

**THE ROLE OF CA 72.4, CA 19.9 AND CEA
IN THE DIAGNOSIS AND FOLLOW-UP OF
GASTROINTESTINAL MALIGNANCIES**

616.9943
A-M

Thesis

Submitted in partial fulfillment for the
requirement of M.D. in **General Surgery**

By

Ahmad Mohamad Ibrahim Khalil

M.B., B.Ch., M.Sc. (Ain Shams University)

59612

Supervised By

Prof. Ahmad Sedki Abdel Rahman

Professor of General Surgery

Faculty of Medicine, Ain Shams University

Prof. Ali Khalifa Ali

Prof. of Biochemistry

Head of Oncology Diagnostic Unit

Faculty of Medicine, Ain Shams University



Dr. Hisham Abdel-Raouf El-Akkad

Lecturer of General Surgery

Faculty of Medicine, Ain Shams University



Dr. Mahmoud El Shafei

Lecturer of General Surgery

Faculty of Medicine, Ain Shams University

General Surgery Department

Faculty of Medicine

Ain Shams University

Cairo - 1998

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وقل رب زدني علما

صدق الله العظيم

طه / آية ١١٤



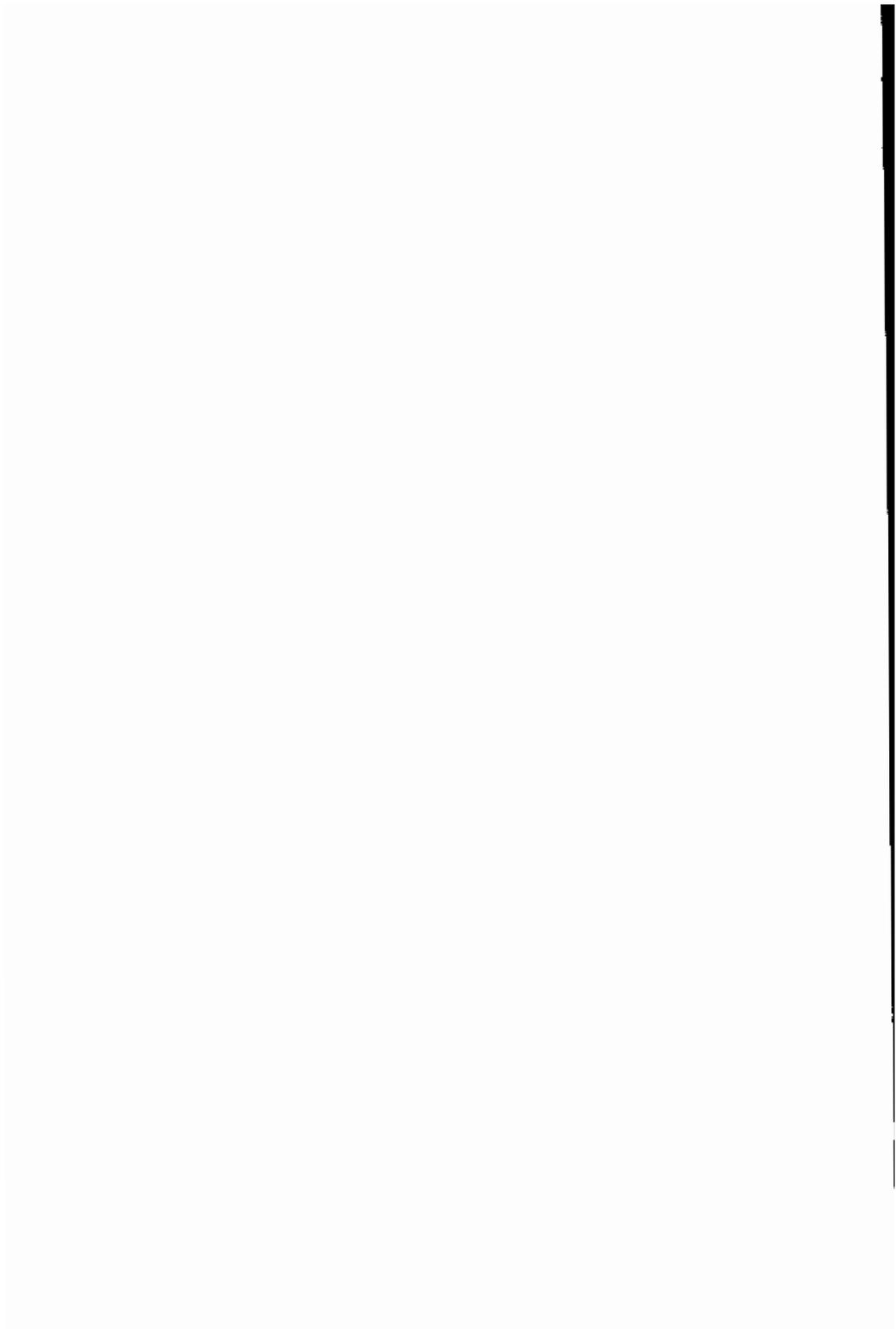
Acknowledgement

I would like to express my deepest gratitude to Prof. Dr. Ahmed Sedki, Professor of General Surgery, Faculty of Medicine, Ain Shams University, who offered me the honor and chance to work under his most fruitful supervision and precious guidance.

I would like to express my deepest thanks and gratitude to Prof. Dr. Ali Khalifa, Professor of Biochemistry, Head of Oncology Diagnostic Unit, Faculty of Medicine, Ain Shams University, for his guidance, his instructive advice and continuous support. I sincerely appreciate his valuable time, effort and understanding.

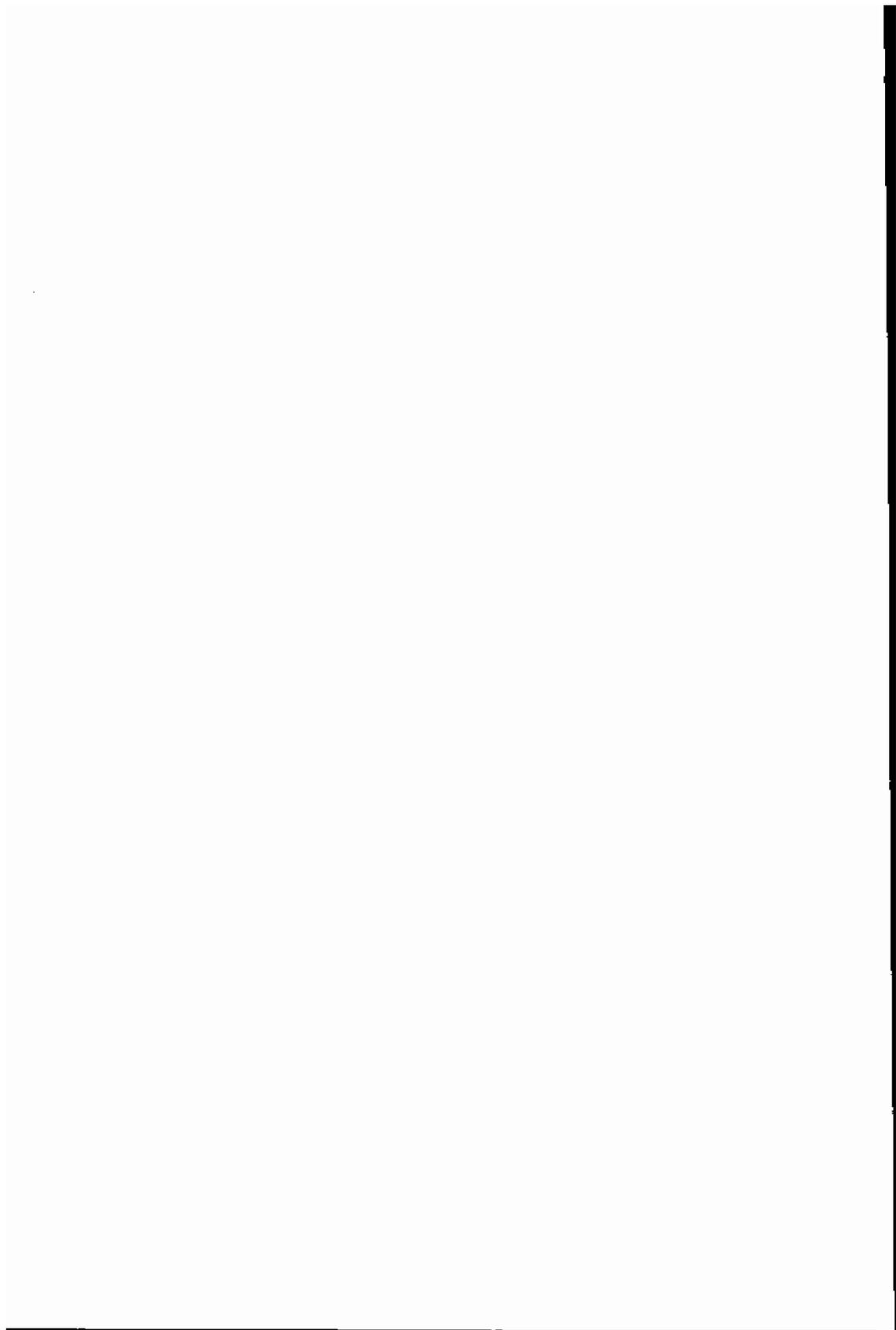
My deepest thanks for Dr. Hisham El-Akkad, Lecturer of General Surgery, Faculty of Medicine, Ain Shams University, whose great effort, patience and endless support crystallized this work.

