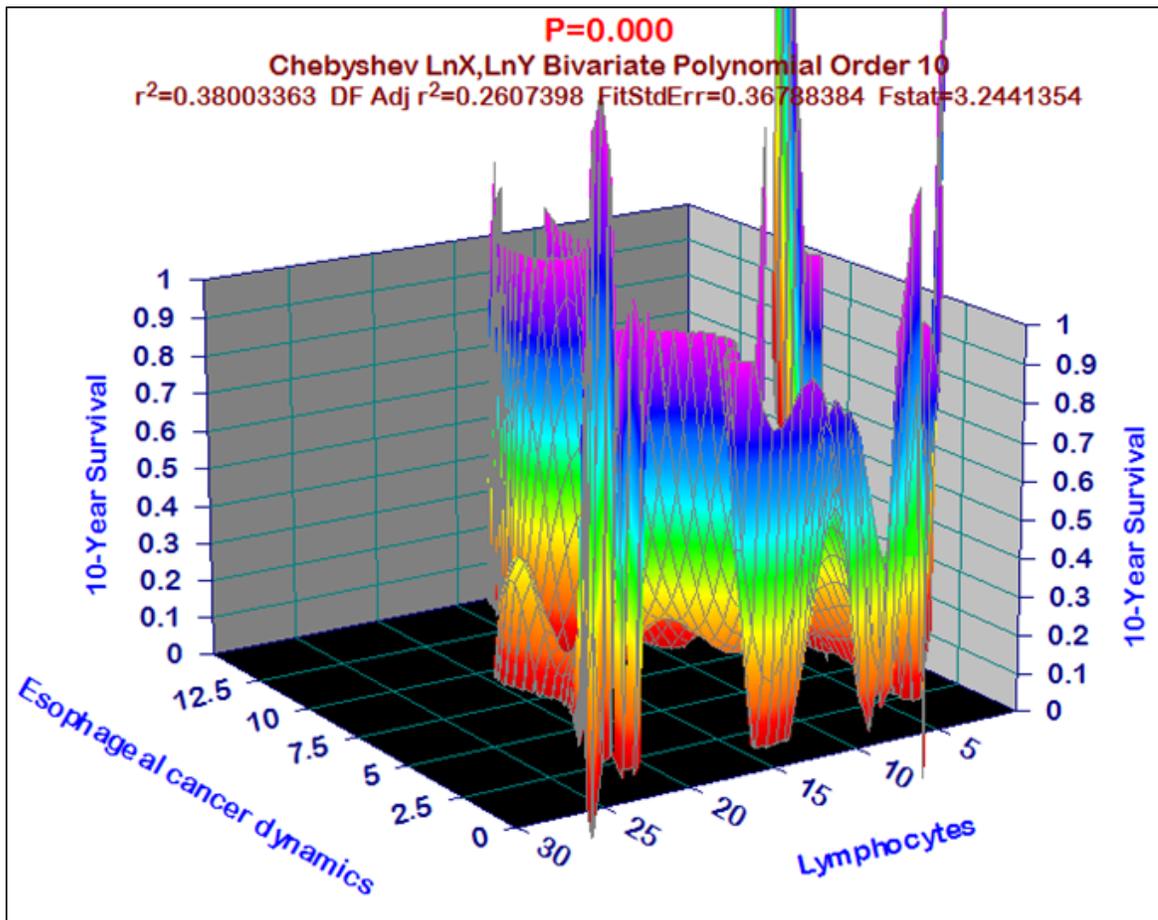


Figure 12

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), esophageal cancer cell dynamics and lymphocytes (P=0.000).

