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MODERN SURGICAL APPROACHES TO MALIGNANT DISEASES OF THE GASTROINTESTINAL TRACT – CLINICAL AND EPIDEMIOLOGICAL ASPECTS IN NORTHEASTERN BULGARIA

ABSTRACT

OF A DISSERTATION

FOR THE ACQUISITION OF THE SCIENTIFIC DEGREE "DOCTOR OF SCIENCES"

Field of higher education – 7. Healthcare and sports
Professional field – 7.1 Medicine

VARNA ● 2026

The dissertation contains 248 pages and is illustrated with 3 panels of photographic material, 29 figures and 61 tables and appendices on electronic media.

The literature used includes 1068 sources, cited as follows: 171 sources listed in the Literature Review, Part I; 33 sources listed in the Literature Review, Part II; 796 literature sources used for the PICOS analysis, and 68 sources distributed throughout the other chapters of the dissertation.

The numbering of the figures and tables in the abstract has been adapted to the volume of information included and differs from that in the dissertation. The numbering of the bibliographic sources cited in the abstract is in accordance with the numbering in *Section X. References used* in the dissertation.

The research related to the dissertation is based on medical documentation from the Clinic of General and Operative Surgery at UMHAT "Sv. Marina" EAD – Varna.

The dissertation has been discussed and scheduled for defence by the Department Council of the Department of General and Operative Surgery, Faculty of Medicine, Medical University – Varna, before

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The materials related to the defence of the dissertation are published on the website of MU – Varna and are available to interested parties at the Secretariat of the Department of General and Operative Surgery, UMHAT "Sv. Marina" EAD – Varna.

The official defence of the dissertation will take place on **04.05.2026** at **13:00 – Rectorate of the Medical University – Varna, in the Conference Hall – 2nd floor.**

CONTENTS

ABBREVIATIONS USED

Latin abbreviations:

5-FU	5-fluorouracil
ACC	Acynarocell carcinoma
AFP	Alpha-fetoprotein
APHE	Arterial phase hyperamplification
APR	Abdominoperineal excision
ASGE	American Society for Gastrointestinal Endoscopy
CEA	Carcinoembryonic antigen
CEUS	Contrast-enhanced ultrasound
CHA	Common hepatic artery
CIN	Chromosomal instability
CME	Complete mesocolon excision
CRC	Colorectal cancer
CRM	Circumferential resection margin
CRS	Cytoreductive surgery
ctDNA	Circulating tumour DNA
CTE	Computer enterography
DFS	Disease-free survival
DGE	Delayed gastric emptying
DSS	Difficulty scoring systems
EATL	Enteropathy-associated T-cell lymphoma
EBV	Eppstein-Bar virus
ECIS	European cancer information system
EGC	Early-Onset Gastric Cancer
EMVI	Extramural vascular invasion
ERAS	Enhanced Recovery After Surgery
ESMO	European Society of Medical Oncology
EUS	Endoscopic ultrasonography
EUS-FNA	Endoscopic echography with fine-needle aspiration
FAP	Family adenomatous polyposis
FLR	Future liver remnant
FNA	Fine needle aspiration biopsy
GEJ	Gastroesophageal junction
GIST	Gastrointestinal stromal tumours
GPC3	Glipican-3
HBV	Hepatitis virus type B
HCV	Hepatitis virus type C
HDGC	Hereditary diffuse gastric cancer
HIPEC	Hyperthermic Intraperitoneal Chemotherapy
HPV	Human Papilloma virus
IBD	Irritable bowel disease
ICG	Indocyanine green

IPMN	Intraductal papillary mucinous neoplasms
LAR	Lower anterior resection
LDG	Laparoscopic distal gastrectomy
LND	Lymph node dissection
LVI	Limpho-vascular invasion
MC	Mucinous carcinoma
MCN	Mucinous cystic neoplasm
MELD	Multiparametric assessment, encompassing liver function
MIE	Minimally invasive esophagectomy
MIPS	Minimally invasive pancreatic surgery
MMC	Mitomycin C
MMR	Mismatch repair
MRCP	Magnetic resonance cholangiopancreatography
MRD	Minimally residual disease
MRE	Magnetic resonance enterography
MSI	Microsatellite instability
MSI-high	High microsatellite instability
MWA	Microwave ablation
NCCN	National Comprehensive Cancer Network
NEC	Neuroendocrine carcinomas
NET	Neuroendocrine tumours
NGS	New generation sequencing
NOS	Not otherwise specified
OE	Open esophagectomy
OS	Overall survival
PanNETs	Pancreatic neuroendocrine neoplasms
pCR	Pathological complete response
PDAC	Pancreatic ductal adenocarcinoma
PEI	Percutaneous ethanol injection
PERT	Pancreas-enzyme replacement therapy
PFS	Progress-free survival
PJS	Peutz-Jeghers syndrome
PNI	Perineural invasion
POPF	Postoperative pancreatic fistula
PPH	Post-pancreatectomy haemorrhage
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROs	Patient reported outcomes
PRRT	Peptide-receptor radionuclide therapy
PSC	Primary sclerotic cholangitis
PV	Portal vein
PVE	Portal vein embolisation
RCT	Randomised controlled trials
RDG	Robotised distal gastrectomy

RFA	Radiofrequency ablation
RTKs	Receptor tyrosine-kinases
SAGES	Society of American Gastrointestinal and Endoscopic Surgeons
SBRT	Stereotactic radiotherapy
SCC	Squamous cell carcinoma
SD	Standard deviation
SEMS	Self-expanding metal stents
SI-NET	Small intestine neuroendocrine tumours
SIRT	Selective internal radiation therapy
SMJN	Sister Mary Joseph nodule
SMV	Superior mesenteric vein
SNNS	Sentinel node navigation surgery
SRCC	Signet-ring cell carcinoma
SSA	Somatostatin analogues
SSTR	Somatostatin receptors
TACE	Transarterial chemoembolisation
TCGA	The Cancer Genome Atlas
TD	Tumour deposits
TME	Total mesorectal excision
TME	Tumour microenvironment
TNT	Total neoadjuvant therapy
VCE	Capsule endoscopy

I. INTRODUCTION

Malignant neoplasms of the gastrointestinal tract are one of the main causes of morbidity and mortality in Bulgaria. According to data from *the National Centre for Public Health and Analysis* (NCPHA), in 2023, the incidence of cancer of the digestive organs is estimated at 87.9% per 100,000 and ranks third in frequency after breast cancer in women (92.2% per 100,000) and cancer of the male reproductive organs (91.8% per 100,000). There are regional differences in the number of newly diagnosed malignant neoplasms per 100,000 population. The highest incidence is in the Ruse region (569.1% per 100,000), and the lowest is in the Sofia region (171.8% per 100,000). The Varna region ranks fourth with an incidence of 514.2% per 100,000 [1, 2].

I.1. DEMOGRAPHIC CHARACTERISTICS OF THE REGION

Varna is the largest city in Northern/ Northeastern Bulgaria and the Bulgarian Black Sea coast , as well as the third largest in the country – the administrative centre of the municipality and region of the same name. According to data from the National Statistical Institute (NSI) as of2020 , the city's population is 332,394 inhabitants [271].

The north-eastern planning region includes the districts of Varna, Dobrich, Silistra, and Shumen. The population of the region is 826,742, or approximately 12.84% of the total population of the country [272]. Over the last 10 years, there has been a trend towards population concentration in the Varna district at the expense of the Shumen and Dobrich districts. The population in the region is characterised by a relatively favourable gender and age structure, which is due to certain features of its ethno-cultural profile and economic specialisation. The share of men is 49%, which is higher than the national average. In a number of municipalities in the region, men account for ≥ 50% of the population, while in the larger cities in the region their share is around 48%. These differences are due to both migration and differences in the natural reproduction of the population [3].

I.2. DATA ON THE INCIDENCE OF CANCER OF THE DIGESTIVE ORGANS

According to data from the National Centre for Public Health and Analyses, newly diagnosed cases of digestive organ neoplasms in Bulgaria for 2022 and 2023 are 90.2 and 87.9 per 100,000 population, respectively, or 5,833 and 5,664 cases in absolute terms. The highest proportion is accounted for by new growths in the large intestine – 3,515 cases in 2022 and 3,421 in 2023. In second place are stomach diseases – 886 cases compared to 814. New growths in other digestive organs account for 24.5% of the total number for 2022 and 25.2% for 2023 (Table 1).

This dissertation presents research on the epidemiological and clinical aspects of malignant diseases of the gastrointestinal tract in North-Eastern Bulgaria. The analyses are based on electronic medical records, which have been processed retrospectively, and a systematic review of contemporary surgical approaches to the treatment of this type of disease has been made, based on both literature data and data from actual clinical practice.

Table 1. Newly diagnosed malignant neoplasms by location ***(source: National Centre for Public Health and Analysis)***

Localization of Neoplasm by ICD-10			
Localization of Neoplasm (ICD-10)	2022	2022	2023
	Number	Per 100,000 population	Per 100,000 population
Total	**26 235**	**405.8**	**406.5**
Lip, oral cavity and pharynx	691	10.7	635
including: lip	99	1.5	100
Digestive organs	**5,833**	**90.2**	**5,664**
including: stomach	886	13.7	814
colon	2,023	31.3	2,044
rectosigmoid junction, rectum, anus and anal canal	1,492	23.1	1,377
	1,492	23.1	1,377

The choice of the topic of the dissertation and its formulation are dictated by the fact that:

1. Malignant diseases of the gastrointestinal tract have a high mortality and morbidity rate among the population.
2. The majority of those affected are of working age.
3. They account for a high proportion of the causes of death among the population, especially among people of working age.
4. Malignant diseases account for a high proportion of the costs of treatment and rehabilitation.
5. These types of diseases require highly qualified and specialised medical care, complex treatment with expensive drugs and the use of high-tech processes.
6. Malignant diseases cause significant social, economic and psychological damage to individuals, their families and society as a whole, and result in prolonged incapacity for work and disability of the patient.
7. There is no evidence that such studies have been conducted in Bulgaria.

II. OBJECTIVES AND TASKS

II.1. OBJECTIVE

To analyse the clinical and epidemiological aspects of malignant diseases of the gastrointestinal tract in North-Eastern Bulgaria and the results of modern surgical approaches to their treatment.

To analyse surgical approaches through the prism and standards for health technology assessment [217].

The objective set in this dissertation is achieved through the completion of the following tasks:

II.2. TASKS:

Task 1: To conduct an epidemiological study of malignant diseases of the gastrointestinal tract in Bulgaria based on literature data.

Task 2: To analyse contemporary surgical approaches to the treatment of malignant diseases of the gastrointestinal tract.

Task 3: To conduct an epidemiological study of malignant diseases of the gastrointestinal tract in North-Eastern Bulgaria.

Task 4: To evaluate the clinical aspects, classify and stage malignant diseases of the gastrointestinal tract in North-Eastern Bulgaria depending on their location and evolution.

Task 5: To analyse contemporary surgical approaches to the treatment of malignant diseases of the gastrointestinal tract in North-Eastern Bulgaria.

Task 6: To assess the loco-regional characteristics and social significance of malignant diseases of the gastrointestinal tract at the micro and macro levels.

Task 7: To forecast the main trends in the development of malignant diseases of the gastrointestinal tract in the short and long term at regional and national level.

III. MATERIALS AND METHODS

III.1. MATERIALS AND METHODS FOR TASKS 1 AND 2

III.1.1. Documentary analysis and content analysis of publicly available documents containing information on the epidemiology of gastrointestinal cancer in Bulgaria

Reports from the National Centre for Public Health and Analysis (NCPHA), the National Cancer Registry (NCR), as well as data from the European Commission for Bulgaria (ECIS – European Cancer Information System), registers, scientific publications, scientific communications, data from European and national institutions, etc.

III.1.2. Review of scientific publications by Bulgarian authors on the systematisation of modern surgical approaches to malignant diseases of the gastrointestinal tract used in real clinical practice (real world evidence) in Bulgaria

III.1.3. Review of scientific publications by foreign authors on the systematisation of modern surgical approaches to malignant diseases of the gastrointestinal tract used in real clinical practice (real world evidence).

III.2. MATERIALS AND METHODS FOR TASKS 3, 4, 5, 6, 7

III.2.1. Main method – review of retrospective databases.

Study design – a retrospective observational (observational) single-centre study of electronic medical records was conducted. An observational study is a research method for documenting clinical, economic and/or medico-social and medico-biological outcomes in current medical practice. This type of study measures the effectiveness of treatment. *Effectiveness shows whether a treatment* "works" *in everyday medical practice*. Observational studies can be retrospective or prospective. Retrospective observational studies analyse treatment and outcomes that have already occurred [214].

The centre of the study is the University Hospital "St. Marina" – Varna, Clinic of General and Operative Surgery. Study period: The analysed period includes electronic medical records for the period from 2013 to 2023, inclusive.

Study period: The analysed period includes electronic medical records for the period from 2013 to 2023, inclusive.

Legal basis for conducting the study: The study we have planned is essentially a non-interventional observational retrospective study of electronic medical records. The trial does not fall under the provisions of the Health Act, Chapter Seven. Section IV. Medical research on humans. Medical science [216], as it concerns a retrospective study of electronic medical records.

The study does not analyse medicinal products, therefore the provisions of the Law on Medicinal Products for Human Use are not applicable [217]. For this reason, no trial protocol has been submitted for approval by the Local Ethics Committee of the centre conducting the study.

Ethical norms and standards: The study design was prepared in accordance with the Declaration of Helsinki and the Guidelines for Good Clinical Practice and Good Medical Practice [218, 219, 220].

The use of personal data is limited to age and gender. No personal contact with patients has been made, thus preserving their physical and mental integrity. Personal data is protected in accordance with the Personal Data Protection Act [221].

Inclusion criteria:

1. Availability of an electronic medical record for patient hospitalisation.

2. Age over 18 years.

Sample size: Probable number of electronic medical records subject to analysis – over 2000.

Analysed parameters: We consider the set parameters to be important and inherent to the results of the study, which can meet the set goals and objectives!

Demographic data – gender and age.

The analysis of age parameters includes stratification:

- 18 to 45,
- 46-65,
- 66-75,
- over 76.
- Clinical pathway (CP) upon admission.
- CP upon discharge, with determination of the degree of correspondence.
- ICD code of the disease upon admission.
- ICD code upon discharge, with determination of the degree of correspondence
- Deceased – relative share.
- Comorbidities – ICD code, number of comorbidities per patient.
- Histological diagnosis.
- Admission type – planned or emergency.
- Bed days – by gender, age, ICD
- Admission diagnosis – ICD code.
- Leading diagnosis – ICD code.
- Correspondence between admission and primary diagnosis.
- Staging according to TNM classification.
- Staging according to ECOG.

Acceptable assumptions: We assume that electronic medical records are kept clearly, accurately, and in strict accordance with the hospital's established standard operating procedures.

Sensitivity analysis: Sensitivity analysis allows us to determine how the results of the analysis would change when the "best assumptions or estimates" change within an acceptable range of values. By using an acceptable range of values for key assumptions or estimates, sensitivity analysis will allow us to calculate the impact of these assumptions on the conclusions and findings of the study.

Statistical approaches used: The study applies descriptive statistical analysis, which aims to systematically present and summarise the empirical data extracted from electronic medical records. This approach provides a quantitative description of the observed population, while creating a reliable basis for subsequent analytical procedures.

Descriptive analysis includes the calculation of summary characteristics for central tendency (arithmetic mean, median, mode) and measures of statistical dispersion (standard deviation, coefficient of variation and range), which are used to assess both the "typical" value of the observed variables and the degree of their variation.

The study uses frequency analysis – one-dimensional and two-dimensional frequency distributions by categorical and variational (measured) characteristics. The descriptive characteristics of these distributions are absolute frequencies (number of observations for each value or category) and relative frequencies (share or percentage of the total number of observations). This provides a clear picture of the structure of the data by individual characteristics. Within the two-dimensional frequency distributions (cross-tabs), dependencies between two characteristics are examined simultaneously, which allows correlations and patterns in the observed data to be identified.

Prior to statistical processing, a preliminary assessment of the completeness and logical consistency of the data was carried out in order to ensure the validity of the results. The analysis of the empirical data was performed using the specialised software product IBM SPSS Statistics.

III.2.2. Identified advantages and disadvantages of retrospective databases, given limitations

Advantages – retrospective studies include a wider range of patients; low costs; larger sample size; longer analysis period; easier sensitivity analyses.

Disadvantages – incomplete and missing data; inaccurate coding of patients and diseases; limited population or restriction within a specific population; missing records of data on the results of clinical and prospective studies during the analysis period; errors in patient and data selection.

Relevant summaries, reliable conclusions. We declare no conflict of interest, no external funding and no specific financial and economic interests, which guarantees the relevance of the summaries and the reliability of the conclusions.

IV. ANALYSIS OF STUDY RESULTS

IV.1. RESULTS FROM TASK 1

IV.1.1. Epidemiology of gastrointestinal cancer in Bulgaria

Bulgaria is one of two EU countries, along with Cyprus, where cancer mortality increased between 2011 and 2021 (from 229 to 242 cases per 100,000 people) [222]. The National Cancer Registry (NCR) was closed at the end of 2023, and the latest publicly available and official information is from 2017 [223]. According to these data, the overall incidence of cancer of the digestive organs (ICD-10 code: C15-C26) in 2017 was 592.8 per 100,000 people (41,948 cases) [223].

The National Centre for Public Health and Analysis (NCPHA) has statistical data available for the period 1980-2024, showing a downward trend in the incidence of all types of cancer – from 30,338 newly diagnosed cases in 2019 to 25,225 cases in 2024 (from 434.9 to 391.6 per 100,000 people) [224].

Data from the National Centre for Public Health and Analyses also show that the incidence of malignant neoplasms of the digestive organs will decrease in 2023 and 2024 from 5,664 to 5,525 new cases (87.9-85.5 per 100,000 people) [224]. A review of new cases by location reveals the same trend: stomach – from 814 to 801 new cases (12.6-12.4 per 100,000); colon – from 2,044 to 1,984 new cases (31.7-30.8 per 100,000); rectosigmoid region, rectum, anus and anal canal – from 1,377 to 1,327 new cases (21.4-20.6 per 100,000) [224].

According to data from the European Commission for Bulgaria (ECIS – European Cancer Information System), the five-year relative survival rate for colorectal cancer in 2019 is about 51% [222]. This value is higher than the 42.7% reported by the NCR for patients aged ≥ 15 years diagnosed between 2000 and 2007.

ECIS data on stomach cancer show that patients in the 45-54 age group have the highest five-year relative survival rate (15.12%), while the lowest is among those aged 75 and over (9.05%), with the average value according to the NCR being 11.8%. (Table 2). With regard to oesophageal carcinoma, the average survival rate according to the NCR was 5.8%, while ECIS data show the highest rate in the 15 to 44 age group (9.67%) and the lowest in the 65 to 74 age group (4.35%).

For small intestine cancer, an average five-year relative survival rate of 35.6% has been reported, with the highest rate in the 55 to 64 age group (45.25%) and the lowest in the 45 to 54 age group (27.99%).

Table 2. Average five-year relative survival rate in patients aged ≥ 15 years in Bulgaria diagnosed with malignant neoplasms of the gastrointestinal tract during the period 2000–2007, according to ECIS data

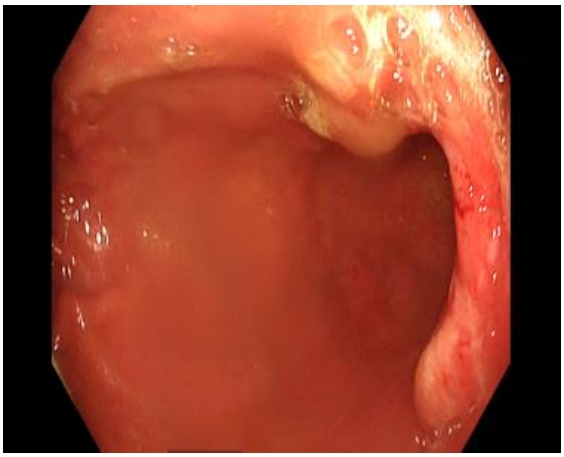
Localisation	Age group				
	15-44 years, %	45-54 years, %	55-64, %	65-74 years, %	75+, %
Oesophagus	9.67	5.35	6.03	4.35	7.36
Stomach	14.18	15.12	13.09	11.97	9.05
Small intestine	35.75	27.99	45.25	29.51	40.43
Colon and rectum	43.92	47.09	45.71	43.96	35.41
Pancreas	10.38	8.23	3.09	4.54	4.53
Liver and intrahepatic bile ducts	8.47	6.21	4.39	3.75	2.78
Gallbladder	11.98	15.42	10	7.82	7.33

IV.1.1.1. Cancer of the oesophagus

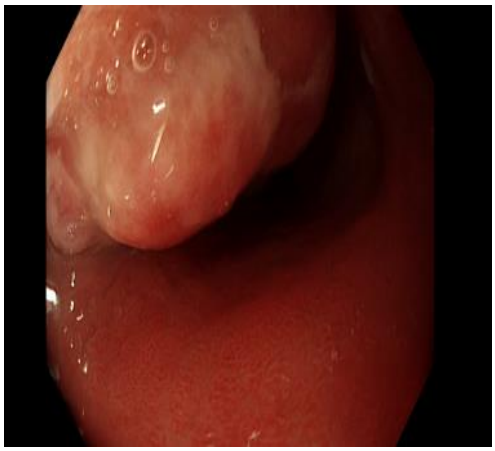
According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of oesophageal cancer in Bulgaria is about 3.3 per 100,000 people, with 226 new cases. The disease ranked 21st in frequency (0.69%) among all newly diagnosed cancer cases and 17th in number of deaths (0.12%). The actual mortality rate was approximately 3.1 per 100,000 people, with 211 deaths. Their estimates also show that the 5-year incidence of oesophageal carcinoma in 2022 will be 4.7 per 100,000 people (322 cases).