I wish to express my sincere thanks to Dr. Mahmoud El-Shafei, Lecturer of General Surgery, Faculty of Medicine, Ain Shams University, for his valuable help, kind supervision and continuous guidance.



Contents

	Page
Introduction	1
Aim of the work	4
Review of Literature	
I. Pathology of gastrointestinal malignancies.....	
A. General oncology	5
B. Malignant neoplasms of the gastrointestinal tract.....	
Malignant neoplasms of the esophagus.....	34
Malignant neoplasms of the stomach	43
Primary malignant neoplasms of the liver.....	55
Malignant neoplasms of the nonendocrine pancreas.....	67
Malignant neoplasms of the colon and rectum	74
II. Tumor markers	
- Introduction	84
- Carcinoembryonic antigen.....	101
- Cancer antigen 19.9	114
- Cancer antigen 72.4	120
Patients and Methods	125
Results	144
Discussion	182
Summary and Conclusion	197
References	202
Appendix	
Arabic Summary	



List of tables in the results

Tab. No.	Title	Page
1	The mean values of the 3 tumor markers in the healthy group	148
2	The mean values of the 3 tumor markers in the nonmalignant group	149
3	The mean values of the 3 tumor markers in the malignant group	150
4	Correlation between the serum values of the 3 serum markers and some clinical variables in the healthy group	154
5	Correlation between the serum values of the 3 serum markers and some clinical variables in patients with nonmalignant GIT diseases	155
6	Correlation between the serum values of the 3 serum markers and some clinical variables in patients with malignant GIT tumors	156
7	Comparison between the mean values of the 3 markers regarding smoking in the 3 groups	157
8	Comparison between the mean values of the 3 markers regarding liver functions in the nonmalignant and malignant groups	159
9	Comparison between the mean values of the 3 markers regarding serosal invasion in the malignant group	161
10	Comparison between the mean values of the 3 markers regarding vascular invasion in the malignant group	162