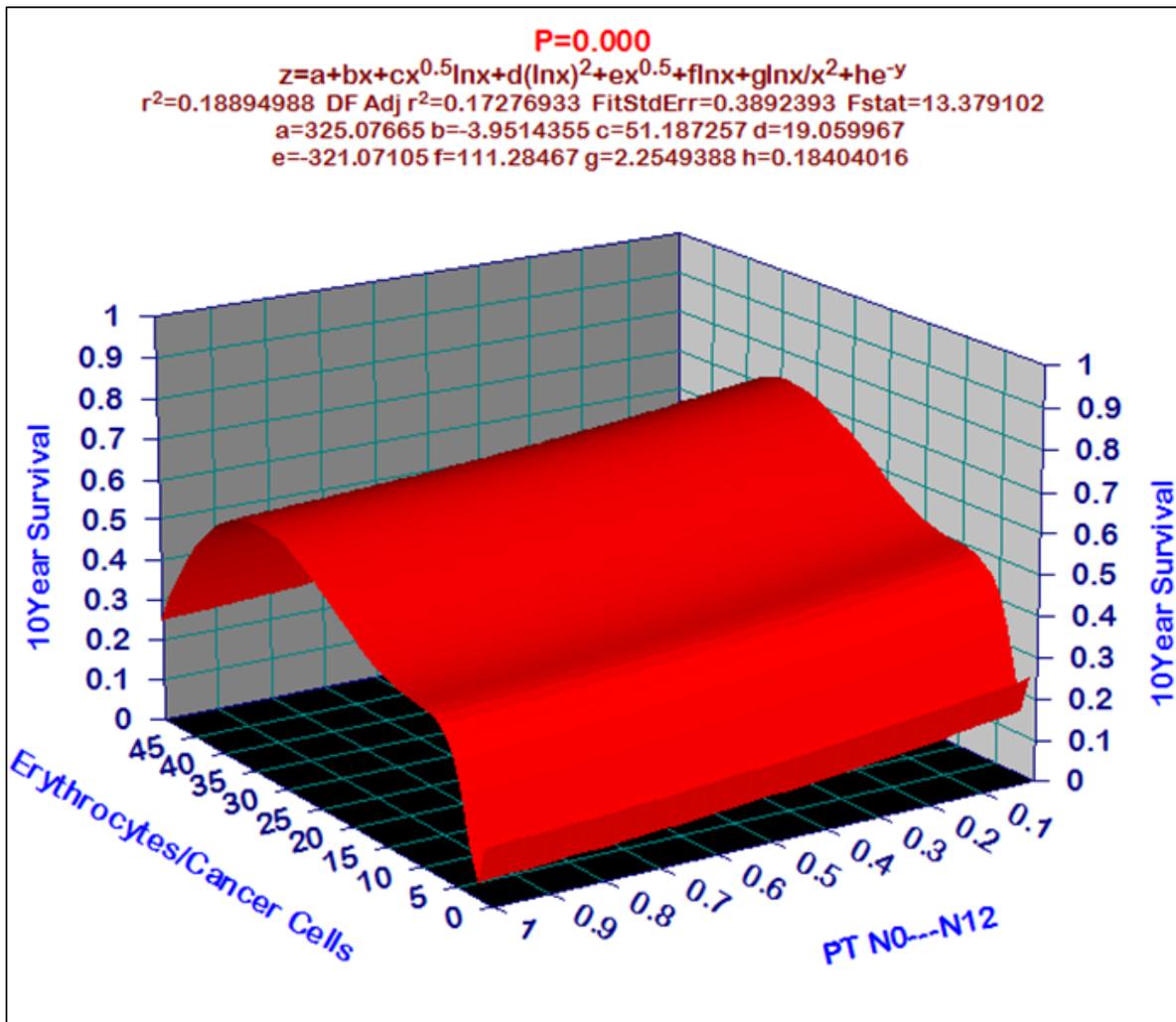


Figure 13

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), phase transition N0–N1-2 and Erythrocytes/Cancer cells (P=0.000).