According to the latest available data from the NCR for 2017, oesophageal cancer is characterised by an unfavourable distribution by stage, with only 24.6% of cases diagnosed at an early stage (I and II). Particularly alarming is the extremely low percentage of stage I (3.4%), which reflects the difficulty of early detection of the disease. Stage II accounts for 21.2% of cases, while locally advanced disease (stage III) is observed in 19.7% of patients. The metastatic form (stage IV) is diagnosed in 20.2% of cases. The percentage of cases with an undefined stage is significant (35.6%), which is the highest rate among all localisations of the gastrointestinal tract and is probably due to the technical challenges of staging and the advanced condition of patients at diagnosis. The 2017 NCR data show that the predominant number of patients with oesophageal carcinoma is 412, which is an actual morbidity of 5.8 per 100,000 people (*Image 1 – endoscopic findings*).

Image 1. Endoscopic findings from the gastrointestinal tract[1]

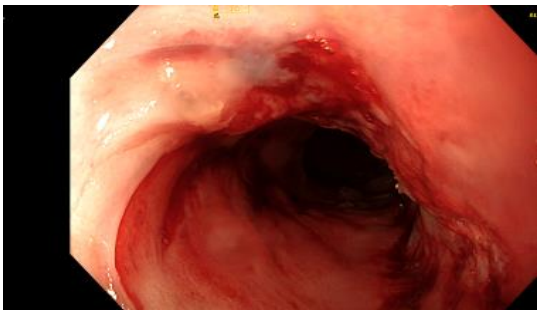


Stomach - at the border of the antrum, more on the anterior wall and the lesser curvature, there is an area measuring approximately 1.5 x 3 cm, eroded, easily bleeding mucosa.
Malignant neoplasm of the stomach.

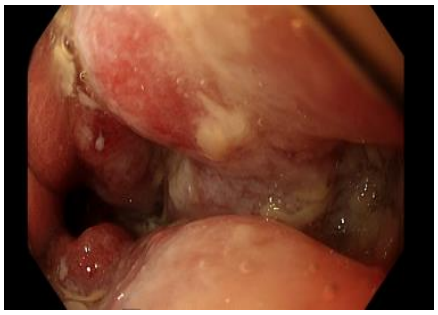


In the fundus of the stomach, a polypoid, ulcerated formation is visible.
ulcerated formation is visible in the fundus of the stomach.
Malignant neoplasm of the cardia. Condition after fundoplication

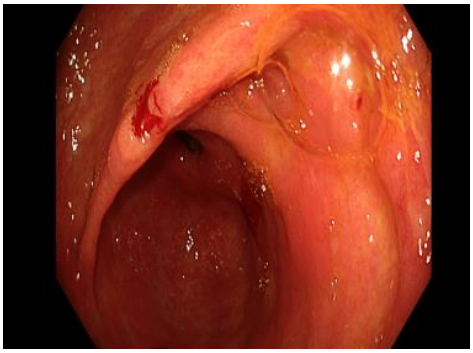
[1] All images presented in this paper are the property of the Surgery Clinic at St. Marina University Hospital – Varna.



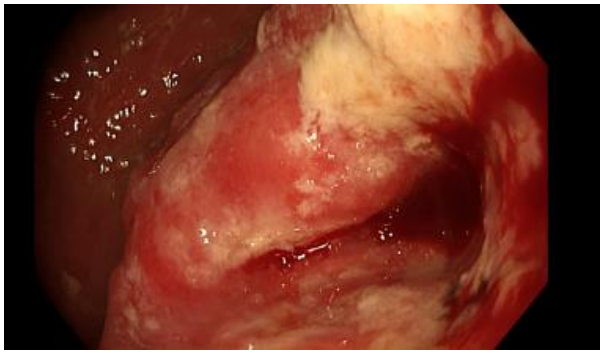
Condition after balloon dilatation of the oesophagus. From 33 cm to 40 cm, there is hyperemic and edematous mucosa, locally lobulated with a TU formation.
Oesophageal carcinoma.



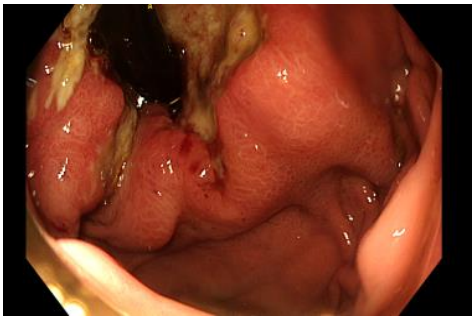
From 35 cm, a polypoid formation begins at the cardia, occupying 1/2 of the circumference. The mucosa is hyperemic, edematous, easily bleeding, with necrotic deposits and formation of a niche with fibrin and necrosis. The formation extends 5-6 cm to about 40 cm from the dentate line.
Carcinoma of the oesophagus with infiltration to the cardia



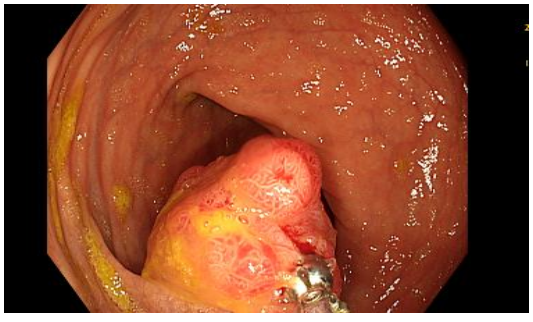
The mucosa of the stomach body is hyperemic and edematous. Two linear ulcers are visible on the lesser curvature, above the gastric angle and towards the posterior wall. The surrounding mucosa is markedly hyperemic and edematous, and the mucosa is mobile when the biopsy is taken. Fine-spotted hyperemia and edema of the antrum.
Early gastric carcinoma.



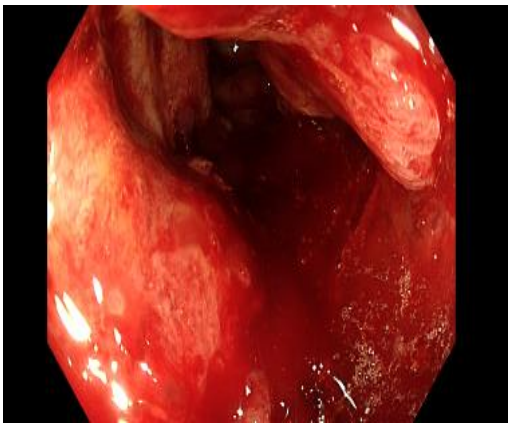
A pre-pyloric ulcer is visible, occupying the area circularly, covered with fibrin deposits. Bleeding on contact and biopsy - "the forceps run along the ulcer".
Malignant neoplasm of the pyloroantral region. Subcompensated pyloric stenosis



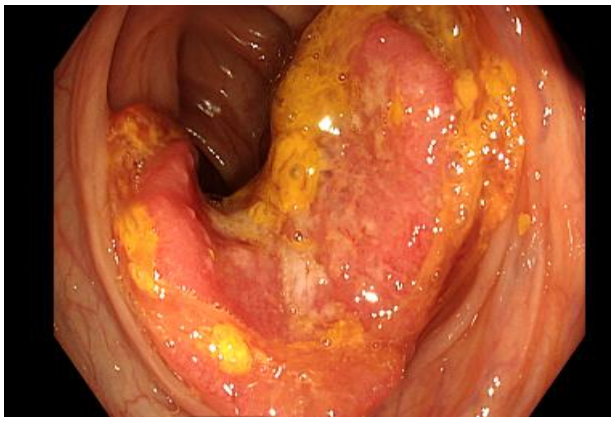
About 5 cm above the GEJ, a tumour formation begins to extend distally, engaging the lumen circumferentially and partially stenosing it. The formation has an uneven surface, is vulnerable and bleeds on contact with the device and biopsy forceps.
Carcinoma of the gastroesophageal junction



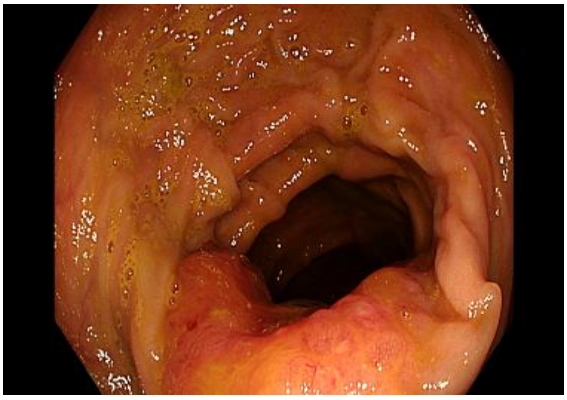
Polyp of the sigmoid-rectal junction



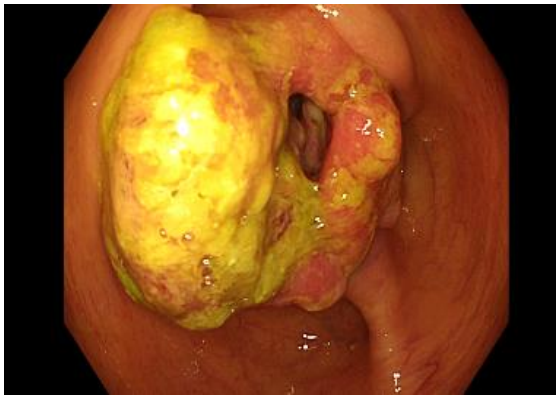
In the descending colon near the sigmoid transition, an exophytic growth is visible, engaging the lumen circumferentially and narrowing it to a residual lumen of about 1.5 cm. The formation is about 5-6 cm long.
Conclusion: **Carcinoma of the descending colon**



Carcinoma of the transverse colon. Flat spreading lesion (LSL) in ascending colon Paris IIa JNET2a



Carcinoma of the hepatic flexure



Malignant neoplasm of the ascending colon-cecum

In terms of gender distribution, oesophageal cancer shows the most pronounced male predominance among all gastrointestinal malignancies, with a ratio of 4.3:1. This means that for every 100 women diagnosed, 430 men are diagnosed, with 169 men versus only 39 women in absolute terms. This dramatic ratio is more than twice as high as that for stomach cancer (1.7:1) and three times higher than colorectal carcinoma (1.34:1), suggesting a significant role for male-specific risk factors such as smoking and alcohol consumption.

IV.1.1.2. Stomach cancer

According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of stomach cancer in Bulgaria was about 21.5 per 100,000 people, with 1,469 new cases. The disease ranked 8th in frequency (4.48%) among all newly diagnosed cancer cases and 6th in number of deaths (5.50%). The actual mortality rate was about 15.1 per 100,000 people, with 1,034 deaths. Their estimates also show that the 5-year incidence of stomach cancer in 2022 was 30.6 per 100,000 people (2,093 cases).

According to the latest data from the National Cancer Registry for 2017, stomach cancer is characterised by an extremely unfavourable distribution by stage, with only 21.4% of cases diagnosed at an early stage (I and II), with stage I accounting for only 9.5% of cases. Locally advanced disease (stage III) is observed in 15.7% of patients, while the most alarming is the extremely high percentage of metastatic form (stage IV) – 36.1%, which

is the highest indicator among the main gastrointestinal localisations together with the pancreas. The percentage of cases with an undefined stage (26.8%) is significant, reflecting the diagnostic challenges and advanced condition at primary diagnosis. The 2017 NCR data show that the predominant number of patients with stomach cancer was 4,865, representing an actual morbidity rate of 68.8 per 100,000 people.

In terms of gender distribution, stomach cancer shows a moderate predominance in men with a ratio of 1.7:1, with 877 men compared to 517 women. This ratio is identical to that for small intestine cancer and is lower than that for oesophageal cancer (4.3:1), but higher than that for colorectal carcinoma (1.34:1).

IV.1.1.3. Pancreatic cancer

According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of pancreatic cancer in Bulgaria was about 18.7 per 100,000 people, with 1,280 new cases. The disease ranked 10th in frequency (3.90%) among all newly diagnosed cancer cases and 5th in number of deaths (6.43%). The actual mortality rate was approximately 17.7 per 100,000 people, with 1,208 deaths. The 5-year incidence of carcinoma in the same year was estimated at 16.6 per 100,000 people (1,137 cases).

According to the latest data from the National Cancer Registry for 2017, new cases of pancreatic cancer, depending on the stage at which the disease was detected, were distributed as follows: stage I – 50 (4.0%), stage II – 159 (12.8%), stage III – 120 (9.7%), stage IV – 508 (41.0%), unknown stage – 401 (32.4%). Pancreatic cancer has the most unfavourable profile among all gastrointestinal malignancies. Only 16.8% of cases are diagnosed at an early stage (I and II), with stage I accounting for only 4.0% – the lowest rate among all localisations. The metastatic form (stage IV), on the other hand, dominates with 41.0%, which is the highest percentage among cancers of the gastrointestinal tract. The high percentage of undefined stage (32.4%) further highlights the aggressive nature and diagnostic challenges of this disease. NRR data for 2017 reveal that the predominant number of patients with pancreatic carcinoma was 2,153, representing an actual morbidity rate of 30.4 per 100,000 people.

The gender distribution shows a slight predominance of men with a ratio of 1.2:1 (686 men versus 552 women), which is the most balanced ratio among the main gastrointestinal localisations and suggests a smaller role of gender-specific risk factors compared to oesophageal or stomach cancer.

IV.1.1.4. Small intestine cancer

No estimates for 2022 are included for this primary site, as they are not available in the ECIS and IARC/GLOBOCAN databases. According to the latest available data from the NCR for 2017, the actual incidence of small intestine cancer was 0.9 per 100,000 people, with 63 new cases in the same year, and the actual mortality rate was 0.4 per 100,000 people (31 deaths). The new cases, depending on the stage at which the disease was detected, were distributed as follows: stage I – 9 (14.3%), stage II – 14 (22.2%), stage III – 8 (12.7%), stage IV – 22 (34.9%), unknown stage – 10 (15.9%). The ratio of newly diagnosed men (40) to women (23) in the same year was 1.7 to 1. Similar to stomach and pancreatic cancer, the highest percentage of new cases are detected in stage IV (34.9%), while 36.5% of cases are in the early stages I and II. The proportion of patients with an undefined stage is relatively low – 15.9%, and the ratio of men to women is identical to that for stomach cancer.

IV.1.1.5. Colorectal cancer

According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of colorectal cancer in Bulgaria was around 74.4 per 100,000 people, with 5,086 new cases. The disease was the third most common (15.50%) among all newly diagnosed cancer cases and the second most common in terms of deaths (14.68%). The actual mortality rate was approximately 40.3 per 100,000 people, with 2,759 deaths. The 5-year morbidity rate for the same year was estimated at 221.1 per 100,000 people (15,133 cases).

According to the latest data from the National Cancer Registry for 2017, new cases of colorectal cancer, depending on the stage at which the disease was detected, were distributed as follows: stage I – 632 (16.2%),

stage II – 1,196 (30.7%), stage III – 743 (19.1%), stage IV – 811 (20.8%), unknown stage – 509 (13.1%). The ratio of newly diagnosed men (2,228) to women (1,663) in the same year was 1.34 to 1. In colorectal cancer, almost half of the cases (46.9%) are diagnosed in the early stages (I and II), with the highest percentage being stage II (30.7%). The percentage of cases with unknown stage is relatively low (13.1%), which indicates good diagnostic practice. When comparing the two locations (colon and rectum), some differences in staging are observed. Rectal carcinoma shows a higher percentage of stage I (23.2% versus 12.5% in the colon), while the percentage of stage II is similar in both localisations (around 30-31%). A significant advantage in this disease is the significantly lower percentage of cases with unknown stage (8.1% vs. 15.8% in the colon), which is probably due to better access to preoperative imaging and endoscopic evaluation. The 2017 NCR data also show that the predominant number of patients with colorectal cancer was 19,026, representing an actual morbidity of 268.9 per 100,000 people.

IV.1.1.6. Anal cancer

According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of anal cancer in Bulgaria was around 1.0 per 100,000 people, with 68 new cases. The disease ranked 30th in frequency (0.21%) among all newly diagnosed cancer cases. The 5-year morbidity rate for the same year was estimated at 3.0 per 100,000 people. According to the latest data from the NCR for 2017, new cases of anal cancer, depending on the stage at which the disease was detected, were distributed as follows: stage I – 10 (15.2%), stage II – 18 (27.3%), stage III – 10 (15.2%), stage IV – 8 (12.1%), undefined stage – 20 (30.3%). The ratio of newly diagnosed men (30) to women (36) in the same year was 0.8 to 1. Unlike the data for colon cancer, in the National Cancer Registry, the predominant number of patients with anal carcinoma is combined with those diagnosed with cancer of the rectosigmoid region and rectum – 13,479 cases, representing an actual incidence of 190.5 per 100,000 people in 2017.

IV.1.1.7. Liver cancer and intrahepatic bile duct cancer

According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of liver cancer in Bulgaria was around 10.4 per 100,000 people, with 713 new cases. The disease ranked 13th in frequency (2.17%) among all newly diagnosed cancer cases and 11th in number of deaths (3.64%). The actual mortality rate was approximately 10.0 per 100,000, with 684 deaths. The 5-year morbidity rate for the same year was estimated at 12.2 per 100,000 people (838 cases).

According to the latest data from the NCR for 2017, new cases of liver cancer, depending on the stage at which the disease was detected, were distributed as follows: stage I – 10 (1.9%), stage II – 44 (8.2%), stage III – 117 (21.8%), stage IV – 96 (17.9%), undefined stage – 269 (50.2%). The ratio of newly diagnosed men (362) to women (174) in the same year was 2.1 to 1. Liver cancer is characterised by an extremely low rate of early diagnosis – only 10.1% of cases are in stages I and II, with stage I accounting for just 1.9%. Most alarming is the record high percentage of patients with an undefined stage (50.2%), which is the highest among all gastrointestinal localisations and reflects serious diagnostic challenges. The NCR data for 2017 also show that the predominant number of patients with liver and intrahepatic duct carcinoma was 928, representing an actual incidence of 13.1 per 100,000 people.

IV.1.1.8. Gallbladder cancer

According to the latest estimates by ECIS and IARC/GLOBOCAN for 2022, the actual incidence of gallbladder cancer in Bulgaria was around 1.1 per 100,000 people, with 77 new cases. The disease ranked 28th in frequency (0.23%) among all newly diagnosed cancer cases and 25th in number of deaths (0.32%). The actual mortality rate was approximately 0.89 per 100,000, with 61 deaths. The 5-year morbidity rate for the same year was estimated at 1.4 per 100,000 people (96 cases).

According to the latest data from the NCR for 2017, new cases of gallbladder cancer, depending on the stage at which the disease was detected, were distributed as follows: stage I – 15 (13.3%), stage II – 19 (16.8%),

stage III – 11 (9.7%), stage IV – 39 (34.5%), undefined stage – 29 (25.7%). The ratio of newly diagnosed men (34) to women (79) in the same year was 0.4 to 1. Gallbladder cancer demonstrates relatively better early diagnosis compared to liver cancer – 30.1% of cases are in stages I and II. However, the metastatic form (stage IV) dominates with 34.5%, while stage III accounts for only 9.7%. The gender distribution shows a marked predominance of women with a ratio of 0.4:1 (79 women versus 34 men), which is the strongest predominance of the female gender among all gastrointestinal localisations and is probably associated with the higher incidence of gallstones in women.

A major limitation remains the lack of up-to-date epidemiological data due to the closure of the National Cancer Registry and late staging at diagnosis.

IV.2. RESULTS FROM TASK 2

IV.2.1. Modern surgical approaches to the treatment of malignant diseases of the gastrointestinal tract. Innovative surgical techniques and added benefits

IV.2.1.1. Minimally invasive laparoscopic surgery

IV.2.1.1.1. Colon and rectum

Laparoscopic surgery of the large intestine involves a set of minimally invasive surgical procedures performed through several small incisions in the abdomen (usually 4-5 in number, between 5 and 10 mm long). In recent decades, a number of large international studies have demonstrated the benefits of minimally invasive surgery in the treatment of colon carcinomas. Patients leave the hospital just a few days after the procedure and return to their daily activities much faster than with "open" surgery. With minimally invasive surgery, the trauma to the patient is many times less than with open surgery.

Ivanov et al. (2025) published a comparative study examining the advantages of laparoscopic versus open surgery in the treatment of colorectal carcinoma, based on clinical experience and analysis of results in Bulgarian surgical practice [225]. The authors compared two groups of patients with colorectal cancer – a laparoscopic and an open surgical group – analysing intraoperative, postoperative and oncological parameters. The study included patients with resectable colorectal carcinoma without distant metastases, suitable for radical surgery [225]. It has been documented that the operating time for laparoscopic procedures is longer in the initial cases due to the learning curve, but it evens out or even shortens with experienced teams. Intraoperative blood loss was significantly lower in the laparoscopic group compared to open surgery, which reduced the need for blood transfusions. The conversion rate to open surgery was low with proper patient selection and was mainly necessary in advanced tumours with local invasion or unexpected intraoperative complications [225].

In addition, Ivanov et al. identified numerous significant advantages of the laparoscopic approach in the postoperative period [225]. Postoperative pain was significantly lower in laparoscopic patients, resulting in a reduced need for analgesics and a shorter period of parenteral analgesia [225]. Recovery of bowel function is faster, with earlier passage of gas and defecation, usually within two to three days compared to four to five days in open surgery [225]. The hospital stay is significantly shorter in the laparoscopic group – an average of four to six days compared to seven to ten days in open surgery [225].The authors also noted a faster return to normal activities and work, usually within two to three weeks with laparoscopy compared to four to six weeks with the open approach [225]. The incidence of postoperative complications was lower in the laparoscopic group. In particular, they noted a reduced risk of wound infections due to smaller incisions, a lower rate of respiratory complications due to less pain and earlier mobilisation, and a reduced incidence of postoperative ileus. Cosmetic results were significantly better with the laparoscopic approach with small incisions, leading to high patient satisfaction [225].