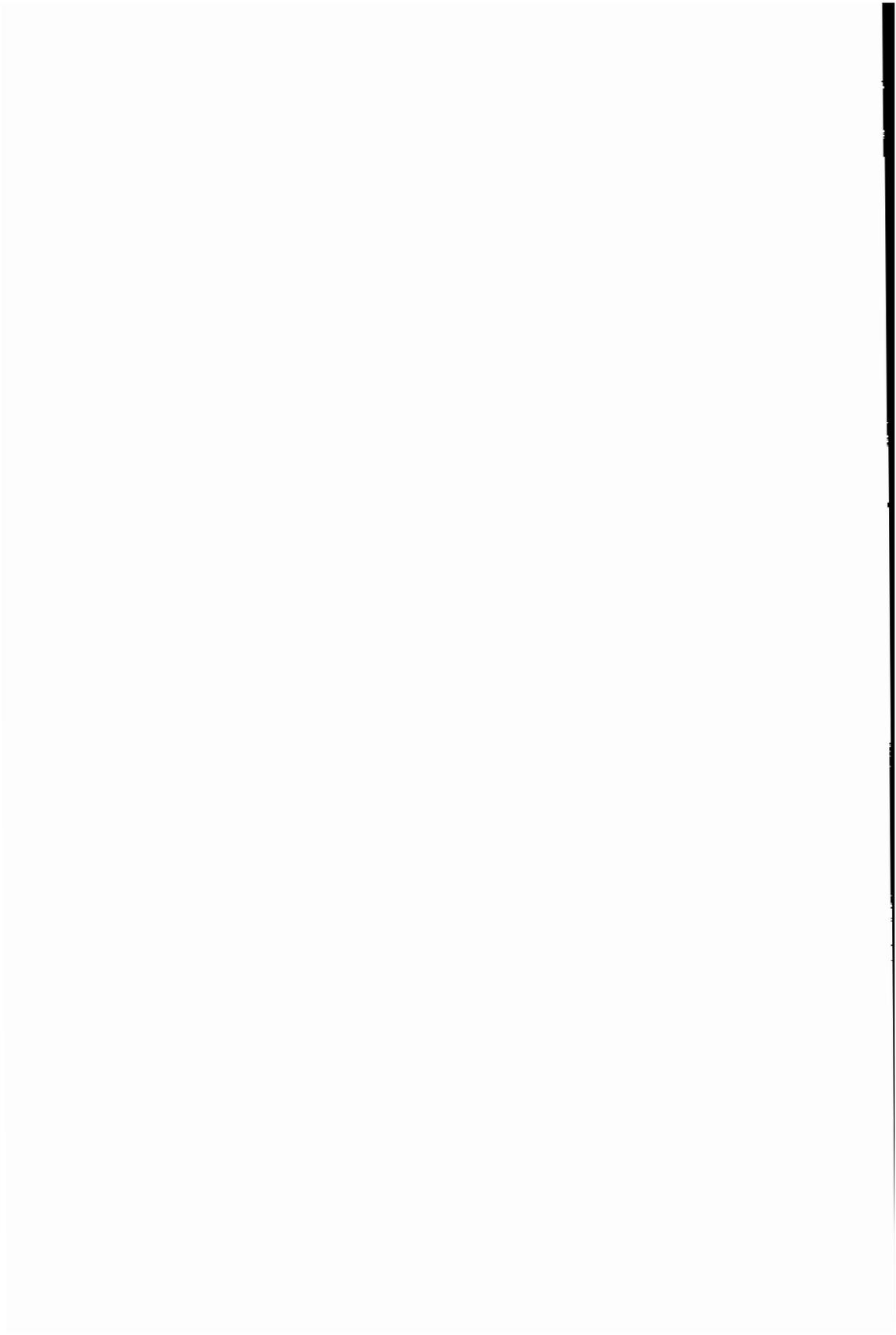
11	Comparison between the mean values of the 3 markers regarding lymphatic invasion in the malignant group	163
12	Comparison between the mean levels of stage 1 and 2 in the malignant group, and the mean levels in the nonmalignant and healthy groups	167
13	Comparison between the mean levels of stage 3 and 4 in the malignant group, and the mean levels in the nonmalignant and healthy groups	168
14	Comparison between the mean levels of stage 1 & 2 and 3 & 4 in the malignant group	169
15	The percentage of sensitivity, specificity, predictive values and test accuracy of single markers and markers combinations	175
16	The mean values of the 3 tumor markers in the preoperative and postoperative samples in the malignant group	176
17	Sensitivity of the three markers at different specificities in the malignant group	180