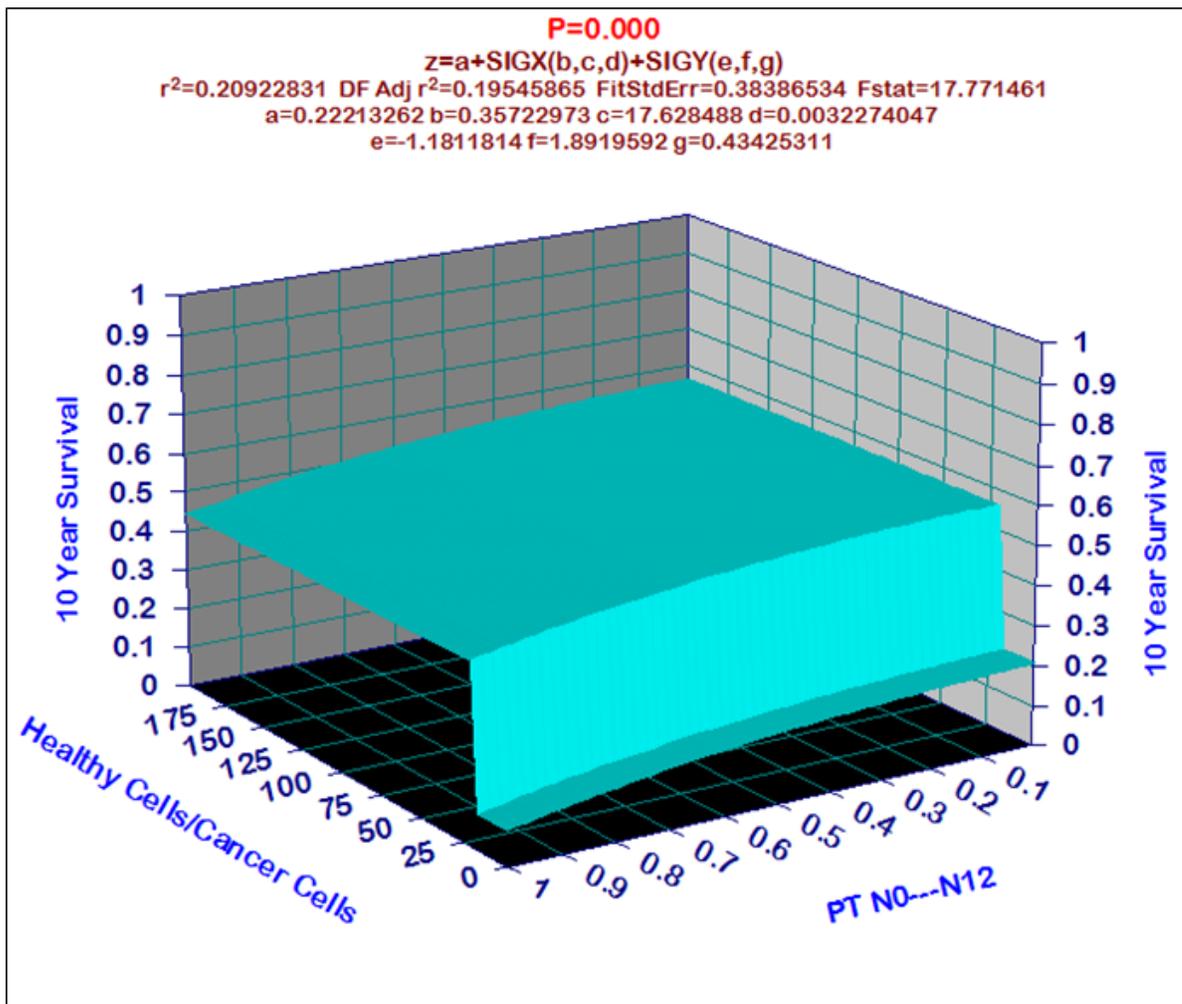


Figure 14

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), phase transition N0–N1-2 and Healthy Cells/Cancer cells (P=0.000).