Ivanov et al. also emphasise that oncological adequacy is comparable between the two groups. The number of lymph nodes removed was comparable, ensuring adequate staging of the disease [225]. Resection margins were negative (R0 resection) at a similar rate in both groups [225]. The quality of TME in rectal carcinoma was excellent in the laparoscopic group due to increased visualisation and precise dissection. Long-term oncological outcomes, including progression-free survival and overall survival, were comparable between the laparoscopic and open groups at a mean follow-up period of three to five years [225]. The incidence of local recurrence showed no statistically significant difference, confirming the oncological safety of the laparoscopic approach [225].

In colorectal carcinoma, Ivanov et al. note specific advantages depending on the location [225]. In colon cancer (right and left colon), laparoscopic mobilisation was facilitated by good visualisation of the mesocolon and vascular structures [225]. In rectal cancer, the laparoscopic approach offered significant advantages in the narrow pelvis, including better visualization of pelvic structures, more precise dissection with better preservation of autonomic nerves, and more accurate TME with a higher percentage of intact mesorectal fascia [225]. The authors have commented that despite the higher initial costs of equipment and consumables in laparoscopic surgery, the overall costs are comparable or even lower due to shorter hospital stays, fewer complications, reduced need for analgesics, and faster return to work for patients. The economic efficiency is particularly pronounced in younger working patients [225].

In another study, **Arabadzhiev et al. (2023)** analysed the advantages and limiting factors of laparoscopic colorectal surgery compared to the traditional open approach [226]. The study is a retrospective comparative analysis involving 42 patients with histologically proven colorectal carcinoma, divided into two equal groups – laparoscopic surgery and open surgery [226]. The main indicators assessed included operating time, length of stay in the intensive care unit, need for analgesia, and the effect of body weight on intraoperative outcomes [226]. In this way, the authors aim to assess both the clinical effectiveness and the practical limitations of the laparoscopic approach in real hospital settings [226].

The results of the study by Arabadzhiev et al. show that the average operating time for laparoscopic surgery is moderately longer than for open surgery, with the difference not reaching clinical significance [226]. Analysis of the impact of body mass index reveals that in patients of normal weight, the laparoscopic approach may even be more time-efficient, while in overweight and obese patients, the operating time tends to increase [226].This highlights the importance of individual anatomical features and body constitution as factors influencing the technical complexity of the procedure [226].

A significant advantage of laparoscopic surgery is observed in the postoperative period [226]. Patients who have undergone laparoscopic surgery demonstrate a significantly shorter stay in the intensive care unit, with more than half of them leaving the intensive care unit within the first 72 hours after surgery [226].In contrast, all patients in the open surgery group remain in the intensive care unit for a longer period. This indicates a milder postoperative course and faster functional recovery with the laparoscopic approach [226]. In addition, analysis of analgesia requirements shows significantly lower consumption of strong opioid analgesics in patients undergoing laparoscopic resection [226]. The reduced need for morphine and other powerful painkillers indirectly reflects the lower level of postoperative pain and contributes to better patient comfort and a reduced risk of adverse drug reactions [226].

In terms of oncological outcomes, Arabadzhiev et al. found no significant differences between the laparoscopic and open approaches, and their observations are consistent with data from the broader scientific literature, according to which laparoscopic colorectal surgery provides equivalent oncological radicality and safety [226].Although the present study does not provide long-term follow-up data, the results support the established concept of the oncological adequacy of the minimally invasive method. [226]. Despite the reported advantages, the authors also highlight some limiting factors of laparoscopic colorectal surgery. [226]. These include longer operating times in certain patient groups, the technical

complexity of the procedure, and dependence on the experience of the surgical team. These factors may limit the applicability of the method in complex cases or in patients with unfavourable anatomical characteristics [226].

IV.2.1.1.2. Gastric carcinoma

Focusing on the surgical treatment of gastric carcinoma in Bulgaria, **Belev et al. (2016)** published a study on the prevention of complications in laparoscopic gastrectomy [227]. The authors systematised the complications according to the stages of the operation and proposed specific preventive strategies [227]. When creating surgical access, careful insertion of the first trocar was recommended, with the Hasson technique being preferred for high-risk patients [227].The authors have identified several critical moments during vascular dissection and lymphadenectomy [227]. The use of a combined technique with ultrasonic scissors and clips or ligatures for larger vessels, such as the left gastric artery and vein, is recommended [227]. Particular attention is paid to dissection around the celiac trunk and its branches, where stepwise vascular ligation with continuous visualisation is recommended [227]. In D2 lymphadenectomy, Belev et al. emphasised the importance of skeletonisation of the common hepatic artery, the lienal artery and the left gastric artery, warning of the risk of pancreatic damage during aggressive dissection around the pancreatic head [227].

Belev et al. have provided detailed recommendations for creating an anastomosis. In esophagojejunal anastomosis after total gastrectomy, emphasis is placed on the need for adequate mobilization of the esophageal stump (at least 2-3 cm intra-abdominally), ensuring good perfusion of the jejunal loop through proper Roux-Y construction, avoiding excessive tension, and using a precise stapling or suturing technique [227]. The authors also recommended intraoperative testing of the anastomosis with air under water or methylene blue to check for leaks [227]. In gastrojejunal anastomosis after distal resection, they emphasised the importance of assessing the perfusion of the gastric remnant, the correct orientation of the jejunal loop (antecolic or retrocolic) and avoiding deformation of the anastomosis [227].

Belev et al. have discussed specific intraoperative risks such as damage to the spleen, pancreas, or colon and have proposed techniques to avoid them [227]. Particular attention is paid to postoperative complications such as anastomotic leakage, pancreatic fistula and intra-abdominal collections, recommending early diagnosis and adequate treatment [227]. The authors have also provided specific recommendations for surgical technique depending on the location of the tumour [227]. In proximal tumours requiring total gastrectomy, the need for adequate mobilisation of the abdominal part of the oesophagus and careful work around the hiatus is emphasised [227]. For distal tumours, an assessment of the adequacy of the proximal resection line and perfusion of the remaining stomach is recommended [227]. For tumours of the middle third, an individualised approach has been discussed depending on the exact location and the possibility of subtotal resection in the case of negative resection lines [227]. Successful laparoscopic gastrectomy requires not only technical skill, but also a systematic approach to the prevention of complications, a good knowledge of anatomy, and a willingness to convert if necessary [227]. The importance of the learning curve and the need for gradual accumulation of experience, starting with simpler cases before moving on to advanced stages of the disease, is emphasised [227].

IV.2.1.1.3. Gastrointestinal stromal tumour

In another study, **Shumarova et al. (2024)** presented a case of a patient with a gastrointestinal stromal tumour (GIST) of the stomach, in whom they successfully performed laparoscopic resection [228]. The tumour was located in a suitable anatomical position, allowing minimally invasive resection without compromising oncological principles [228]. The operation was performed using a standard laparoscopic technique with four trocars, and the tumour was resected with adequate macroscopic margins, without tumour rupture or dissemination of tumour cells [228]. Intraoperative results show minimal

blood loss (less than 50 ml), short operating time compared to the open technique, and no intraoperative complications [228].The authors emphasise that the laparoscopic approach allows excellent visualisation of the tumour and surrounding structures thanks to the magnification, which facilitates precise dissection and preservation of healthy gastric tissue. Postoperative recovery is significantly faster than expected with open surgery [228]. The patient started oral intake of fluids on the first postoperative day and progressed to a regular diet on the second or third day [228]. The hospital stay was short – three to four days, which is significantly shorter than the typical five to seven days for open resection [228]. Postoperative pain was minimal, requiring only a short period of analgesia with non-steroidal anti-inflammatory drugs, without the need for opioid analgesics [228].

Shumarova et al. emphasised the cosmetic advantages of the laparoscopic approach with small incisions (5-12 mm), leading to excellent aesthetic results and high patient satisfaction [228]. Functional recovery was also rapid, with the patient returning to normal activities within one to two weeks [228]. From an oncological point of view, pathological analysis confirmed R0 resection (negative microscopic margins) with intact tumour pseudocapsule and no tumour rupture [228]. The authors emphasised that the laparoscopic approach did not compromise oncological principles and allowed for adequate resection comparable to open surgery [228]. According to Shumarova et al., laparoscopic resection of GIST tumours is a safe and effective alternative to open surgery in selected cases [228]. The approach combines oncological adequacy with significant advantages of minimally invasive surgery, including less postoperative pain, shorter hospital stay, faster recovery, excellent cosmetic results and high patient satisfaction [228]. The authors emphasised the importance of proper patient selection based on tumour size, location and characteristics, as well as the need for experience in laparoscopic surgery for optimal results [228].

IV.2.1.1.4. Liver

Laparoscopic liver surgery has undergone significant development over the last decade, with the increasing technical complexity of liver resections posing new challenges for surgical teams and requiring adequate assessment of the risk and difficulty of interventions. To facilitate the selection of patients for a laparoscopic approach and to assess the expected difficulty of the procedure, numerous difficulty scoring systems (DSS) have been developed in the literature. The use of such systems aims to support clinical decision-making by optimising both the planning of the operation and the prognosis for intraoperative and postoperative parameters.

Kostadinov et al. (2022) prospectively analysed a database for the period from January 2019 to January 2022, identifying patients who underwent laparoscopic liver resections [229]. All included patients were assessed using four different difficulty scales: Iwate, Institut Mutualiste Montsouris (IMM), Southampton, and Hasegawa. These scales were created with various criteria in mind, such as anatomical features of the lesions, previous surgery, lesion size, location, and technical aspects of the resections that affect the expected complexity of the intervention [229]. By correlating the calculated difficulty levels with the corresponding intraoperative parameters – duration of the Pringle manoeuvre, volume of blood loss, frequency of blood transfusion and operating time, as well as analysis of postoperative results, the study aims to assess the validity of these scales for the Bulgarian population and their applicability in routine clinical practice [229].

The study by Kostadinov et al. included a total of 60 patients who met the predefined criteria for analysis. The average age of the patients was 60 years, with 43% of them being men [229]. The correlation analysis between the four difficulty scales and the actual intraoperative parameters showed a positive correlation, supporting the concept that most of the DSS used reflect to some extent the actual surgical complexity of laparoscopic liver resections. However, the study found that none of the scales considered adequately predicted the risk of conversion to open surgery or adverse postoperative outcomes with strong discriminatory ability [229]. When assessing the risk of conversion, the IMM scale showed the

best results in terms of discriminatory ability, while the Hasegawa scale demonstrated the highest ability to predict postoperative complications among the instruments considered [229].

The analysis of intraoperative data conducted by Kostadinov et al. reveals that the application of fair statistical methods, including Jonckheere-Terpstra analysis and AUROC (area under the ROC curve), allows for an objective comparison between the predicted difficulties according to the scales and the actual clinical parameters [229]. The positive correlation shows that as the predicted level of difficulty increases, parameters such as the duration of the Pringle manoeuvre, the volume of blood loss and the operating time also increase, which is in line with the principles for assessing the complexity of laparoscopic interventions [229]. However, the limited predictive value for conversion and postoperative complications highlights the need for additional risk stratification factors that can optimise prognostic models [229].

The results of the study by Kostadinov et al. also show that, despite the relative usefulness of the available difficulty scales for laparoscopic liver resections, they have limitations, especially when it comes to predicting key clinical outcomes such as conversion and postoperative complications [229]. Such risk and difficulty assessment is particularly important given that laparoscopic liver resections are technically challenging procedures requiring a high level of surgical expertise and adequate planning [229]. Not all aspects of clinical risk can be fully integrated into existing scales, which highlights the need for continued refinement of stratification tools [229].

IV.2.1.2. Robotic surgery (Da Vinci system)

Robotic platforms provide 3D visualisation, finer manipulation and better ergonomics, which reduces conversion rates, often reduces bleeding and may increase the volume of lymph node dissection in some procedures (especially in narrow anatomical spaces such as the small pelvis). However, differences in long-term oncological survival between robotic and laparoscopic methods remain a subject of research. Several systematic reviews and meta-analyses show improvement in short-term outcomes. Robotic surgery has specific applications in surgical interventions in the small pelvis, which apply to all diseases of the rectum, including tumours, cysts, etc. In the surgical treatment of stomach cancer, it allows for extremely precise lymph node dissection, which is key to oncological outcomes and patient survival. Robotic instruments are designed to work with devices to achieve very good haemostasis and reduce blood loss in the surgical field. During surgery, conventional laparoscopic images are obtained from a single camera, while robotic surgery uses two high-resolution cameras that provide a three-dimensional image with 10 to 12 times magnification. Pain after robotic surgery is much less severe, mobilisation is early and recovery is relatively quick [230]. Less blood loss during surgery, smaller incisions and therefore fewer scars, less postoperative pain, limited risk of infection, shorter hospital stay, rapid recovery [230]. Patients who need chemotherapy or radiotherapy can start this treatment earlier [230].

IV.2.1.2.1. Gastric carcinoma

In a randomised phase II clinical trial conducted by **Lu et al. (2024)**, robotic distal gastrectomy (RDG) was compared with laparoscopic distal gastrectomy (LDG) in patients with resectable gastric carcinoma, with the primary endpoint being 3-year recurrence-free survival (DFS) and secondary endpoints including 3-year overall survival (OS) and recurrence patterns [237]. The study included a total of 300 patients with clinical stages cT14a and N0/+ randomised into two groups, with 283 patients (141 in RDG and 142 in LDG) participating in the modified intention-to-treat population analysis [237]. All patients underwent R0 resection and D2 lymph node dissection and were followed up for a minimum of 36 months after surgery [237]. The comparison between the two approaches shows that the 3-year DFS is significantly higher in the RDG group (85.8%) compared to LDG (73.2%), with a difference of 12.6%, which not only meets the criteria for non-inferiority but also shows a trend towards a possible advantage

of RDG [237]. Multivariate Cox regression analysis, including age, tumour size, gender, ECOG PS, lymphovascular invasion, histology, and pathological stages pT and pN, confirmed that RDG is a factor with an independent protective effect for 3-year DFS (HR: 0.541; 95% CI: 0.3140.932). With regard to recurrence patterns, clinical analysis shows a lower cumulative recurrence rate with RDG (12.1% vs. 21.1%), reflecting better controlled local recurrence compared to laparoscopy [237]. Looking at different subgroups according to pT and pN stage also shows a more pronounced benefit of RDG in more advanced stages (pT24 and pN+), which may be due to the more precise lymphadenectomy technique and lower local recurrence rate [237]. Based on these data, RDG demonstrates non-inferiority and potentially improved 3-year recurrence-free survival and recurrence profile, providing a high level of evidence supporting the use of robotic surgery in resectable gastric cancer [237].

The systematic reviews and meta-analyses by **Tuohuti et al. (2025)** and **Liu et al. (2025)** compare robotic (RG/RTG) and laparoscopic (LG/LTG) surgery for gastric cancer, evaluating both perioperative and oncological outcomes in different clinical contexts [238-239]. Tuohuti et al. analysed four uncontrolled (retrospective observational) studies involving a total of 569 patients with locally advanced gastric carcinoma after neoadjuvant therapy [238]. They show that robotic gastrectomy is associated with longer operative time, but at the same time faster recovery of intestinal function (shorter time to first flatulence and liquid intake) and a greater number of lymph nodes removed, with no significant differences in postoperative complications, blood loss, conversion to open surgery, hospital stay, reoperations or readmissions in the 30-day period after surgery, suggesting comparable safety and also positive early clinical effects for RG despite the duration of the intervention [238]. Due to the predominantly uncontrolled design of the included studies and the lack of randomisation, the results of this meta-analysis should be interpreted as associative and hypothesis-generating rather than as evidence of a causal superiority of one of the two minimally invasive approaches in patients with gastric cancer after neoadjuvant therapy.

Liu et al., on the other hand, cover comparative (retrospective controlled cohort) studies of robotic versus laparoscopic total gastrectomy, demonstrating that RTG reduces severe (Clavien-Dindo ≥ 3) complications, the incidence of abdominal infections, intraoperative blood loss, and length of hospital stay, while the number of lymph nodes removed is higher, with no significant differences in three-year overall or recurrence-free survival rates, supporting comparable oncological efficacy and more favourable short-term operative profiles for RTG [239].

Du et al. (2025) conducted an extensive systematic review and the largest meta-analysis to date, including 68,755 patients from 86 separate studies comparing RG with LG gastrectomy in patients with gastric cancer, with the main measures being intraoperative parameters, postoperative complications, and short-term clinical outcomes [240]. The analysis shows that RG is associated with longer operating times, but with less intraoperative blood loss, more lymph nodes removed, shorter hospital stay, earlier time to flatulence and oral intake, as well as lower frequency of conversion to open surgery, repeat operations, general and severe complications, including pancreatic complications [240]. There are no significant differences between RG and LG in terms of resection margins, mortality, anaesthesia, uncontrolled recurrences or recurrence rates, which supports the safety and efficacy of the robotic approach in the surgical treatment of gastric carcinoma, despite higher operating costs and duration of the intervention [240].

Currently, one of the few meta-analyses based on randomised controlled trials has been conducted by **Deng et al. (2025)**, which included six RCTs with a total of 1055 patients (547 RG vs. 508 LG) with gastric cancer in Asia, focusing on short-term postoperative outcomes [240, 241]. Their analysis shows that RG is associated with reduced intraoperative blood loss, more lymph nodes removed, shorter hospital stay, lower incidence of postoperative complications, and earlier recovery of bowel function [241]. There are no significant differences between RG and LG in terms of operating time or time to first ambulatory mobilisation, and perioperative mortality remains similar between the two groups [241].

IV.2.1.2.2. Colon and rectum

With regard to colorectal cancer, systematic reviews and meta-analyses conducted by **Thrikandiyur et al. (2024)** and **Gahunia et al. (2025)** compare the use of robotic and laparoscopic surgery, including their specific significance in high-risk patients [242, 243]. The analyses cover over 4,000 patients from various randomised and observational studies and evaluate parameters such as conversion rate, blood loss, operating time, postoperative complications and long-term oncological outcomes [242, 243]. The data show that robotic surgery is associated with a lower conversion rate and reduced blood loss, with these benefits being particularly pronounced in high-risk surgical patients, including those with comorbidities, advanced age, or previous abdominal surgery [242-243]. Despite slightly longer operating times, the incidence of general and oncological complications does not differ significantly between the two approaches, highlighting the safety and effectiveness of robotic surgery as an alternative to the laparoscopic method. In high-risk patients, the robotic technique additionally offers better surgical control and accelerated postoperative recovery, including a shorter hospital stay, demonstrating significant clinical advantages of the minimally invasive robotic approach [242, 243].

In 2014, robotic surgery was performed for the first time in Bulgaria on a patient with colorectal cancer, with **Delyiski et al. (2015)** publishing early clinical results from the application of this innovative technology [230]. The authors emphasise that rectal surgery is a significant technical challenge due to the anatomical features of the small pelvis – narrow spaces, proximity to critical structures (ureters, vessels and nerves of the autonomic nervous system), and the need for precise dissection to achieve oncological radicality while preserving function [230]. Conventional laparoscopic surgery for rectal cancer, although minimally invasive, is associated with a long learning curve and technical limitations in the deep pelvis [230]. The authors include patients with rectal adenocarcinoma who are suitable for curative resection and have no contraindications for a laparoscopic approach [230]. Robotic TME was performed, with the technique involving positioning of robotic ports, use of a medial to lateral approach for mobilisation, precise identification and preservation of autonomic nerves (hypogastric and pelvic splanchnic nerves), sharp dissection in the operative field between the visceral and parietal fascia of the pelvis, and distal resection with adequate oncological margins [230]. Intraoperative parameters showed minimal blood loss thanks to precise dissection and good visualisation, excellent bleeding control through precise coagulation and the possibility of preserving autonomic nerves even in deep tumour locations [230]. From an oncological point of view, high-quality TME with intact mesorectal fascia was achieved in all cases, negative distal resection margins with adequate distance from the tumour, negative circumferential resection margins (a critical factor for locoregional control) and an adequate number of lymph nodes removed for accurate staging [230]. The postoperative results published by Delyiski et al. include a low incidence of early complications, rapid recovery of bowel function, short postoperative stay compared to open surgery, and low level of postoperative pain. Functional results showed preservation of urinary function thanks to the nerve-sparing technique, preservation of sexual function in men, and good functional results of the anastomoses [230]. When compared to laparoscopic and open surgery, robotic TME shows potential for oncological results comparable to or better than laparoscopic and open surgery, with a lower conversion rate to open surgery compared to laparoscopic TME (based on data from the world literature) and similar short-term results compared to laparoscopic surgery, but with the potential for better functional results [230].

Despite the positive results, Delyiski et al. identify a number of challenges and limitations [230]. The high cost of the robotic system and consumables is a major barrier to widespread application. The lack of tactile feedback requires the surgeon to adapt their technique, as they cannot feel the tissue tension

directly [230]. Robot docking and instrument adjustment prolong operating time, especially at the beginning of the experiment. The team requires specific training to work with the robotic system, and implementation requires appropriately equipped operating rooms and technical support [230].