List of figures in the results

Fig. No.	Title	Page
1	Sex distribution in the three groups	145
2	Frequency of cigarette smoking in the three groups	145
3	Frequency of patients with liver function abnormalities in the nonmalignant and malignant groups	146
4	Frequency of different stages in patients with malignancy	147
5	Frequency of different grades of differentiation in patients with malignancy	147
6	Frequency of different anatomical sites in patients with malignancy	147
7	Comparison between mean values of CEA in the three groups	151
8	Comparison between mean values of CA 19.9 in the three groups	152
9	Comparison between mean values of CA 72.4 in the three groups	153
10	Mean values of the three tumor markers in smokers and nonsmokers in the three groups	158
11	Mean levels of the three tumor markers in patients with normal and abnormal liver functions in the nonmalignant and malignant groups	160

12	Mean values of serum level of CEA in the presence and absence of serosal, vascular and lymphatic invasions in patients with malignancy	164
13	Mean values of serum level of CA 19.9 in the presence and absence of serosal, vascular and lymphatic invasions in patients with malignancy	165
14	Mean values of serum level of CA 72.4 in the presence and absence of serosal, vascular and lymphatic invasions in patients with malignancy	166
15	Correlation between serum levels of the 3 markers and the stage of the malignant group	170
16	CEA mean values in relation to clinicopathological stage	171
17	CA 19.9 mean values in relation to clinicopathological stage	172
18	CA 72.4 mean values in relation to clinicopathological stage	173
19	Correlation between serum levels of the 3 markers and the grade of differentiation in malignant tumors	174
20	Preoperative, early and late postoperative mean levels of CEA in patients with malignancy in comparison with healthy group and patients with non malignant lesions	177
21	Preoperative, early and late postoperative mean levels of CA 19.9 in patients with malignancy in comparison with healthy group and patients with non malignant lesions	178

-
- 22 Preoperative, early and late postoperative mean levels of CA 72.4 in patients with malignancy in comparison with healthy group and patients with non malignant lesions 179
- 23 Specificity-sensitivity diagram of CEA, CA 19.9 and CA 72.4 in patients with gastrointestinal malignancies 181



List of Abbreviations

AC	Adenocarcinoma
ACTH	Adrenocorticotrophic hormone
AJC	American joint committee
BHCG	Betasubunit human chroionic gonadotrophin
CA50	Cancer Antigen 50
CA72.4	Cancer antigen 72.4
CA125	Cancer Antigen 125
CA15.3	Cancer Antigen 15.3
CA19.9	Cancer Antigen 19.9
CC	Cholangiocarcinoma
CEA	Carcinoembryonic antigen
DNA	Deoxynucleic acid
EBV	Epstein barr virus
EDGF	Epidermal growth factor
EGC	Early gastric cancer
FHC	Fibrolamellar hepatocellular carcinoma
G	Grade
GFR	Growth factor receptor
GIM	Gastro intestinal malignancies
HBV	Hepatitis B virus
HPV	Human papilloma virus
IL-2	Interleukin-2
JJC	Japanese joint committee
L.Inv.	Lymphatic invasion
MCA	Mammary carcinoma antigen
NIH	National Institute of Health
NK	Natural killer cell
p-TNM	Postoperative tumor node metastasis
PSA	Prostate specific antigen
RNA	Ribodeoxy nucleic acid
S	Stage
S.Inv.	Serosal invasion
SCC	Squamous cell carcinoma

Sis	Simian sarcoma oncogene
TAA	Tumor associated antigen
TAG 72	Tumor associated glycoprotein 72
TGF- α	Transforming growth factor alpha
TGF- β	Transforming growth factor Beta
TM	Tumor markers
TNM	Tumor node metastasis
TSA	Tumor specific antigen
UICC	Union Internationale Contre Le Cancer
V.Inv.	Vascular invasion