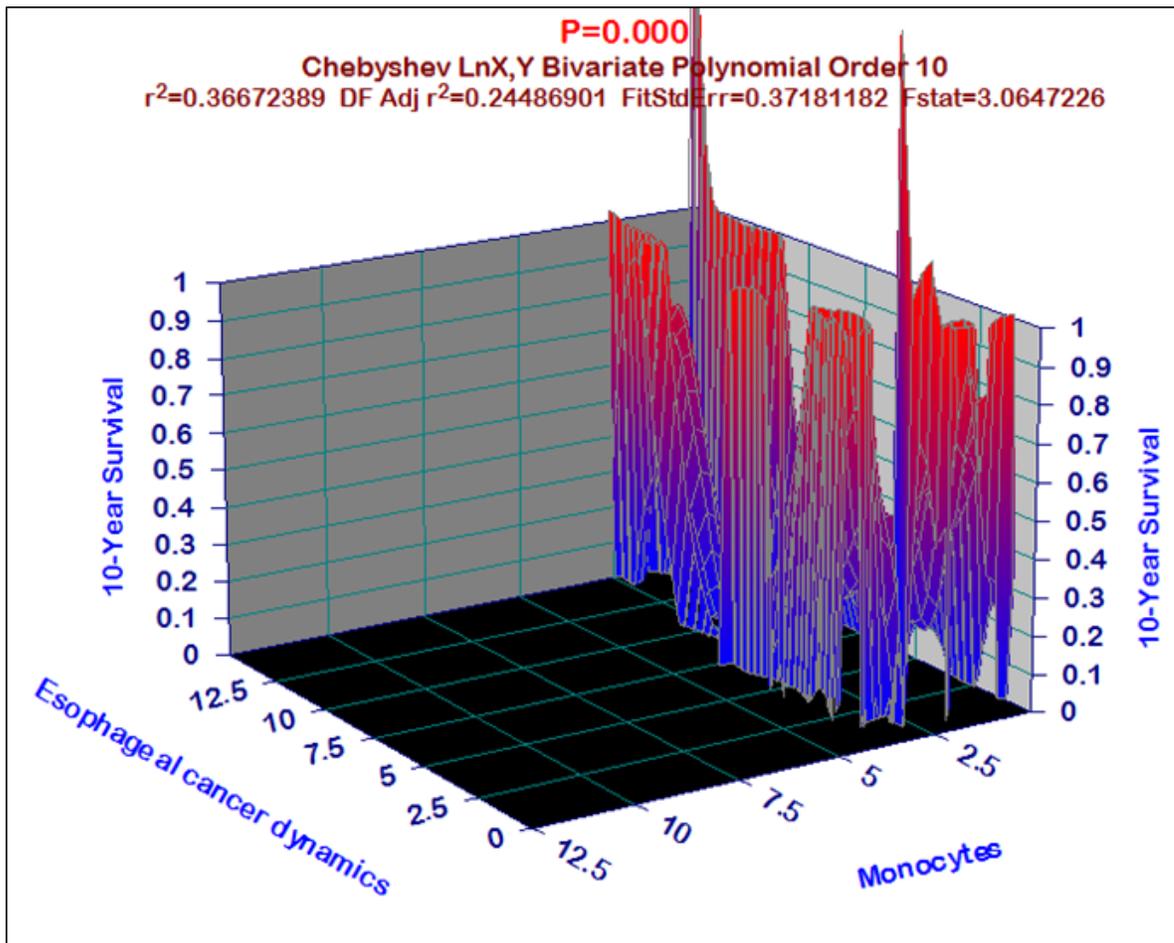


Figure 15

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), esophageal cancer cell dynamics and monocytes (P=0.000).