IV.2.1.3. Enhanced recovery after surgery protocol

The enhanced recovery after surgery protocol is a set of pre-, intra- and post-operative procedures, including preoperative patient education, reduction of fasting with carbohydrate drinks before surgery, multimodal pain management, prevention of venous thromboembolism, and early mobilisation. This multidisciplinary approach reduces the physiological stress of surgery and accelerates patient recovery after various surgical interventions, including abdominal surgery, with the main goals being shorter hospital stays, fewer complications and improved early functional rehabilitation. Although analyses in Bulgarian sources focus mainly on gynaecological surgery (where ERAS shows a reduction in length of stay and complications), the conceptual principles are easily transferable to gastrointestinal oncology practice due to the similar pathophysiological mechanisms of surgical stress and recovery [244]. International evidence included in systematic reviews and meta-analyses of ERAS in gastrointestinal cancer surgery shows that in gastrectomy for stomach cancer, ERAS protocols shorten hospital stays, accelerate first bowel function, and reduce costs without increasing the incidence of surgical complications, although some analyses have observed higher rates of readmission after discharge [244]. In colorectal surgery for cancer treatment, ERAS protocols are also associated with significantly shorter hospital stays, a trend towards fewer overall complications and effective recovery time, without negatively affecting safety or the frequency of complications [244]. One of the largest retrospective observations shows that in patients with colorectal cancer, ERAS has no adverse effect on 5-year cancer survival compared to conventional recovery, supporting the long-term safety of ERAS [247].

ERAS, combined with laparoscopic techniques for the treatment of colorectal cancer, is a safe and feasible strategy that not only accelerates the recovery of gastrointestinal function but also improves the perioperative nutritional status of patients.

IV.2.1.4. Hyperthermic intraperitoneal chemotherapy (HIPEC)

HIPEC is a complex, innovative surgical-oncological strategy that combines cytoreductive surgery (CRS) for maximum removal of visible tumours and subsequent application of intraperitoneal hyperthermic chemotherapy to improve local control of the disease and increase survival and other clinical outcomes in patients with peritoneal carcinomatosis of gastrointestinal origin. Hyperthermic intraperitoneal chemotherapy uses a solution heated to 41-42 °C, as the high temperature improves the effect of chemotherapy on tumour cells. During the HIPEC procedure, the chemotherapeutic mixture is heated to 42-43 °C and then infused into the abdominal cavity for about 60-80 minutes. HIPEC is used in the treatment of colon, stomach and, more recently, pancreatic cancer. Although international data show potential benefits in selected patients and in a specific context, the current evidence remains inconclusive, making HIPEC an area of active research and still experimental in relation to the routine treatment of gastrointestinal tumours. The conflicting evidence surrounding the role of HIPEC in gastrointestinal malignancies is summarised in a systematic review and meta-analysis that analyses some RCTs in patients with gastric and colorectal cancer, evaluating both the prevention and treatment of peritoneal carcinomatosis through CRS plus HIPEC [248]. The included RCTs show that, according to current data, there is no proven overall improvement in OS for patients with gastrointestinal and biliary neoplasms, which makes the role of HIPEC in this context experimental and requires additional large multicentre studies to determine its effectiveness [248]. Although reduced event risks are observed in some subgroups (such as

peritoneal carcinomatosis of gastric origin), the evidence is still uncertain and limited in scope and quality, which places HIPEC outside the standard treatment recommendations for gastrointestinal tumours until convincing results from phase III RCTs are obtained [248].

Another systematic literature review focuses on the results of cytoreductive surgery and HIPEC in patients with gastric cancer that has developed peritoneal carcinomatosis, where traditional systemic chemotherapy without local control leads to a very poor prognosis [249]. Data show that in patients with complete cytoreduction and subsequent HIPEC, median survival can be significantly increased compared to supportive care, and five-year overall survival varies significantly depending on the degree of cytoreduction and specific patient characteristics [249]. This approach aims to remove visible tumour masses and destroy microscopic residual cells through the local application of heated chemotherapy solution, which is thought to improve survival in selected patients, but with numerous limitations related to the design of available studies, the lack of large randomised data and variability in results [249].

IV.2.1.5. ICG (indocyanine green) fluorescent labelling for lymphatic navigation and vascular assessment

ICG navigation routinely improves the visualisation of lymphatic pathways and venous/arterial blood flow, leading to a higher degree of lymph node dissection in gastrectomies and more accurate lymphadenectomy without increasing overall complications. and some randomized controlled trials (RCTs) and meta-analyses have also shown a reduction in certain perioperative markers (e.g., bleeding and anastomotic leakage in certain situations). In a phase 3 randomized clinical trial conducted by **Chen et al. (2023)** comparing ICG-guided laparoscopic lymphadenectomy with conventional approaches in patients with gastric carcinoma, the long-term results showed that ICG-guided navigation improved surgical precision and potentially increased lymph node yield, contributing to better oncological outcomes [250]. After conducting a systematic review and meta-analysis of studies investigating the broader role of ICG in intraoperative navigation in the surgical treatment of gastric carcinoma, **Mourdi et al. (2025)** confirmed that this method significantly improves the visualisation and identification of perigastric and regional lymph nodes, including small and deeply located nodes that could be missed in conventional surgery [251]. ICG provides excellent visualisation of the blood supply, including identification of associated arteries and veins, which aids in precise vascular dissection and reduces the risk of vascular injury [251]. Overall, fluorescent navigation facilitates more accurate determination of resection margins and helps to assess the radicality of the resection, especially in tumours with unclear anatomical boundaries. ICG also allows intraoperative assessment of anastomotic perfusion, which may reduce the risk of anastomotic leaks and other postoperative complications [251].

Lv et al. (2025) published a study focusing specifically on the benefits of ICG in laparoscopic total gastrectomy for advanced upper gastric carcinoma, an anatomical location where lymphadenectomy is particularly challenging [252]. ICG significantly improved the visualisation of lymph nodes in the splenic artery and pancreatoduodenal region, which are often metastatic in upper gastric tumours. ICG fluorescence has allowed for more precise identification and preservation of the splenic artery and vein, while ensuring adequate lymphatic dissection, reducing the need for splenectomy [252]. No increase in complications related to the pancreas (pancreatic fistula) or spleen was observed, despite more extensive dissection in the ICG group. Short-term oncological results showed better locoregional control in the ICG group, with the authors planning long-term follow-up to assess survival [252].

In another study published by **Zhong et al. (2025)**, the five-year oncological results from the randomised clinical trial FUGES-012 provide the longest-term data on the efficacy of ICG-guided lymphadenectomy in gastric carcinoma. The results support the inclusion of ICG technology as a standard of care

in laparoscopic gastrectomy, especially in cases requiring D2 lymphadenectomy in advanced disease (stage II or III) [253].

In an individual patient data (IPD) meta-analysis conducted by **Calì et al. (2025)**, the effect of ICG-guided lymphadenectomy on survival in gastrectomy was investigated in 17 studies covering a total of over 2,200 patients [254]. Subgroup analyses showed that the benefits of ICG are present regardless of the surgical approach (laparoscopic versus open), the type of resection (total versus subtotal gastrectomy) and the geographical region [254].

In 2025, the Society of American Gastrointestinal and Endoscopic Surgeons (**SAGES**) published a current systematic review and meta-analysis of fluorescent imaging navigation in gastrointestinal surgery using ICG [255]. In gastric cancer, the review confirms that ICG significantly improves the identification of perigastric and regional lymph nodes, with pooled estimates showing a 20-30% increase in the number of lymph nodes removed. Special attention is paid to the role of ICG in intraoperative assessment of anastomotic perfusion, with data showing a significant reduction in anastomotic leaks (relative risk reduction of 30-50%) [255]. SAGES provides conditional recommendations for the inclusion of ICG fluorescent navigation in routine practice in complex gastrointestinal oncological procedures, especially when precise lymphadenectomy is required [255].

IV.2.1.6. Sentinel nodes/navigation strategies (SN-navigation)

Laparoscopic sentinel lymph node navigation surgery (SNNS) as an alternative to standard gastrectomy in patients with early gastric cancer has been investigated in a significant randomised clinical trial, the results of which were published by **Kim et al. (2022)** [256]. The study confirms SNNS as an alternative to standard gastrectomy for selected patients with early gastric carcinoma. [256]. The sensitivity for detecting lymph node metastasis by sentinel biopsy is high (> 90%), with a very low false-negative rate (< 5%). [256]. In a significant proportion of patients in the SNNS group (> 60%), the stomach was successfully preserved, avoiding radical gastrectomy, with only local or segmental resection performed [256]. At a 3-year follow-up, there was no statistically significant difference in recurrence-free survival between the SNNS group and the standard gastrectomy group, confirming the oncological safety of the approach. It offers "personalised" surgery, in which the extent of resection is adapted to the individual lymphatic drainage pattern and metastatic status [256]. SNNS is particularly suitable for young patients with a long life expectancy, for whom maintaining activity and quality of life are priorities [256].

A literature review published by **Booka et al. (2023)**, summarising the latest developments in sentinel lymph node navigation surgery for early gastric cancer, discusses the use of radiocolloidal tracers in combination with ICG fluorescence imaging [257]. ICG offers the advantages of real-time imaging, better tissue penetration and no radiation exposure, with the dual tracer approach with radiocolloids providing the highest identification rate [257]. Experimental new fluorescent agents such as IRDye800CW and other tracers from the near-infrared region may offer improved imaging [257]. The best results are obtained in tumours with a diameter ≤ 4 cm, where lymphatic drainage is more predictable [257]. Optimal candidates are T1a (intramucosal) and selected T1b (submucosal SM1) tumours without lymphovascular invasion, with differentiated adenocarcinomas being more suitable than undifferentiated tumours due to a lower risk of lymphatic metastasis [257]. Tumours in the lower and middle third of the stomach are more suitable, while proximal tumours are challenging due to complex lymphatic drainage. Additional immunohistochemical assessment (e.g., with cytokeratins) may identify isolated tumour cells [257]. The review by Booka et al. (2023) presents data showing > 95% identification rate and < 3% false-

negative rate when selection criteria are strictly adhered to [257]. In properly selected patients, the five-year overall survival rate is > 95% and the progression-free survival rate is > 90%. The rare recurrences are predominantly haematogenous or peritoneal rather than lymphogenous, confirming the adequacy of lymphatic control [257].

Among the limitations of the technique are that it requires specialised training and experience, with success rates increasing significantly after the first 30-50 cases [257]. The lack of universally accepted protocols for dosing, injection, and pathological assessment leads to variability between medical centres, and although rare, false-negative results remain a major concern, especially in patients with larger or undifferentiated tumours [257]. In addition, some tumours have unpredictable lymphatic drainage, which can lead to the omission of metastatic nodes [257].

In a systematic review and meta-analysis, **Huang et al. (2021)** focused specifically on optimising imaging and marking protocols in sentinel lymph node biopsy for gastric carcinoma [258]. The meta-analysis included > 50 studies (randomised cohort and observational) with over 5,000 patients in total. The compared marking methods include: isolated blue staining, isolated radiocolloid tracer (^{99}mTc), combined method (blue staining + radiocolloid), standalone ICG fluorescent imaging, and combined method (ICG + radiocolloid) [258]. Due to the highest scores on all criteria (combining the advantages of both methods), the combined ICG + radiocolloid method has been accepted as the "gold standard" [258]. Based on the results of the meta-analysis, the authors propose the following optimised protocol: a combined method of ICG + radiocolloid labelling for the highest accuracy, and as an alternative for centres without access to radiocolloids – ICG alone. [258]. The recommended injection technique for T1a tumours is endoscopic submucosal injection, with laparoscopic subserosal injection also acceptable for T1a and selected patients with T1b SM1 tumours [258].The criteria for defining a sentinel node include: any lymph node with radioactivity > 10% of the hottest node, any lymph node with fluorescence visible on ICG imaging, any primary node along a visual lymphatic channel, with a minimum of 3-4 sentinel nodes required for biopsy for optimal test sensitivity [258]. The economic evaluation included in the meta-analysis shows that the combined method is initially more expensive, but can be cost-effective by avoiding unnecessary gastrectomies in the case of negative sentinel nodes, while reduced complications and improved quality of life with preservation of the stomach lead to long-term cost savings [258]. Sentinel node biopsy and combined mapping techniques (radioisotope + ICG) provide high levels of detection and diagnostic accuracy in early gastric tumours, enabling organ-preserving surgery in carefully selected patients [258]. Available multicentre reviews and meta-analyses show a high detection rate, but implementation requires standardisation and trained personnel [258].

IV.2.1.7. 3D modelling, AR/VR and intraoperative navigation

Three-dimensional (3D) modelling and navigation using augmented reality (AR) and virtual reality (VR) improve preoperative planning and orientation in the operating theatre, reducing orientation time, assisting with complex resections (e.g. liver segmentectomies) and facilitating multidisciplinary decision-making during surgery [259-262]. Numerous advantages increasingly establish 3D modelling as an important tool in preoperative planning for the surgical treatment of malignant diseases of the gastroin-

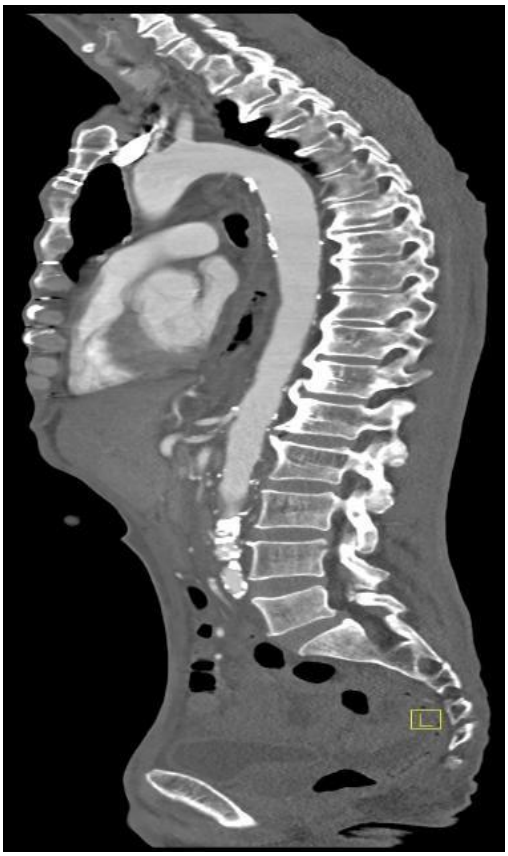
testinal tract [259]. Using imaging methods such as computed tomography and magnetic resonance imaging, patient-specific 3D reconstructions are created that allow precise visualisation of tumour location, vascular anatomy and connections to adjacent organs [259, 260]. This helps in choosing the optimal surgical strategy, especially in complex resections of the liver, pancreas, and stomach, reducing the risk of intraoperative complications and improving the radicality of the resection [261, 262].

AR and VR navigation methods are also finding increasingly widespread application in both training and clinical practice. VR is mainly used for surgical training and simulations, allowing surgeons to practise complex oncological procedures in a controlled environment without risk to the patient [263]. AR, on the other hand, has the potential for direct clinical application by superimposing digital information, including 3D anatomical models, vascular structures and tumour boundaries onto the actual surgical field, which aids orientation and increases precision during minimally invasive and robotic interventions [264, 265]. Currently, most data comes from pilot studies, but the trend is towards wider application and integration with ICG and ultrasound navigation. Intraoperative navigation is a logical extension of 3D modelling and AR technologies, combining preoperative imaging data with real-time intraoperative information from reality. Navigation systems allow surgical instruments to be tracked relative to anatomical structures and the tumour, which is particularly valuable in oncological resections with narrow margins or in repeat operations. In gastrointestinal tumour surgery, these technologies help achieve R0 resection, limit unnecessary tissue trauma and can improve short-term clinical outcomes [266-268].

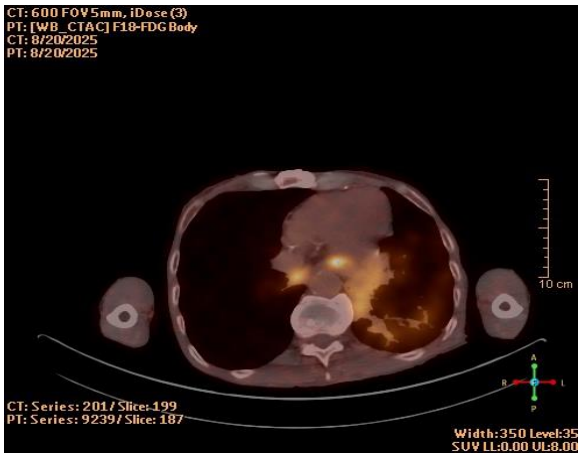
IV.2.1.8. Combined multidisciplinary strategies (MIS + neoadjuvant therapies + navigation)

With the application of ICG, robotics and navigation in a multidisciplinary plan, more and more medical centres are achieving a higher percentage of R0 resections after neoadjuvant therapy and are expanding the indications for surgical treatment in selected cases of oligometastatic disease. The result is personalised surgery with an improved benefit/risk ratio. Combined multidisciplinary strategies in the surgical treatment of malignant diseases of the gastrointestinal tract combine MIS approaches, neoadjuvant therapies and intraoperative navigation to improve oncological and functional outcomes (*Figure 2*). MIS, including laparoscopic and robot-assisted surgery, reduces surgical trauma and speeds up recovery compared to open procedures, while maintaining equivalent oncological outcomes in appropriately selected cases [243, 269]. Neoadjuvant therapies (chemotherapy, immuno- and targeted therapy) administered prior to resection aim to reduce tumour volume and invasiveness, improve the chances of R0 resection and reduce the risk of recurrence, especially in locally advanced and high-risk GIT tumours. The integration of intraoperative navigation techniques, including intraoperative ultrasound (IOUS), fluorescent navigation with ICG, and 3D reconstructions/AR overlay, aids in the real-time visualisation of tumour margins, vascular structures, and lymphatic pathways, contributing to more precise radical resection. The combined use of these approaches in multidisciplinary programmes involving oncologists, radiologists, surgeons and imaging specialists is associated with more favourable short- and long-term clinical outcomes, including reduced complication rates, shorter hospital stays, reduced risk of recurrence, and improved overall survival, according to data from systematic reviews and clinical series [267-270].

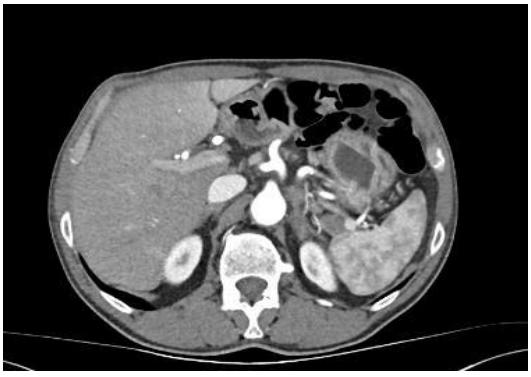
Image 2. Examples of CT and PET application in navigation



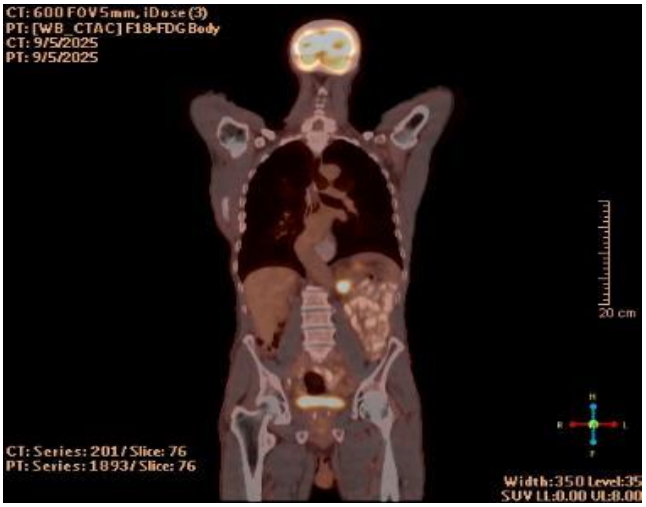
A dilated oesophagus (within the scan volume) measuring 22 mm is noticeable. In order to rule out prestenotic dilation and given the patient's consumptive syndrome and dysphagia, gastroscopy is recommended.



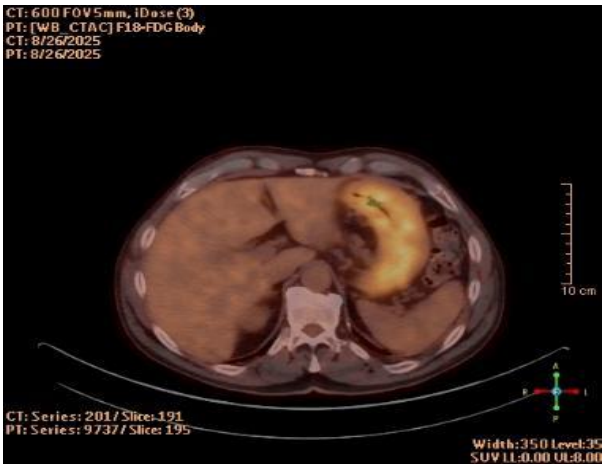
Oesophageal carcinoma, cT3 cN3 cM0. Condition after gastroscopy (14 February 2025) with histological result – squamous cell carcinoma. Distant staging with PET/CT (26 February 2025) – evidence of diffuse pathologically elevated glucose metabolism in the middle and distal third of the oesophagus. Metabolically active lymph nodes with a metastatic appearance in the thorax and upper abdomen



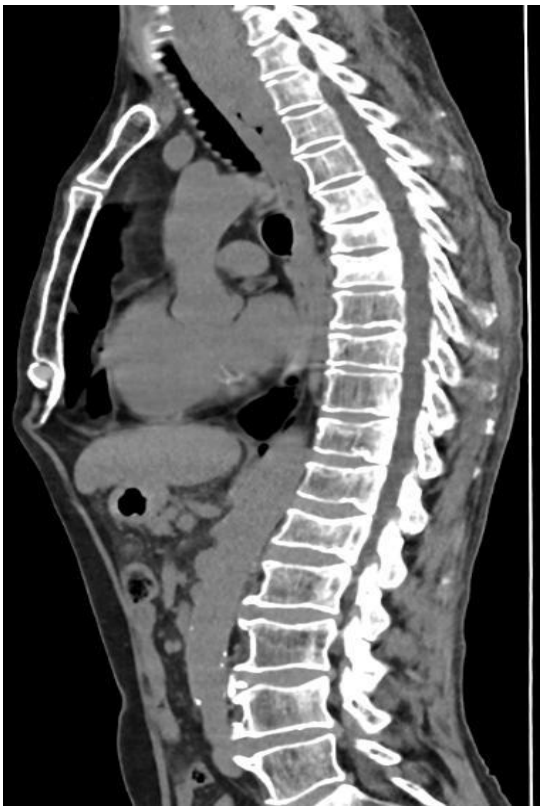
Condition after robotic oesophagectomy. Oesophagogastric plasty. Enterostomy. Postoperative control



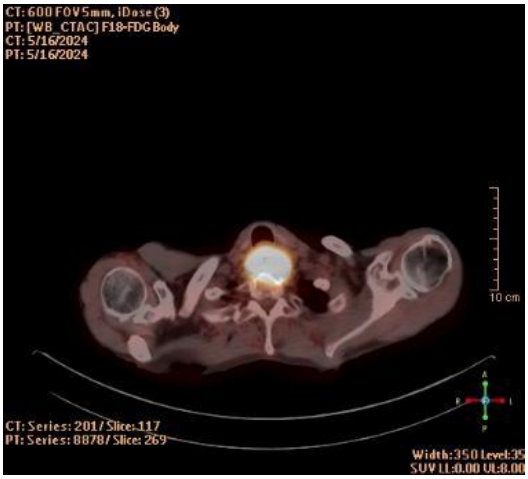
They are ventricles. pT4pN2M1. Condition after robot-assisted oesophagectomy, oesophagogastric plasty. Condition after CT. PET/CT data for an area with focal pathologically elevated glucose metabolism ventrally in the medial pole of the spleen. DD malignant lesion, inflammatory focus



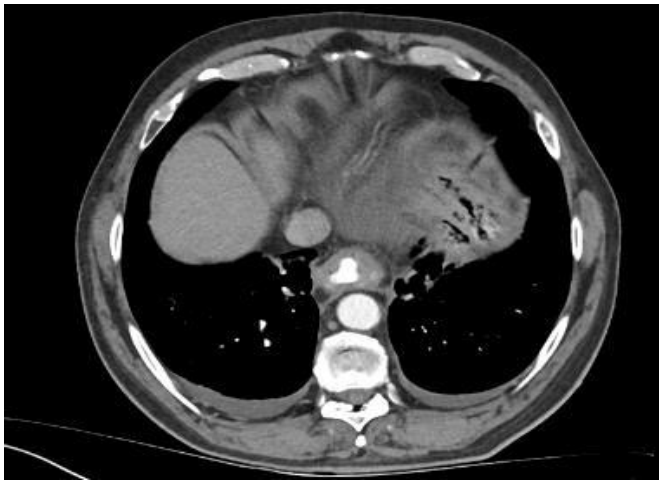
Ca recti pT3 N0 cM0. Histological result – squamous cell carcinoma. From staging PET/CT (23 May 2023) – with data for metabolically active tumour in the rectum. No metabolically active areas representative of local recurrence/malignant persistence, regional malignant lymphadenopathy and/or distant metastatic lesions are scanned. No newly appeared hypermetabolic lesions suspected of being metastatic are scanned.
Additional findings: Diffuse moderately increased activity in the stomach, likely of inflammatory origin



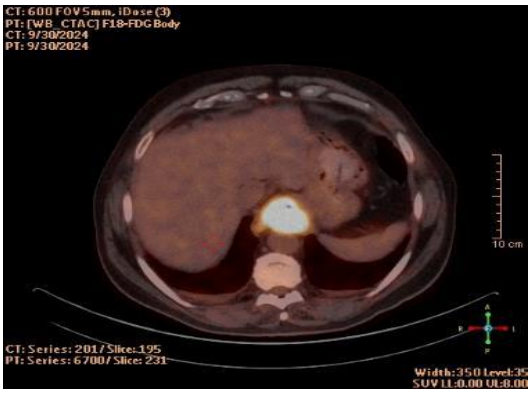
CT data for a mass in the upper third of the oesophagus, without infiltration of adjacent structures. Pneumothorax



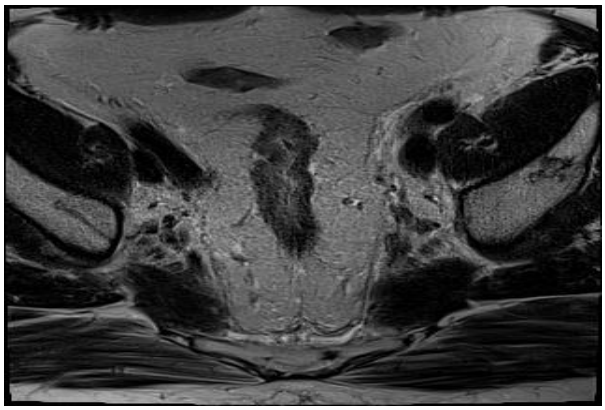
PET/CT data for carcinoma in the proximal third of the oesophagus. Metastatic cervical lymph node on the left in level III.



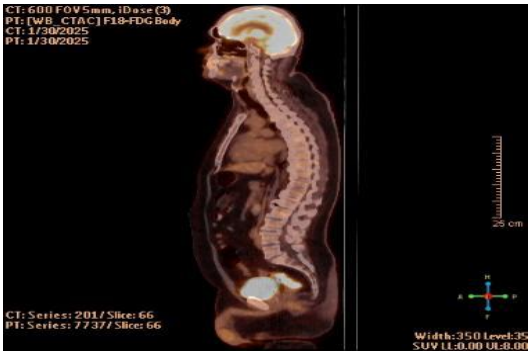
Tumour formation in the distal oesophagus and cardia of the stomach. Secondary involvement of adjacent lymph nodes. Lymph nodes in the upper mediastinum and retrocranial region highly suspicious for secondary involvement



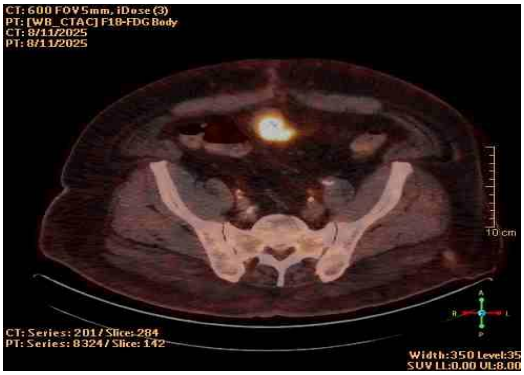
Squamous cell carcinoma of the oesophagus. St post biopsy. Staging prior to planning LL.



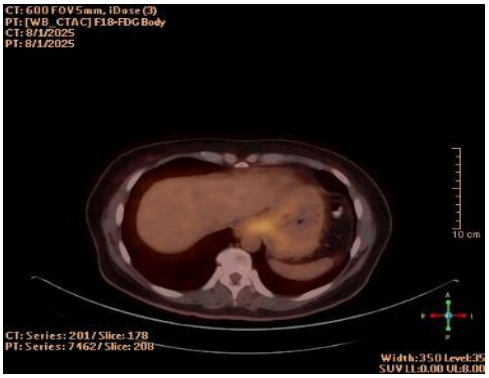
MRI examination of: SMALL BOWEL
Tumour formation of the rectum, stage T3aN2a. Number of regional LEs suspected of involvement: one high rectal LE with a transverse diameter of 13 mm. Four smaller high rectal LEs with a transverse diameter of up to 5.5 mm, two of which are rounded and the other two are oval but with uneven contours – also suspected of malignant involvement.



PET/CT data for circumferential thickening of the rectal wall with pathologically increased glucose metabolism and striation of the perirectal adipose tissue – with the appearance of a primary neoplastic process. Metastatic presacral lymph node. No evidence of distant secondary lesions. cM0



PET/CT data for Ca of the descending colon. No PET/CT data for distant metastatic lesions.



PET/CT data for a segmental area with increased metabolic activity circularly involving the lumen of the distal third of the oesophagus, the gastro-oesophageal junction and the cardia of the stomach, with the appearance of a primary neo-process. No PET/CT data for malignant regional lymphadenopathy or distant secondary lesions. cN0 cM0

IV.2.2. Conclusion

Available Bulgarian publications show that minimally invasive and robot-assisted surgeries performed in Bulgaria demonstrate typical MIS benefits: reduced bleeding, faster recovery, shorter hospital stay, and good lymph node dissection in some cases. This supports the hypothesis that most of the benefits described in the world literature are also applicable to the Bulgarian population. Publications with Bulgarian sources mainly describe implementation, early results and validation of scales, but at the same time, the lack of large RCTs, meta-analyses and long-term data means that the scientific level of evidence remains limited.

Minimally invasive techniques such as laparoscopy and robotics are gradually replacing open surgery in the treatment of many localised gastrointestinal tumours, as they improve postoperative recovery without compromising the effectiveness of treatment in suitable patients. In oesophageal cancer, minimally invasive oesophagectomy (MIE) is increasingly being used as a way to reduce post-operative morbidity, but with comparable long-term results. In rectal carcinoma, total mesorectal excision (TME) remains the standard of care, while new approaches such as TaTME and robotic TME are still being evaluated to improve the quality of resection and reduce potential conversions. Extended and synchronous resections for hepatopancreatobiliary tumours (including resections of liver metastases), as well as a multidisciplinary approach (neoadjuvant therapy + surgical treatment) are becoming more common in selected patient groups. Unresolved issues such as cost-effectiveness, the learning curve for robotics, the optimal selection of patients for organ-preserving procedures, and the place of neoadjuvant treatment before surgical intervention are still under discussion.

Contemporary surgical approaches to malignant diseases of the gastrointestinal tract are characterised by the progressive integration of multimodal therapeutic strategies. In addition to the evolution of surgical techniques, significant emphasis is placed on perioperative guidance and personalisation of treatment based on the molecular characteristics of the tumour.

In locally advanced and metastatic diseases, neoadjuvant chemotherapy, chemoradiotherapy and immunotherapy play a critical role in reducing the stage of tumour development, increasing the percentage of patients with R0 resection and providing the possibility of organ-preserving surgery. Comprehensive neoadjuvant therapy is now an established standard in rectal cancer, improving treatment compliance and distant metastasis-free survival. [235, 236]. In selected cases of oligometastatic disease, aggressive surgical treatment is considered, supported by advances in systemic therapy. [233, 234]. Innovative techniques such as sentinel lymph node biopsy and fluorescence-guided surgery are emerging as promising approaches to organ preservation in early gastric cancer, particularly in East Asia, where these methods are gradually gaining clinical validity. They aim to improve quality of life without compromising oncological radicality, although they are not yet widely accepted in Western countries. [233, 234].

National and international epidemiological data show persistent geographical differences in morbidity and outcomes, with higher rates of gastric cancer and colorectal carcinoma observed in Eastern Europe and East Asia [236]. These differences highlight the need for regionally adapted screening programmes and treatment protocols. The future of surgical oncology in the gastrointestinal tract is increasingly defined by multidisciplinary collaboration, molecular profiling of tumours, and the integration of digital navigation and planning tools. These factors encourage the use of precision medicine and personalisation of surgical treatment according to the individual characteristics of each patient [236].

IV.3. RESULTS OF TASKS 3 TO 7

The analysis covers an 11-year period – from 01.01.2013 to 31.12.2023. The total number of patients for the analysed period is 2103.

IV.3.1. Demographic parameters

The distribution by gender shows a higher proportion of male patients (58.9%) compared to female patients (41.1%).

Table 3. Distribution by gender

Gender	Number	Relative share (%)
Men	1239	58.9
Women	864	41.1
Total	2103	100.0

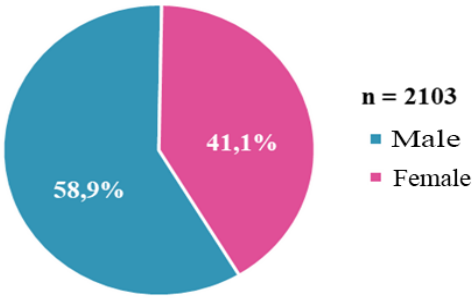


Figure 1. Graphical representation of distribution by gender

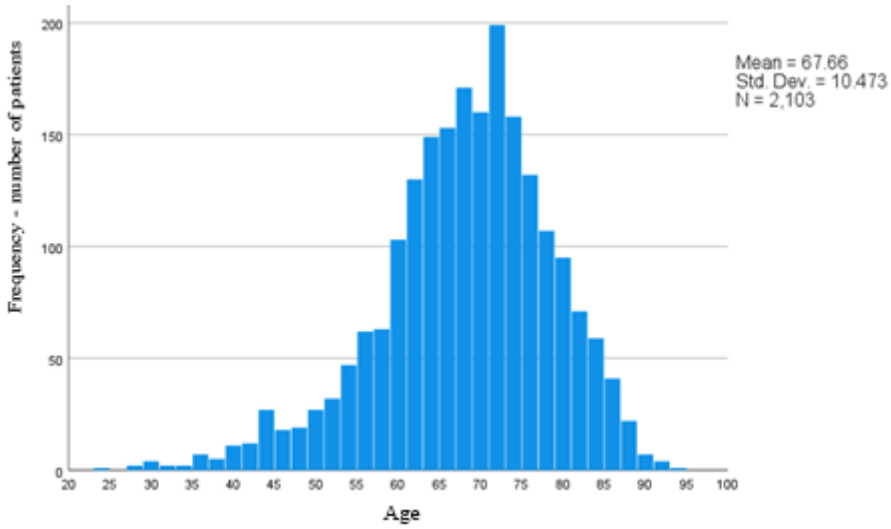


Figure 2. Histogram of age distribution

The mean age of patients is 67.66 years (SD = 10.473), the median age is 69.00 years, and the mode is 72.00 years (at 5.0%). The youngest patient is 24 years old, and the oldest is 94 years old.

The average age for men is 67.41 (SD = 9.870) and is slightly lower than that for women – 68.01 (SD = 11.277).

The age group "66-75 years" has the highest relative share – 40.4%, followed by "46-65 years", whose share is 33.9%. Patients under 45 years of age account for 3.7%, and those in the last age group (over 75) account for 22.0% (Table 4).

Table 4. Distribution by age group

Age	Number	Relative share (%)	Cumulative share (%)
18 to 45	78	3.7	3.7
from 46 to 65	712	33.9	37.6
from 66 to 75	850	40.4	78.0
over 75	463	22	100.0
Total	2103	100.0	

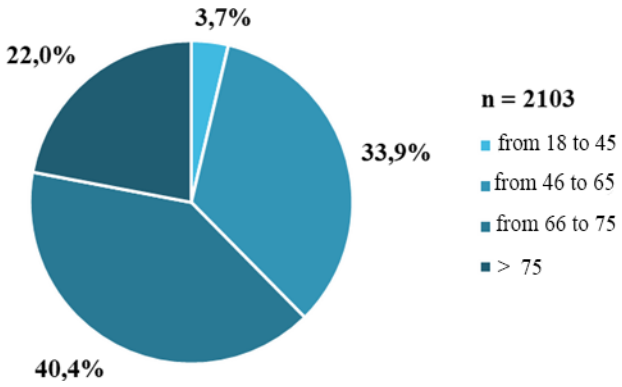


Figure 3. Distribution by age groups

IV.3.2. Clinical pathway (CP) upon admission

Patients were admitted under 74 clinical pathways, most commonly under **CP No. 175**: Surgical procedures on the small and large intestines, including diseases of the mesentery and retroperitoneum, with large and very large volume and complexity in persons over 18 years of age, under which 29.62% of patients were admitted during the period. The share of the next most common clinical pathway, **CP No. 160**, is more than twice as small: Surgical procedures on the small and large intestines, including diseases of the mesentery and retroperitoneum, with large and very large volume and complexity, in persons over 18 years of age, under which 13.12% of patients were admitted. This is followed by **CP No. 197**: Conservative treatment of acute abdominal diseases – with 9.37%; **CP No. 171**: Surgical procedures on the oesophagus, stomach and duodenum with high and very high volume and complexity in persons over 18 years of age – with 7.61%; **CP No. 156**: Surgical procedures on the oesophagus, stomach and duodenum with high and very high volume and complexity in persons over 18 years of age – with 4.56%; **CP No. 183**: Surgical procedures for hernias with incarceration – with 3.52%, and **CP No. 72.1**: Endoscopic and medical treatment for acute bleeding from the gastrointestinal tract in persons over 18 years of age – by 3.38% (Fig. 4). For 10 clinical pathways, the admission rate ranges from 1.05% to 2.33%. For 35 clinical pathways, the admission rate ranges from 2 (0.1%) to 20 (0.95%) patients. For 22 clinical pathways, one patient (0.05%) was admitted.

IV.3.3. CP upon discharge, with determination of the degree of coincidence

The number of CP at discharge is significantly lower than that at admission – 15 clinical pathways are registered (Fig. 5). Almost half of the patients – 46.55% – were discharged under **CP No. 175** *Surgical procedures on the pancreas and distal choledoch, with average volume and complexity*. Next is **CP No. 160** *Surgical procedures on the small and large intestine, including diseases of the mesentery and retroperitoneum with high and very high volume and complexity, in persons over 18 years of age* with 19.92%, and **CP No. 171** *Surgical procedures on the oesophagus, stomach and duodenum with high and very high volume and complexity in persons over 18 years of age* with 12.03% of discharged patients In a total of 1198 (56.97%) of 2103 admitted patients, there is a complete match between the CP at admission and the CP at discharge.

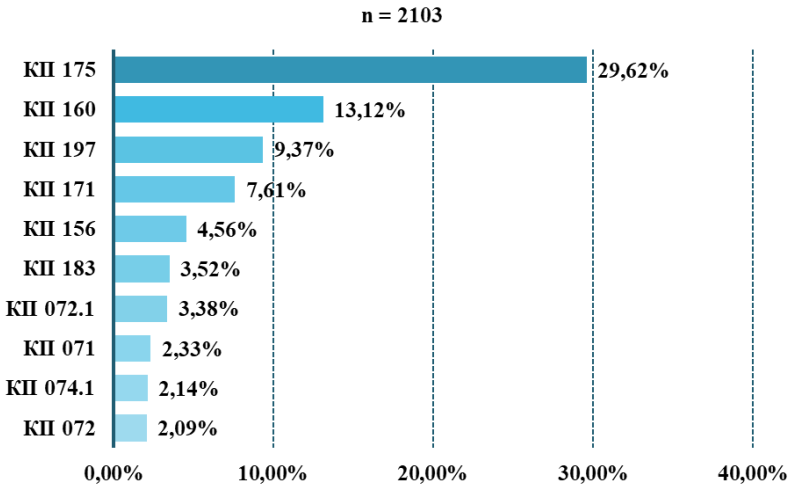


Figure 4. Top ten clinical pathways by frequency pathways at admission

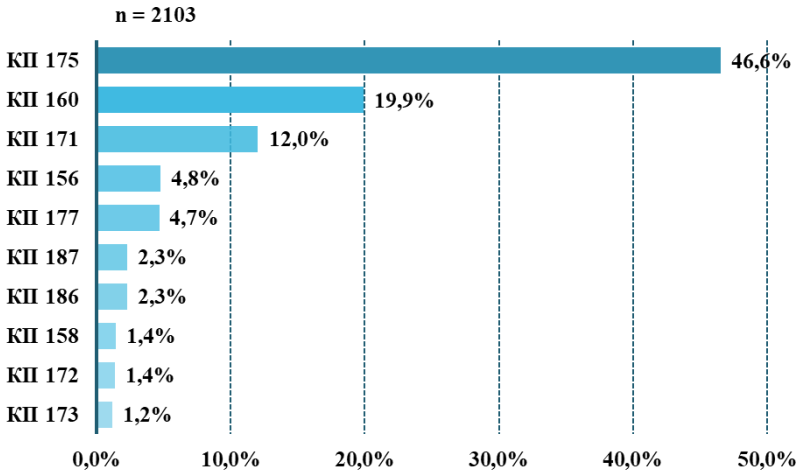


Figure 5. Top ten clinical pathways by frequency at discharge

IV.3.4. International Classification of Diseases (ICD) code at admission

The total number of diagnoses upon admission is 144. **C20** *Malignant neoplasm of the rectum* is the diagnosis with which the largest proportion of patients were admitted during the period – 15.22%. Next in line are those admitted with a diagnosis **of C18.7** *Malignant neoplasm of the sigmoid colon* – 9.03%. Those admitted with a diagnosis **of K56.6** *Paralytic ileus and intestinal obstruction without hernia* account for 7.94%, with **K62.5** *Haemorrhage from the anus and rectum* – 5.33%, with **C18.2** *Malignant neoplasm of the ascending colon* – 4.71, and with **C16.0** *Malignant neoplasm of the cardia of the stomach* – 4.14%. With diagnoses **C16.2** *Malignant neoplasm of the body of the stomach* and **C18.0** *Malignant neoplasm of the cecum*, 3.52% were admitted. There are two patients registered for 29 diagnoses (0.10%), and 50 diagnoses for which one patient is registered (Fig. 6).