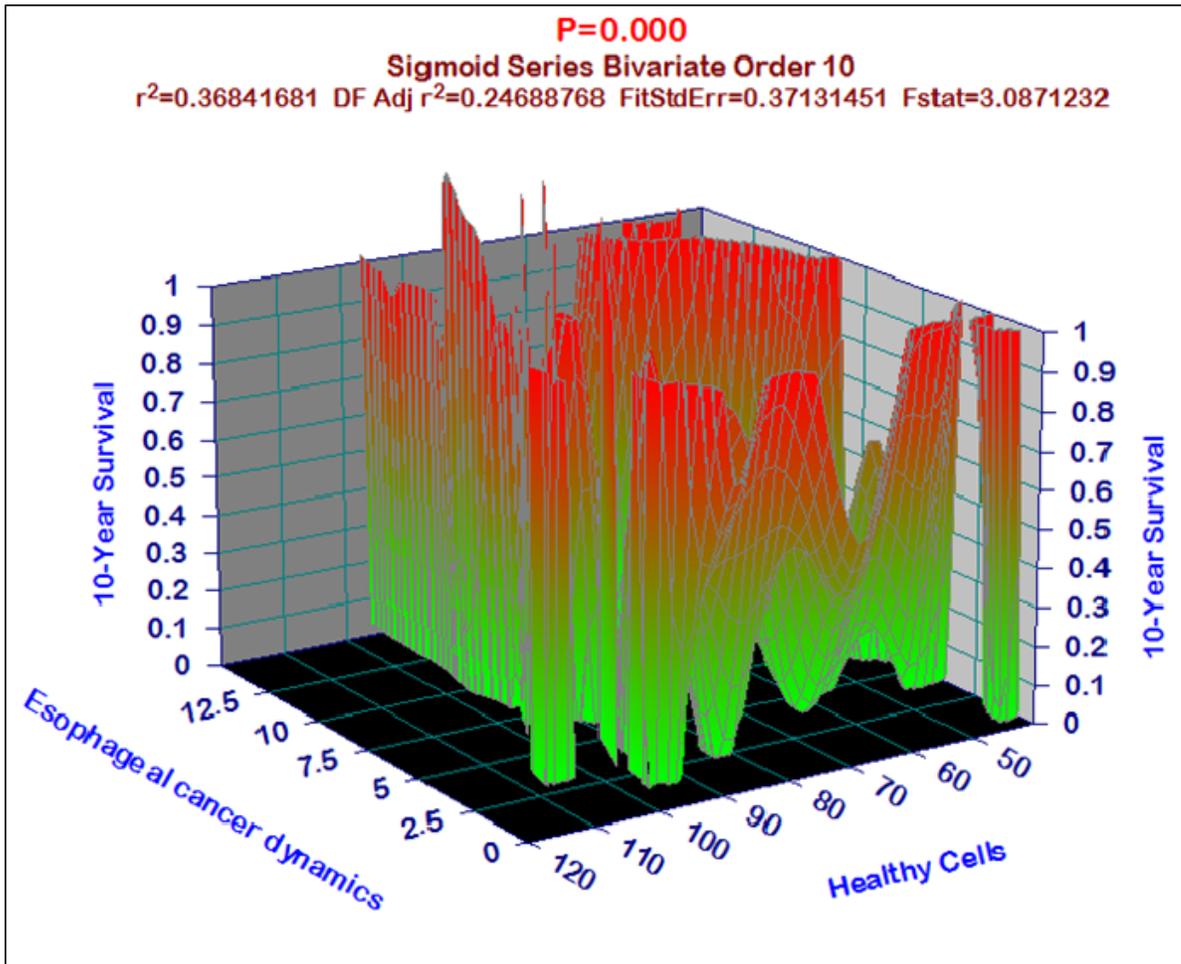


Figure 16

Prognostic equation model of 10-year survival of esophageal cancer patients (n=410), esophageal cancer cell dynamics and healthy cells (P=0.000).

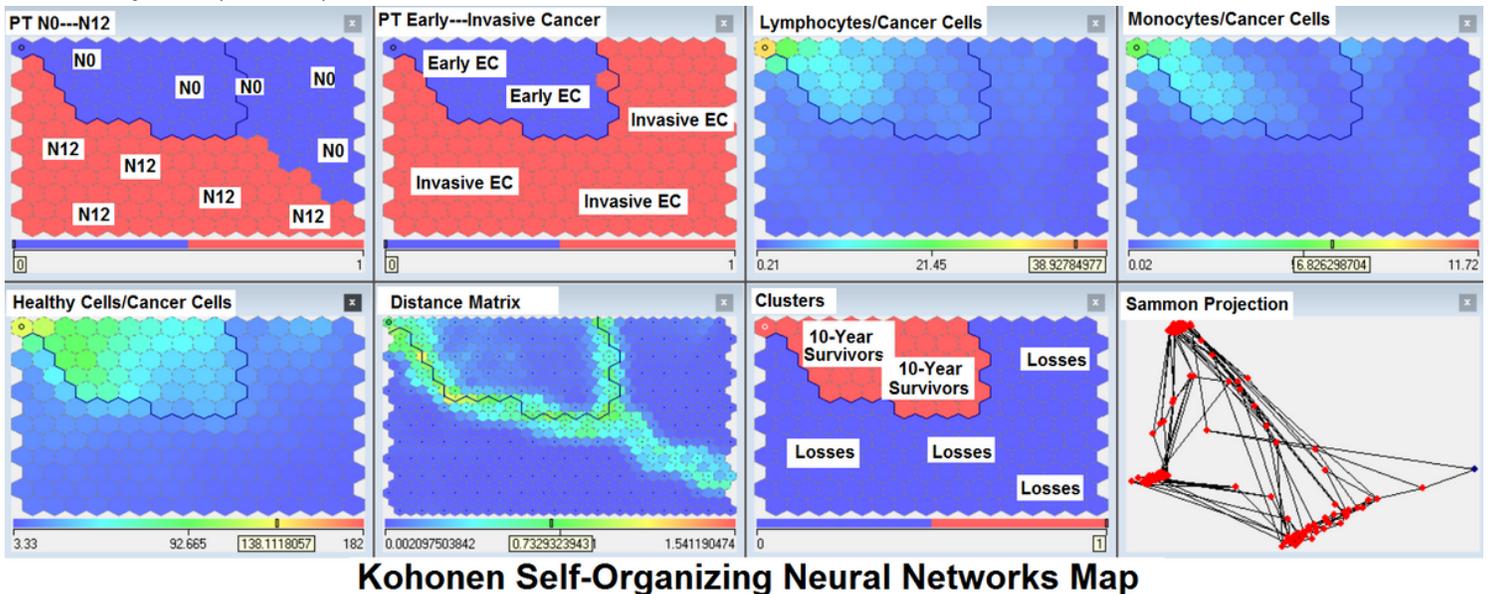


Figure 17

Results of Kohonen self-organizing neural networks computing in prediction of ECP 10-year survival after esophagectomies (n=410).