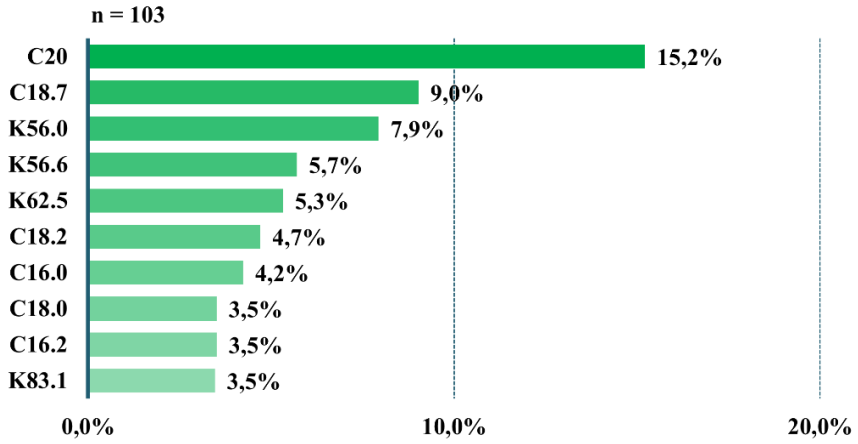


Figure 6. Top ten diagnoses by frequency, coded according to the International Classification of Diseases (ICD) upon admission

IV.3.5. International Classification of Diseases (ICD) code at discharge

The number of patients with diagnoses at discharge is 2055 (97.72%), while 48 (2.28%) patients have missing values. The number of diagnoses at discharge was 105. **C20** – *Malignant neoplasm of the rectum* was the main diagnosis at discharge, given to 19.42% of patients during the analysed period. The second most frequent diagnosis is **C18.7** *Malignant neoplasm of the sigmoid colon*, which has a relative share of 15.04%. The following diagnoses have significantly lower relative shares: **C18.0** *Malignant neoplasm of the cecum* – 6.86%, **C18.2** *Malignant neoplasm of the ascending colon* – 6.23%, **C16.3** *Malignant neoplasm of the antrum of the stomach* and **C18.4** *Malignant neoplasm of the transverse colon*, each with 4.48%, **C25.0** *Malignant neoplasms of the pancreas* – 3.65%, **C78.6** *Secondary malignant neoplasms of the retroperitoneum and peritoneum* – 3.36%, **C18.5** *Malignant neoplasm of the flexura coli lienalis* – 3.11%, and **C16.0** *Malignant neoplasm of the cardia of the stomach* – 3.02%. In 18 histological diagnoses, the frequency of patients is 2 people (0.10%), and in 41 – only one patient.

All ICD codes that represent symptoms and syndromes (**K56.0** *Paralytic ileus and intestinal obstruction, without hernia***; K56.6** Other unspecified intestinal obstruction; **K62.5** Haemorrhage from the anus and rectum; **K83.1** Obstruction of the common bile duct) are specified and refined at discharge and replaced with ICD codes from group **C** (Fig. 7).

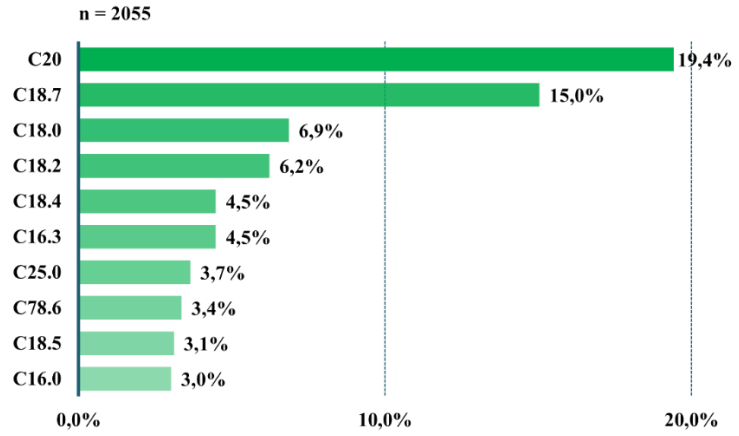


Figure 7. Top ten diagnoses by frequency, coded according to the International Classification of Diseases (ICD) at discharge

IV.3.6. Hospital mortality – relative share of deaths to admissions

Of the patients admitted during the period 2013-2023, 91.9% were discharged and 8.1% died.

Table 5. Relative proportions of discharged/deceased patients for the study period

Status	Number	Relative share (%)
Discharged	1933	91.9
Deceased	170	8.1
Total	2103	100.0

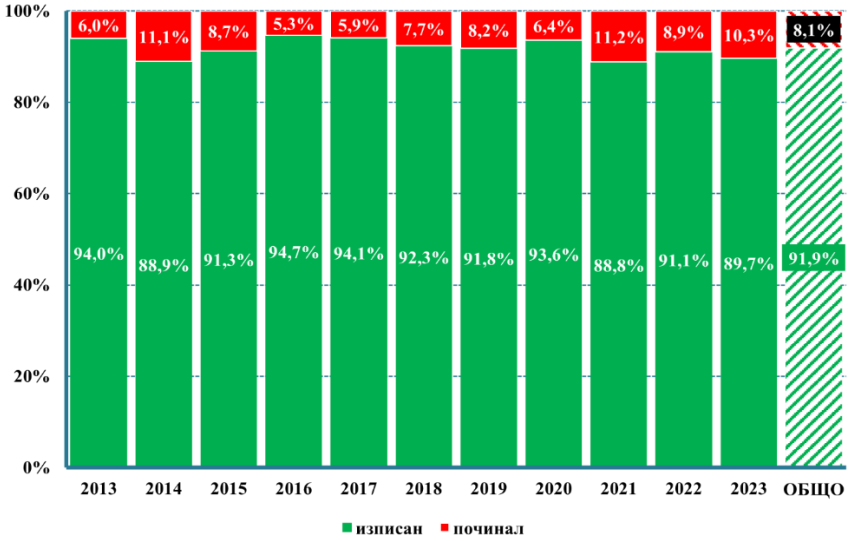


Figure 8. Proportion of discharged and deceased patients by year

IV.3.7. Comorbidities (CC) – ICD code, number of comorbidities diseases per patient

As already mentioned in the section on age parameters, over 62% of patients are over 66 years of age. For this reason, we decided to analyse comorbidity in the assessed population as a factor influencing the quality and effectiveness of surgical treatment.

91.87% of patients have at least one accompanying disease, with 261 diseases reported according to the ICD (Table 6).

The main accompanying disease is **I11.9** *Hypertensive heart without (congestive) heart failure*, which occurs in 22.62% of patients with accompanying diseases. The next most common diseases have more than twice lower rates: **D63.0** *Anaemia in neoplasms* with 8.13%, **C78.7** *Secondary malignant neoplasm of the liver* with 8.02%, **K56.6** *Other and unspecified intestinal obstruction* with 6.94%, **E11.9** *Non-insulin-dependent diabetes mellitus, without complications*, with 3.99%, and **C78.6** *Secondary malignant neoplasm of the retroperitoneum and peritoneum*, with 3.83%. For 145 underlying comorbidities, only one patient is reported.

74.4% of all patients have more than one comorbidity, with cases of 8 comorbidities (2.8%) also observed. **The average number of comorbidities is 3.11** (Fig. 9)**.** The total number of comorbidities in patients during the period 2013-2023 is 511. Table 7 presents comorbidities that occur in more than 1.0% of patients (or the minimum frequency is more than 20 patients) during the study period. This group includes 49 comorbidities (or 10.0%).

Table 6. Number of comorbidities per patient

Number of comorbidities	Number	Relative share (%)
1 (main)	1932	91.87
2	1565	74.4
3	1126	53.5
4	647	30.8
5	373	17.7
6	199	9.5
7	109	5.2
8	59	2.8
Total	6010	

Table 7. Absolute number of comorbidities and relative share recalculated based on the number of patients in the study (n = 2103), including the primary one (with a relative share above 1.0%) – the top 10 are marked in red

ICD code	Number	Relative share (%)		ICD code	Number	Relative share (%)
I11.9	1063	55.02		J44.9	29	1.50
E11.9	327	16.93		N18.8	29	1.50
D63.0	308	15.94		D12.5	27	1.40
C78.7	255	13.20		D12.8	26	1.35
Z98.8	226	11.70		Z99.8	25	1.29
K56.6	182	9.42		Z85.4	24	1.24
I11.0	155	8.02		Z43.3	23	1.19
I48	151	7.82		I25.0	22	1.14
C78.6	142	7.35		K43.9	22	1.14
I20.8	133	6.88		K83.1	22	1.14
I25.9	131	6.78		Z95.5	22	1.14
N40	75	3.88		K52.8	21	1.09
K65.0	69	3.57		K56.0	20	1.04
K29.5	61	3.16		K44.9	40	2.07
I69.3	58	3.00		K74.6	38	1.97
K81.1	58	3.00		K57.3	37	1.92
Z85.0	57	2.95		I25.8	35	1.81
K76.0	56	2.90		C77.2	34	1.76
K29.4	50	2.59		I25.2	33	1.71
K29.3	49	2.54		I67.9	32	1.66
C78.0	48	2.48		K62.5	32	1.66
K80.2	47	2.43		K56.4	31	1.60
K80.1	45	2.33		N20.0	31	1.60
I49.9	41	2.12		J44.9	29	1.50
K44.9	40	2.07		N18.8	29	1.50

Table 7. Continued

ICD code	Number	Relative share (%)		ICD code	Number	Relative share (%)
K74.6	38	1.97		D12.5	27	1.40
K57.3	37	1.92		D12.8	26	1.35
I25.8	35	1.81		Z99.8	25	1.29
C77.2	34	1.76		Z85.4	24	1.24
I25.2	33	1.71		N20.0	31	1.60
I67.9	32	1.66		K56.4	31	1.60
K62.5	32	1.66		Z43.3	23	1.19

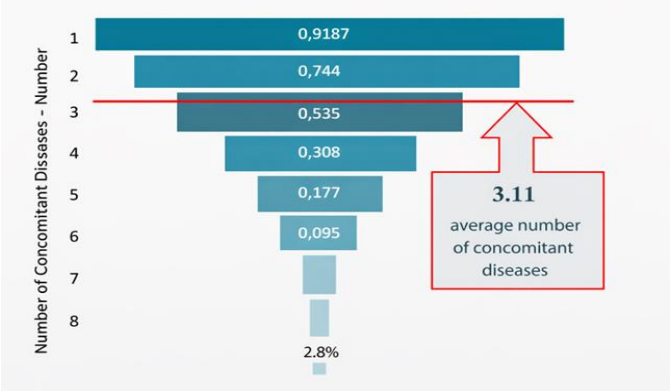


Figure 9. Average number of comorbidities per patient

I11.9 Hypertensive heart without (congestive) heart failure is the concomitant disease found in the highest proportion of patients – 55.02%. The following are next in relative terms: **E11.9** *Non-insulin-dependent diabetes mellitus, without complications* (16.93%), **D63.0** *Anaemia in neoplasms* (15.94%), **C78.7** *Secondary malignant neoplasm of the liver* (13.20%), **Z98.8** *Other specified conditions following surgery* (11.70%), **K56.6** *Other and unspecified intestinal obstruction* (9.42%), and the last accompanying disease in this group is **Z43.3** *Colostomy care* with 1.19%.

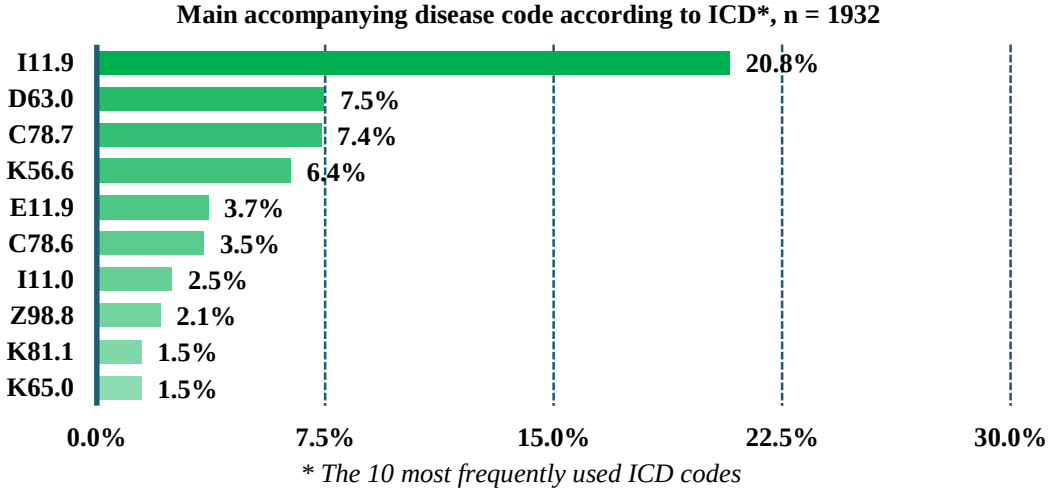


Figure 10. Graphical representation of the top 10 leading accompanying diseases

Table 8 presents all other comorbidities that occur in less than 1.0% of patients (or a minimum frequency of less than 20 patients) during the analysed period. This group includes 462 comorbidities (or 90.0%). For 250 comorbidities, the frequency is only one patient for the entire eleven-year period.

Table 8. Distribution of patients by concomitant disease, including the primary disease (with a relative share below 1.0%)

ICD code	Number	Relative share (%)
I50.1	19	0.98
J90, R18	18	0.93
B18.1, Z93.3	17	0.88
E78.8, I67.8, I84.2	16	0.83
E10.9, H40.9, K22.2, Z85.3	15	0.78
E11.4, I69.4	14	0.72
D12.3, I34.0, J45.9, Z90.4	13	0.67
C18.7, D13.4, E06.3, J44.8, K36, M10.99, N28.1, Z85.5, Z95.0	12	0.62
C79.5, D12.4, D62, I20.0, I44.7, K29.8, K86.1, N17.8, U07.1	11	0.57
C61, G20, I20.9, I26.9, I45.1, K21.0, K31.5, K42.9, K92.0	10	0.52
D12.6, D50.0, G45.1, K76.6, Z90.7	9	0.47
C79.6, I35.0, I50.0, K63.5	8	0.41
C79.1, D12.2, D63.8, E03.9, E04.2, E11.7, E11.8, I25.1, I36.1, I80.2, I84.9, K20, K63.1, K82.8, M17.9, Z85.8, Z86.0	7	0.36
B18.2, C79.8, D64.9, G63.2, I69.8, J42, J91, K21.9, K40.9, K52.0, K62.1, K66.0, K80.4, K80.5, K80.8, N18.9, Z87.4	6	0.31
C20, C34.1, C64, C77.8, C78.4, C78.5, D13.1, D27, G40.6, G45.0, I47.1, J18.9, K29.0, K31.7, K56.5, K92.1, L03.3, Z85.2, Z93.2	5	0.26
C18.0, C18.3, C78.8, D35.0, E04.9, F20.0, F33.9, I44.4, I45.0, I70.2, J45.0, K26.7, K29.9, K35.9, K61.0, K74.0, K75.0, L02.2, N11.8, N13.1, Z95.9	4	0.21
C16.2, C18.2, C77.1 E78.4, C79.7, D12.7, D13.2, D13.3, D18.0, D50.8, E10.8, H35.0, H40.8, I13.2, I35.1, I44.1, I49.8, I83.9, I84.1, I84.5, J93.8, J96.0, K25.7, K31.1, K51.2, K57.1, K65.8, K81.0, K83.0, M16.0, M17.0, N13.3, N17.9, R40.0, Z85.1, Z86.7, Z90.5, Z95.2	3	0.16
A41.8, C16.8, C18.6, C25.0, C34.3, C50.9, C73, C77.9, C78.1, C82.7, C91.1, D12.0, D39.1, D50.9, E11.0, E66.9, E78.2, E78.5, E90, F07.0, F31.9, F41.2, G30.9, G40.3, G93.4, H54.0, I10, I21.0, I26.0, I42.0, I80.3, I95.8, I95.9, I98.2, J12.8, J20.9, J47, J84.1, J86.9, J93.9, J95.2, J96.1, K22.6, K25.3, K26.3, K26.9, K31.6, K40.2, K51.3, K51.8, K55.0, K56.7, K62.7, K63.2, K66.1, K82.3, K85, L23.9, M16.9, M19.99, M81.99, N10, N13.2, N30.0, R16.1, R40.1, R57.1, R73.0, T90.5, Z43.2, Z86.1, Z87.3, Z95.1, Z95.8, Z98.0, Z99.2	2	0.10

Table 8. Continued

ICD code	Number	Relative share (%)
A41.9, B18.9, C15.8, C17.2, C18.5, C18.8, C19, C23, C24.1, C32.0, C34.0, C34.2, C38.3, C48.1, C48.8, C50.0, C54.1, C67.0, C67.2, C67.9, C77.0, C77.4, C77.5, C81.9, C90.0, C93.1, D01.0, D13.0, D17.1, D20.1, D22.9, D25.1, D25.9, D35.2, D46.2, D48.6, D56.1, D56.9, D68.8, D69.6, D73.8, E01.0, E03.8, E05.2, E06.9, E10.6, E10.7, E11.2, E11.3, E22.0, E44.0, E64.0, E66.8, E78.0, E78.3, E78.6, E78.9, F01.3, F03, F10.8, F29, F33.1, F33.4, F41.8, F45.0, F92.0, G25.5, G30.8, G40.8, G54.1, G80.9, G93.0, G96.8, H25.8, H25.9, H26.9, H33.2, H35.3, H35.7, H42.8, H44.2, H44.3, H47.2, H50.9, H54.1, H68.0, H81.4, H90.0, H90.6, H91.3, I07.1, I12.0, I13.1, I15.9, I21.9, I24.9, I25.4, I27.0, I35.2, I44.0, I44.2, I46.0, I46.1, I47.2, I63.0, I63.2, I63.3, I63.8, I63.9, I68.8, I69.0, I70.8, I70.9, I71.2, I71.4, I71.5, I74.1, I74.8, I80.0, I80.1, I83.2, I85.0, I85.9, I87.0, I89.0, I95.0, J15.8, J18.0, J30.4, J31.2, J32.4, J35.0, J38.0, J41.0, J43.9, J44.0, J44.1, J45.1, J45.8, J70.8, J86.0, J93.1, J95.4, J98.1, J98.3, K22.1, K22.8, K23.8, K25.1, K25.9, K29.1, K29.6, K29.7, K51.0, K51.9, K52.9, K56.1, K57.2, K57.5, K57.9, K58.9, K59.3, K61.3, K62.4, K62.8, K70.1, K70.3, K74.2, K76.7, K76.8, K80.0, K80.3, K83.4, K83.8, L02.3, L02.8, L40.9, L50.0, M02.39, M05.90, M06.09, M06.90, M06.99, M16.1, M16.6, M17.1, M17.4, M17.5, M19.29, M19.88, M45.0, M45.9, M46.00, M47.89, M47.92, M47.96, M47.99, M48.99, M51.0, M51.1, M51.2, M51.9, N05.0, N05.9, N08.3, N11.0, N11.1, N11.9, N13.9, N18.0, N20.2, N21.0, N30.2, N30.8, N31.0, N32.1, N80.1, N83.0, N83.2, Q05.9, Q61.3, R34, R45.1, R48.0, S01.0, S37.20, S72.00, S79.9, T78.4, T79.8, T80.1, T81.4, T92.9, T93.1, Z43.4, Z43.6, Z53.0, Z80.4, Z85.6, Z86.6, Z87.1, Z89.0, Z90.8, Z92.1, Z92.4, Z93.0, Z93.6, Z96.6, Z99.1, Z99.9	1	0.05

There is significant comorbidity in the analysed group of patients. Arterial hypertension is observed in 50% of patients, and type II diabetes mellitus in 16.9%.

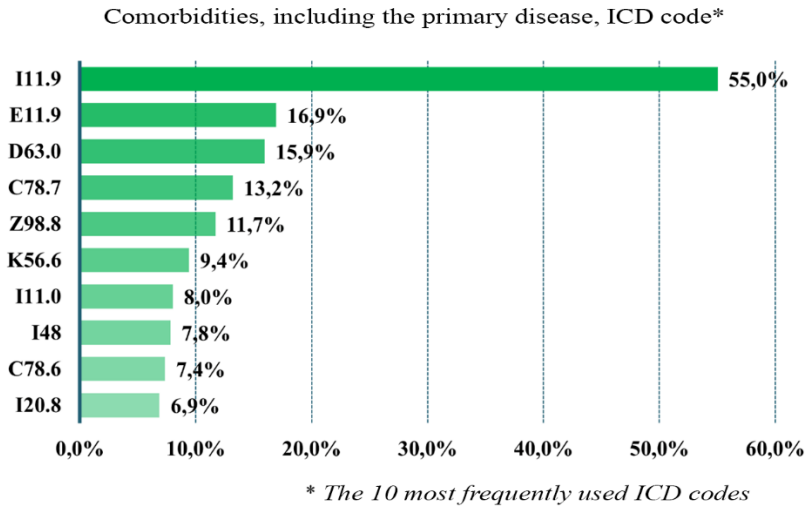


Figure 11. Total number of comorbidities

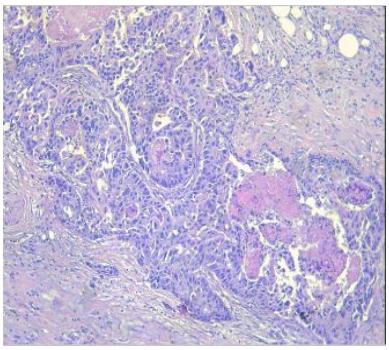
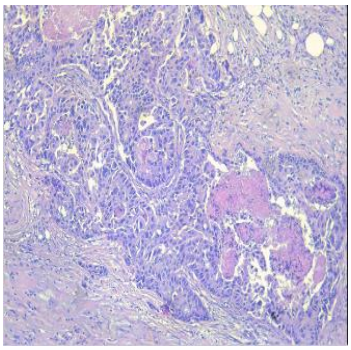
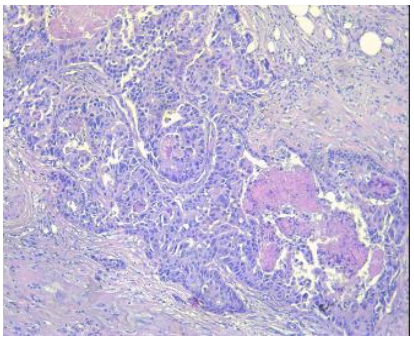
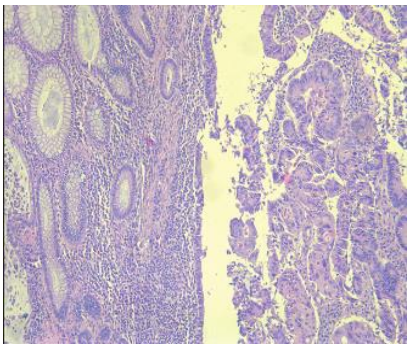
IV.3.8. Histological diagnoses (analysed using ICD codes)

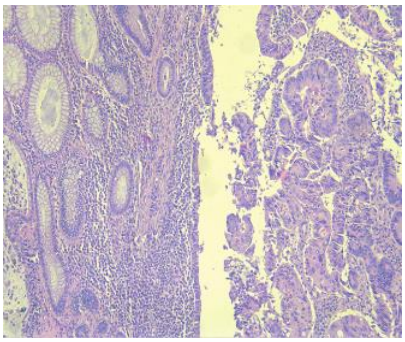
The results obtained in the histologically confirmed diagnosis section fully correspond to the data in section IV.3.7 (Table 6). There are 2,055 patients (97.72%) with verified histological diagnoses at discharge. Only 48 (2.28%) patients did not have a verified histological diagnosis or rather lacked data. The number of diagnoses at discharge was 105.

C20 *Malignant neoplasm of the rectum* is the main diagnosis at discharge, which was made in 19.42% of patients during the analysed period. The second most frequent diagnosis is **C18.7**, which has a relative share

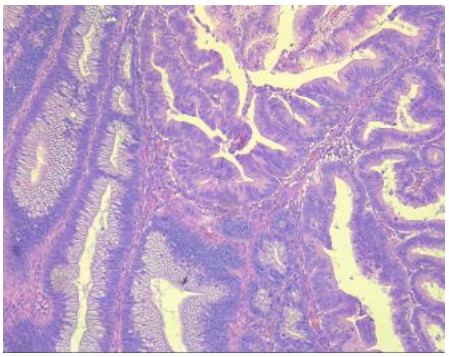
of 15.04%. The following diagnoses have significantly lower relative shares: **C18.0** – 6.86%, **C18.2** – 6.23%, **C16.3** and **C18.4** – 4.48% each, **C25.0** – 3.65%, **C78.6** – 3.36%, **C18.5** – 3.11%, and **C16.0** – 3.02%. In 18 histological diagnoses, the frequency of patients is 2 (0.10%), and in 41 – only one patient.

Table 9. Sample of morphological studies of biopsy material from the analysed patient population – 14 cases confirming histological verification

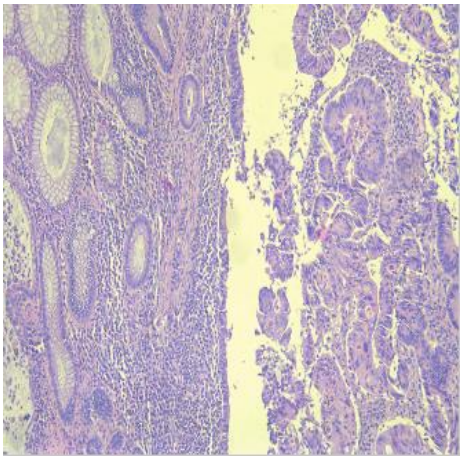
	
Morphological result: terminal ileum: small intestine mucosa with preserved villous structure with the inflammatory population typical for the location in the chorion, no signs of acute inflammation, no parasites, no dysplasia; transverse colon: polypoid material from the large intestine mucosa with superficial tubular glands with mild dysplasia; descending colon: polypoid material with tubular large intestine glands with mild dysplasia; rectum: multiple colonic fragments with villous glands with severe dysplasia, section with desmoplastic stroma. Diagnosis: Rectal adenocarcinoma. Tubular adenomas of the transverse and descending colon.	Macroscopic description: One specimen measuring 1.5/0.6/0.7 cm with an uneven surface, greyish-white in colour; one fragment covered with multilayered flat keratinising epithelium with pronounced acanthosis, intraepithelial lymphocytes, dysplasia in the lower third of the covering epithelium, an area with proliferation of nests and strands of atypical squamous cells penetrating in depth, superficial ulceration, areas with haemorrhages. Diagnosis: Squamous cell carcinoma.
	
Morphological result: material from a tumour formation in the large intestine with superficial ulceration and fibrinoid necrosis, represented by proliferating atypical cells forming irregular glandular and cribriform structures, infiltrating deeply into the wall and merging with the visceral peritoneum, presence of necrotic material in part of the lumens of the irregular structures, as well as necrotic areas with focal calcium deposits, perineural invasion, atypical cells in cleft-like spaces with erythrocytes in them, stroma with pronounced desmoplastic reaction and lymphoplasmacytic infiltration; material from the colon wall with superficially desquamated epithelium, lymphoplasmacytic infiltration in the chorion, hyperemic vessels, focal haemorrhages, no involvement of the tumour process; five lymph nodes with sinus histiocytosis and focal lipomatosis, no metastases. Diagnosis: adenocarcinoma of the colon with a single tumour deposit in the peritoneal fat tissue, no metastases in the 5 lymph nodes examined, pT4a pN1c, low grade (G2), Pn1, V1.	Morphological result: sigmoid colon: Colonic wall with tumour invasion by well-differentiated tumour glands with mucous secretion in the lumen: depth of invasion – in the mesenteric adipose tissue, without involvement of the visceral peritoneum, clean resection lines, 13 LY without tumour metastases. Diagnosis: colon adenocarcinoma, pT3 N0 R0 G1, V1. Diagnosis: Large intestine adenocarcinoma, pT3 N0 R0 G1



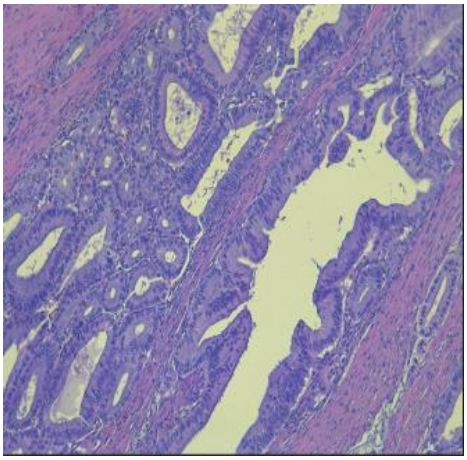
Morphological result: Material from the colon with a proliferating tumour formation, represented by small malignant acini, lined with atypical cells with hyperchromic nuclei, some with prominent nucleoli, forming cribriform structures, infiltrating the wall and peritoneal fat tissue, areas of necrosis, tumour emboli, lymphoplasmacytic infiltration in the stroma, tumour deposits in the peritoneal fat tissue, a total of ten lymph nodes, one of which has metastasis from the tumour process. Resection line without invasion by the tumour process
Diagnosis: Moderately differentiated adenocarcinoma of the colon; pT3 N1c Mx G2 L1 R0



Morphological result: polypoid formation of the colon, as well as fragments thereof with proliferating atypical cells forming villous and tubular structures with areas of stratified epithelium of cells with hyperchromic nuclei, in places reaching the lumen of the glands, areas with destruction of the basement membrane and fusion of glands, involvement of the resection line of the leg by the tumour process;
Diagnosis: Morphological picture of: tubulovillous adenoma of the colon with severe dysplasia and foci of intramucosal carcinoma, without possibility of assessing submucosal invasion due to lack of submucosa. Tubulovillous adenoma of the colon with foci of severe dysplasia at a clean resection line.

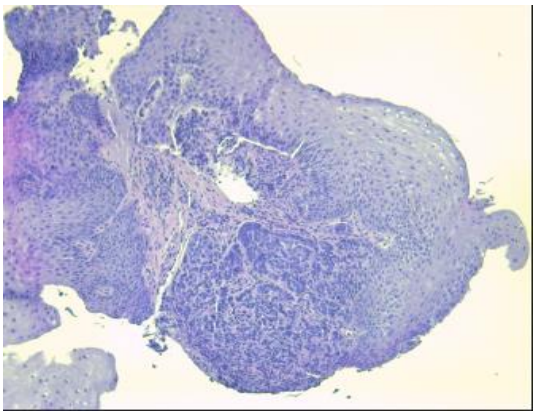


Morphological result: Material from the colonic mucosa with proliferating atypical acini with destroyed basement membranes, lined by atypical cells with hyperchromatic nuclei, some with prominent nucleoli, located among desmoplastic stroma, areas of necrosis, lymphoplasmic infiltration in the stroma, mixed with neutrophilic leukocytes. Material from polypoid proliferating colonic mucosa, represented by tubular structures lined by stratified epithelium, areas of reduced or increased mucus formation and lymphoplasmacytic infiltrate in the stroma mixed with eosinophilic leukocytes
: Moderately differentiated adenocarcinoma of the colon; G2



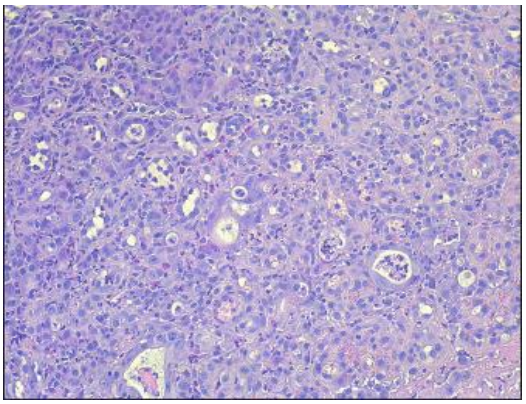
Morphological result: proximal small bowel resection line without involvement by the tumour process; distal colon resection line without involvement by tumour process; colon with tumour formation of proliferating malignant intestinal-type glands with focal extracellular mucus production, invasion into the submucosa, muscle layer of the wall and subserosal fatty tissue by the tumour process, desmoplastic stroma with sparse lymphocytic stromal reaction (intermediate budding Bd2);

Diagnosis: Morphological picture of adenocarcinoma of the colon without metastasis in one examined lymph node. pT3N0, G2, Bd2



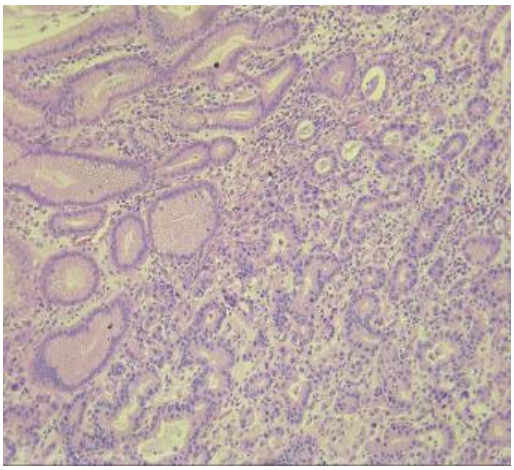
Morphological result: biopsy material, antrum, shortened and slightly deformed pit layer, slight separation of the glandular layer, edematous lamina propria with mild to moderate lymphoplasmacytic inflammatory infiltrate, HP (-); punch material, oesophagus, squamous epithelial lining with dysplasia and associated infiltrative tumour process, represented by squamous cells with nuclear hyperchromasia, mitoses, very focal desmosomes, infiltrative growth present, focus with ulceration, underlying granulation tissue.

:



Morphological result: three materials from a punch biopsy of the gastric mucosa with ulceration and focal proliferation of atypical polymorphic cells forming glands, nests and single infiltrating cells among desmoplastic stroma with mixed inflammatory infiltrate, vascular congestion.

Diagnosis: morphological picture of intestinal-type adenocarcinoma of the stomach.



M

orphological result: stomach wall with tumour formation,

c

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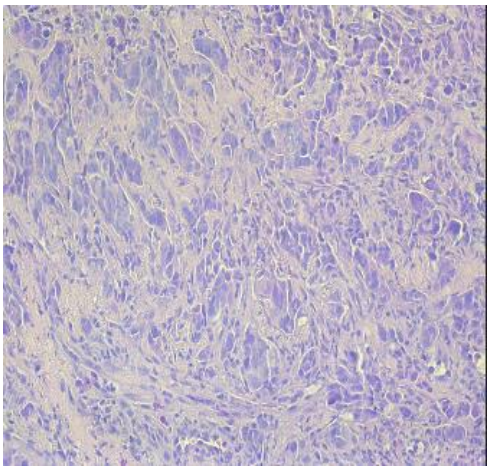
p

o**Moderately differentiated adenocarcinoma of the stomach, pT1bN2Mx, G2. Metastases in 3 of the 13 l**ymph nodes examined

d

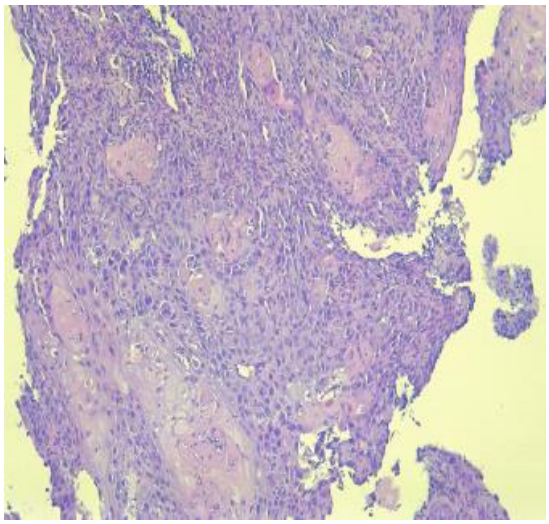
o

f



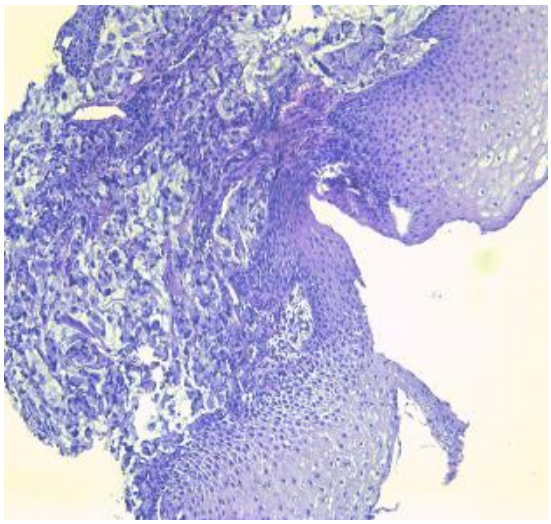
Morphological result: biopsy material from the antral mucosa, relatively preserved architecture, sparse inflammatory infiltrate in the chorion (mainly plasma cells), HP (-) biopsy material, two fragments, one lined with dysplastic squamous epithelium and underlying glands lined with atypical pseudostratified cells with hyperchromatic slightly elongated nuclei, mitoses in places; second fragment, consisting entirely of desmoplastic stroma and solid nests of atypical tumour cells of varying sizes located within it, multiple mitoses, including atypical ones, focal abortive gland formation

, HP (-). Morphological picture of adenocarcinoma.



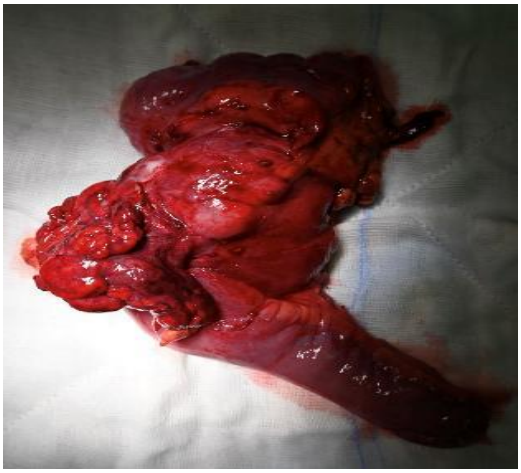
Morphological result: biopsy material consisting of a fragment of gastric mucosa and several fragments consisting of tumour nests of squamous atypical cells with high mitotic activity and necrotic foci

: Morphological picture of squamous cell carcinoma.

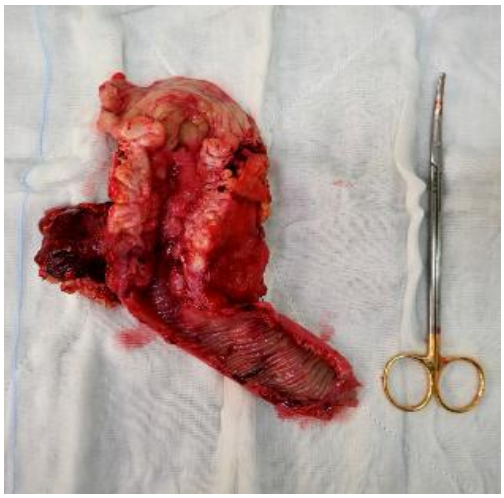


Morphological result: fragmented material with squamous epithelial lining, fragment with granulation tissue, in most fragments, an invasive tumour process is established subepithelially, represented by glandular elements or individually located atypical cells with enlarged hyperchromic nuclei and abundant cytoplasm (some with signet ring morphology), abundant mucin lakes, stromal reaction
: Adenocarcinoma with signs of mucus formation

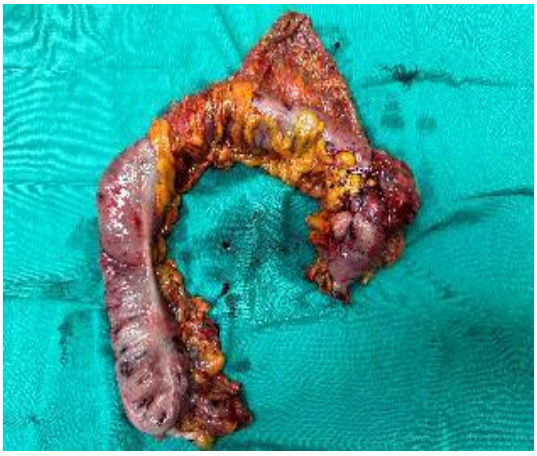
Image 3. Macroscopic preparations



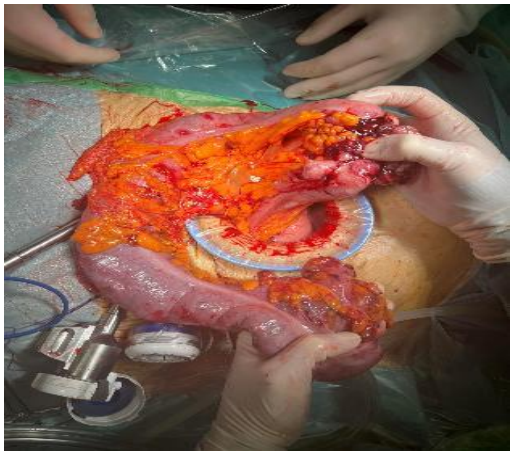
Resected specimen from right hemicolectomy - tumour formation of the caecum



Transected resection specimen after right hemicolectomy - tumour formation of the caecum

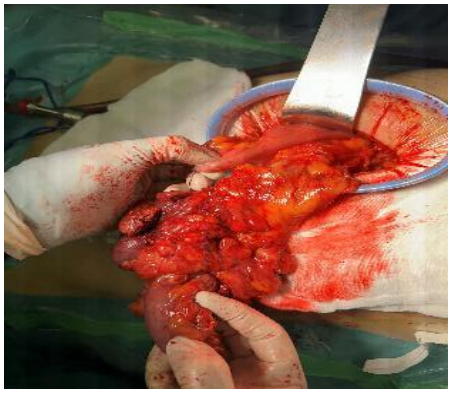


Resected specimen after extended right hemicolectomy - tumour formation in the middle third of the transverse colon

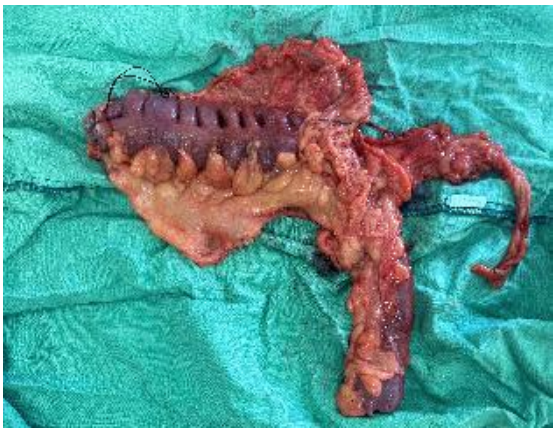


Extraction of specimen through upper-middle minilaparotomy after robotic extended right hemicolectomy

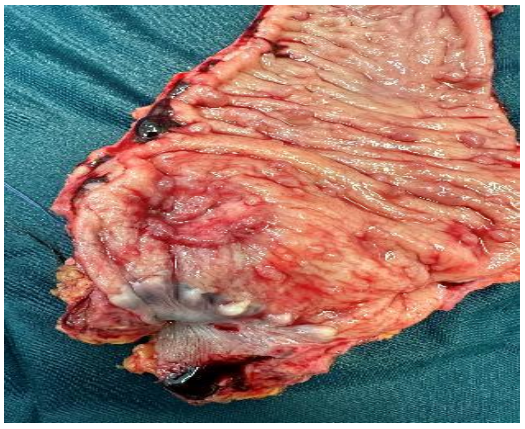
Port placement during laparoscopic right hemicolectomy



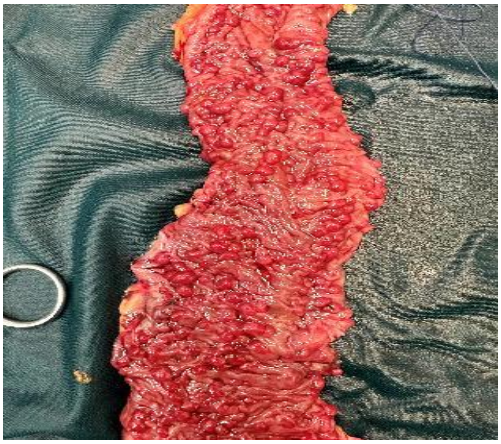
Extraction of specimen after right hemicolectomy through midline minilaparotomy



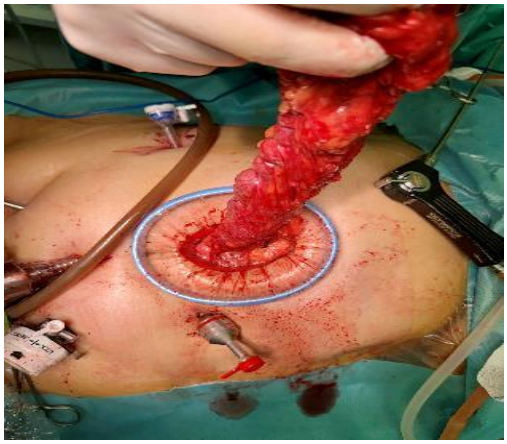
Specimen after left hemicolectomy



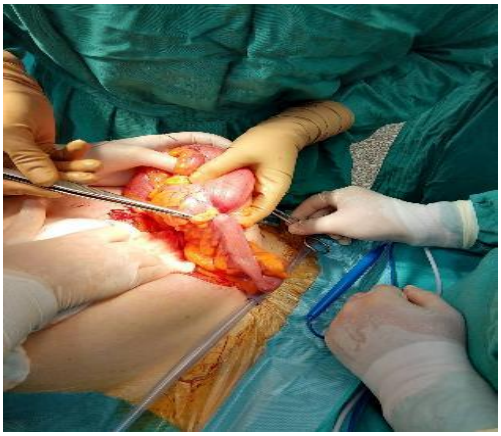
Specimen after rectal extirpation. A 1 cm tumour formation in the anorectal line and rectal polyposis are visible.



Macroscopic view of an open specimen - polyposis of the colon in a patient with familial adenomatous polyposis.

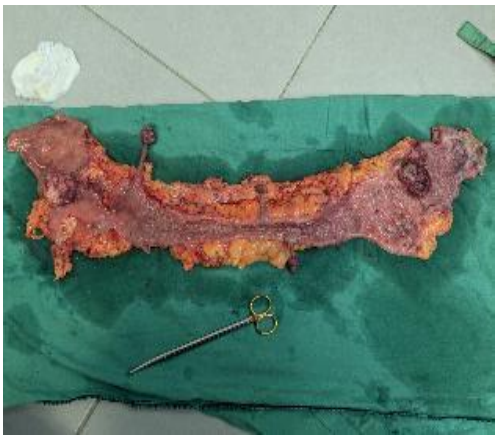


Extraction of specimen after right hemicolectomy through midline minilaparotomy.

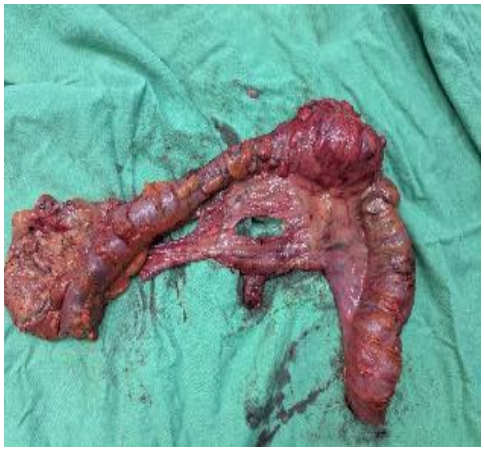


Extraction of specimen after right hemicolectomy through midline minilaparotomy. Visible stenosing tumour in the area of the Bauhin valve.

Macroscopic view of an open specimen - polyposis of the large intestine in a patient with familial adenomatous polyposis.



Transected specimen from the small intestine. Pseudotumour infiltration in the intestinal wall is observed.



Specimen after left hemicolectomy for sigmoid carcinoma.

IV.3.9. Admission – planned or emergency

64.6% of admissions were planned, while 34.4% were urgent to varying degrees, most commonly with an urgency of up to 6 hours or 27.5% (Table 10, Fig. 12).

Table 10. Distribution by type of admission – planned or emergency

Admission	Number	Relative share (%)	Cumulative share (%)
Planned	1359	64.6	64.6
Urgent after 24 hours	65	3.1	67.7
Urgent within 24 hours.	91	4.3	72.0
Urgent within 12 hours	10	.5	72.5
Urgent within 6 hours	578	27.5	100.0
Total	**2103**	**100.0**	

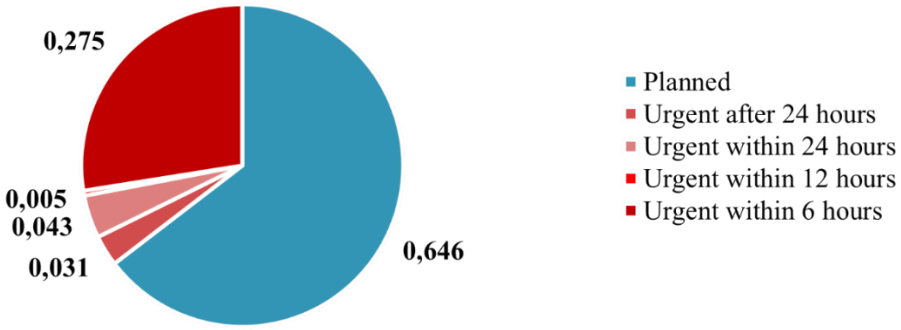


Figure 12. Graphical representation of the type of admission

IV.3.10. Hospital stay measured in bed days – by gender, age, ICD

The average number of bed days is 10.65 (SD = 5.902), the median is 9, and the mode is 7 (in 20.2% of patients). The minimum stay is 1 bed day (0.2%), and the longest is 70 bed days (0.05%).

There is almost no difference in the average number of bed days depending on the gender of the patient: for men, the average is 10.70 (SD = 6.259), and for women, it is 10.58 (SD = 5.352).

With regard to age groups, there are minimal differences in the average number of bed days. The highest value is in the "over 75" group, which is 11.29 (SD = 6.661), and is one day higher than in the other groups. The lowest value is found in the "18-45 years" group. The coefficients of variation in the four age groups are similar, ranging from 53.6 to 59.0%.

Table 11. Hospital stay measured in bed days by age group

Age	Number	Average	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation
from 18 to 45	78	10.26	5.497	2	43	53.6
from 46 to 65	712	10.61	5.948	1	66	56.1
from 66 to 75	850	10.38	5.425	1	53	52.3
over 75	463	11.29	6.661	1	70	59.0
Total	2103	10.65	5.902	1	70	55.4

For the most common admission diagnosis (**C20** *Malignant neoplasm of the rectum*), the average number of bed days is 8.95 (SD = 5.150), which is below the average for the analysed period (10.65 bed days). For the second most common admission diagnosis (**C18.7** *Malignant neoplasm of the sigmoid colon*), the average is also lower – 8.96 bed days (SD = 3.862). Higher values for the average number of bed days are reported for diagnoses with a small number of patients for the period, such as **C15.2**, where the average is 33.50 bed days, but only 2 patients were admitted with this diagnosis. Diagnoses **K92.1** and **K29.4**, which have 15 and 30 admitted patients, also show higher values, with 17.27 bed days and 15.73 bed days. A lower than average number of bed days is also observed for diagnoses with a small number of admitted patients. The coefficient of variation ranges from 4.6% (for C16) to 133.0% (for C15.2). The diagnosis with the highest number of admissions (C20) has a coefficient of variation of 57.5%.

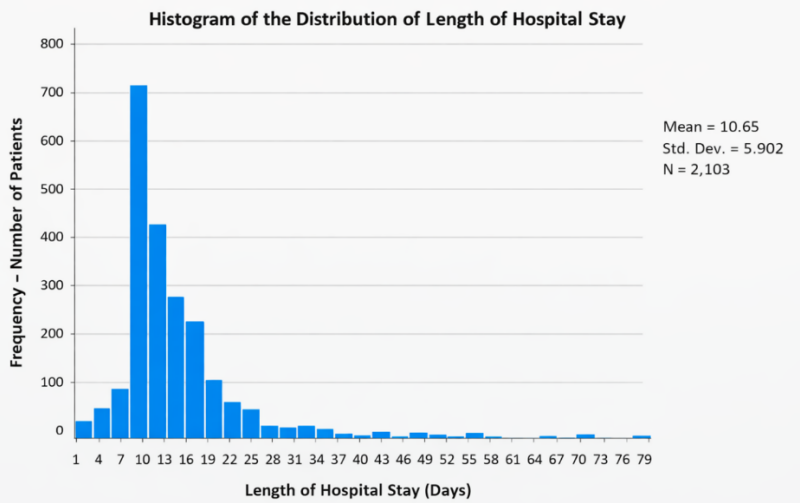


Figure 13. Histogram of hospital stays

The leading diagnosis with the highest number of patients is **C20**, with an average number of bed days of 9.42 (SD = 5.361), which is lower than the average for the entire population during the analysed period. Similarly, for the next most common leading diagnosis, the average value is 9.96 (SD = 6.279). Above-average bed days are again observed for diagnoses with few patients or isolated cases. The coefficient of variation for the most common leading diagnosis (**C20**) is 56.9%, with the highest degree of dispersion observed in **C16.5**, where the coefficient of variation is 103.7%.

In the histological diagnosis with the largest number of patients (**C20**), the mean value of the bedside score is 9.42 (SD = 4.435), while in the next largest group (patients with histological diagnosis – **C18.7**, the average value is 9.99 (SD = 4.411). Higher averages for bedridden patients are found in diagnoses with fewer patients (usually from 1 to 9). Higher values are also observed in some histological diagnoses with more than 10 patients, for example in **C16.4** (12 patients) – 16.42 (SD = 8.586) bed days, **K81.1** (12 patients) – 14.83 bed days (SD = 5.474), **C24.0** (14 patients) – 14.79 bed days (SD = 7.343). The coefficient of variation is high for diagnoses such as **D12.3** (108.1%), **Z03.1** (107.9%), **C16.5** (103.7%) (Table 12), and for the most frequently used histological diagnosis (**C20**), it is 47.1%.

IV.3.11. Admitted diagnoses – ICD code

The results are identical to those in section IV.3.4.

The total number of diagnoses upon admission is 144. The total number of diagnoses upon admission is 144. **C20** *Malignant neoplasm of the rectum* is the diagnosis with which the largest proportion of patients were

admitted during the period – 15.22%. Next in line are those admitted with a diagnosis **of C18.7** *Malignant neoplasm of the sigmoid colon* – 9.03%. Those admitted with a diagnosis of K56.6 *Paralytic ileus and intestinal obstruction without hernia* account for 7.94%, with **K62.5** Haemorrhage from the anus and rectum – 5.33%, with **C18.2** *Malignant neoplasm of the ascending colon* – 4.71, and with **C16.0** *Malignant neoplasm of the cardia of the stomach* – 4.14%. With diagnoses **C16.2** *Malignant neoplasm of the body of the stomach* and **C18.0** *Malignant neoplasm of the cecum,* 3.52% were admitted. There are two patients registered with 29 diagnoses (0.10%), and 50 diagnoses with one patient registered.

IV.3.12. Leading diagnoses – ICD code

There were 53 leading diagnoses. Almost one in four patients (23.40%) had a leading diagnosis of C20. Next, with 15.36% of the leading diagnoses, was C18.7, and third was C18.0 with 7.13%. The leading diagnosis C18.2 was assigned to 6.47%, C16.3 to 4.85%, C18.4 to 4.66%, and C25.0 to 4.37%. Of all leading diagnoses, there are 12 with a frequency of one patient for the entire period, as well as 6 with two patients each.

Table 12. Hospital stay (bed days) according to the leading diagnosis

ICD code	Number	Mean	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation (%)
C15.0	1	10.0		10	1	
C15.1	2	7.50	4.950	4	11	66.0
C15.3	2	4.50	3.536	2	7	78.6
C15.4	5	7.40	4.037	3	14	54.6
C15.5	30	13.13	9.468	2	50	72.1
C15.8	5	14.40	8.706	5	23	60.5
C15.9	2	8.00	0.0	8	8	
C16.0	76	12.45	9.908	3	65	79.6
C16.0[D63.0]	1	7.00		7	7	
C16.1	3	7.33	2.517	5	10	34.3
C16.2	47	11.04	7.074	5	40	64.1
C16.3	102	11.80	4.254	5	30	36.0
C16.4	14	15.29	8.407	7	39	55.0
C16.5	16	12.31	12.774	5	54	103.7
C16.6	8	12.38	5.069	7	22	41.0
C16.8	77	11.45	4.453	5	24	38.9
C16.9	1	8.00		8	8	
C17.0	7	9.71	3.546	6	16	36.5
C17.1	8	11.38	3.543	7	18	31.1
C17.2	8	8.75	2.188	7	13	25.0
C17.3	1	14.00		14	14	
C17.8	1	8.00		8	8	
C17.9	1	14.00		14	14	
C18.0	150	10.54	6.279	1	70	59.6

Table 12. Continued

ICD code	Number	Mean	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation (%)
C18.1	1	7.00		7	7	
C18.2	136	10.15	4.366	3	41	43.0
C18.3	61	10.57	3.263	6	20	30.9
C18.4	98	10.68	4.553	3	32	42.6
C18.5	67	11.75	7.102	2	47	60.5
C18.6	52	9.62	3.951	2	26	41.1
C18.7	323	9.96	4.699	1	43	47.2
C18.8	11	9.91	4.061	3	17	41.0
C19	61	9.69	5.658	2	45	58.4
C20	492	9.42	5.361	0	66	56.9
C21.0	4	3.75	1.258	2	5	33.6
C21.1	6	7.33	4.633	3	16	63.2
C21.8	3	8.00	1.00	7	9	12.5
C22.0	48	11.98	8.073	4	50	67.4
C22.1	3	14.33	4.041	10	18	28.2
C22.2	2	9.50	7.778	4	15	81.9
C22.3	1	11.00		11	11	
C22.4	1	11.00		11	11	
C22.7	1	19.00		19	19	
C22.9	2	7.00	1.414	6	8	20.2
C23	17	10.18	3.972	2	16	39.0
C24.0	24	14.83	6.485	6	33	43.7
C24.1	3	13.33	5.774	10	20	43.3
C24.8	1	15.00		15	15	
C25.0	92	14.15	7.127	4	53	50.4
C25.1	15	10.87	2.722	6	15	25.0
C25.2	2	16.00	12.728	7	25	79.5
C25.8	7	15.29	10.012	7	35	65.5
C25.9	1	20.00		20	20	
Total	2103	10.65	5.902	0	70	55.4

IV.3.13. Match between admission and discharge diagnoses

Table 13 presents the degree of correspondence between admission diagnoses and discharge diagnoses according to the ICD using the "Top 10" rule in absolute values

Table 13. Degree of correspondence between admission diagnoses and discharge diagnoses according to ICD – analysis of the top 10

Admission			Admission		
ICD code	**Number**	**Relative share (%)**	**ICD code**	**Number**	**Relative share (%)**
C20	320	15.22	C20	492	23.40
C18.7	190	9.03	C18.7	323	15.36
K56.0	167	7.94	C18.0	150	7.13
K56.6	120	5.71	C18.2	136	6.47
K62.5	112	5.33	C16.3	102	4.85
C18.2	99	4.71	C18.4	98	4.66
C16.0	89	4.24	C25.0	92	4.37
C16.2	74	3.52	C16.8	77	3.66
C18.0	74	3.52	C16.0	76	3.61
C18.4	59	2.81	C18.5	67	3.19

An analysis of the top 10 diagnoses in both groups reveals a coincidence of only 50%, with the discrepancy being both qualitative and quantitative. The discrepancies in all groups are significant.

IV.4. STAGING ACCORDING TO THE TNM CLASSIFICATION

No TNM data were reported for the period from 2013 to 2015. The number of patients during this period was 579.

For the period from 2016 to 2023, the number of patients was 1,524, of whom 1,068 (70.01%) had data on staging according to the TNM classification. For the entire period, 567 categories of tumour staging according to the TNM classification were observed. For 11 patients, a "non-standard" or "unidentified" category is specified.

448 (79.01% of all) of the TNM classification configurations are unique (occur individually) and account for 41.948% of patients with TNM data.

Several categories with higher frequencies were also identified:

– $T_3\ N_x\ M_0$ occurs in 39 patients (or 0.937% of those with TNM);
– $cT_3\ N_1\ M_0$ occurs in 32 patients (2.999%);
– $cT_3\ N_0\ M_0$ was found in 28 patients (2.624%);
– $cT_3\ cN_x\ cM_0$ occurs in 21 patients (1.968%);
– $T_4\ N_x\ M_0$ occurs in 18 patients (1.687%);
– $cT_2\ N_0\ M_0$ and p $T_3\ N_x\ M_0$ have a frequency of 15 patients (1.406% share for each of the two configurations).

Table 44 presents the summary results for configurations with a frequency of 39 to 4 patients.

Table 14. Distribution of patients according to TNM classification

TNM classification	Number	Relative share (%)	Valid relative share (%)
Non-standard / unidentified	11	0.523	1.030
T3 Nx M0	39	1.854	3.652
c T3 N1 M0*	32	1.522	2.996
c T3 N0 M0	28	1.331	2.622
cT3 cNX cM0	21	0.999	1.966
T4 Nx M0	18	0.856	1.685
c T2 N0 M0	15	0.713	1.404
p T3 Nx M0*	15	0.713	1.404
T3N0M0	12	0.571	1.124
T3NxMx	12	0.571	1.124
c T2 Nx M0	11	0.523	1.030
c T3 N2 M0	11	0.523	1.030
cT3 cN0 cM0	11	0.523	1.030
T2N0M0	11	0.523	1.030
c T4 N2 M0	10	0.476	0.936
p T3 N0 M0	10	0.476	0.936
T2 Nx M0	10	0.476	0.936
p T3 N1 M0	9	0.428	0.843
T3NxM0	9	0.428	0.843
T3 N0 M0	8	0.380	0.749
T3N1M0	8	0.380	0.749
c T3 Nx M0	7	0.333	0.655
cT3 cN2 cM0	7	0.333	0.655
pT3 pN0 cM0	7	0.333	0.655
T4N1M1	7	0.333	0.655
T3 N1 M0	6	0.285	0.562
T3NxM1	6	0.285	0.562
T3N0M0	6	0.285	0.562
c T3 N1 Mx	5	0.238	0.468
c T4 N1 M0	5	0.238	0.468
c T4 N1 M1	5	0.238	0.468

Table 14. Continued

TNM classification	Number	Relative share (%)	Valid relative share (%)
cT2 cN0 cM0	5	0.238	0.468
cT3N0M0	5	0.238	0.468
p T2 Nx M0	5	0.238	0.468
pT3 pN1b cM0	5	0.238	0.468
T1 Nx M0	5	0.238	0.468
T3N1Mx	5	0.238	0.468
c T3 N1 M1(hep)	4	0.190	0.375
c T4 N1 M1hep	4	0.190	0.375
cT3 cN1 cM0	4	0.190	0.375
cT4 cNX cM0	4	0.190	0.375
p T2 N1 M0	4	0.190	0.375
pT2 pNX cM0	4	0.190	0.375
pT3 pN1a cM0	4	0.190	0.375
pT3 pNX cM0	4	0.190	0.375
T1N0M0	4	0.190	0.375
T2-3N1Mx	4	0.190	0.375
T4N2M0	4	0.190	0.375
T4N1M1	4	0.190	0.375
T2N0M0	4	0.190	0.375
Configurations with frequency 3 patients	78	3.709	7.303
Configurations with frequency 2 patients	88	4.184	8,240
Configurations with frequency 1 patient	44	21,303	41,948
Total TNM	106	50.785	100.0
Without TNM	1035	49.215	
Total	2103	100.00	

***Note:** Staging can be "clinical" or "pathological". Clinical staging is based on the results of tests performed prior to surgery, such as physical examination and imaging studies. Pathological staging is generally performed during surgery. Clinical staging is indicated by a lowercase letter **"c "**before the TNM classification. Pathological staging is indicated by a lowercase letter "**p**".

The configurations with 3 patients include 78 patients, with the total relative share of this group being 3.709% of all patients and 7.303% of patients with TNM classification data. The proportion of a single configuration is 0.143% of all patients or 0.281% of patients with TNM. The group of three patients includes a total of 27 different configurations according to the classification.

The configurations with two patients include 88 patients, with the total relative share of this group being 4.184% of all patients and 8.247% of patients with TNM classification data. The share of a single configuration is 0.095% of all patients or 0.187% of patients with TNM. The group with two patients includes a total of 44 different configurations according to the classification.

The configurations with 1 patient include 448 patients, with the total relative share of this group being 21.303% of all patients and 41.948% of patients with TNM classification data. The share of a single configuration is 0.048% of all patients or 0.094% of patients with TNM. The group with one patient includes a total of 448 different configurations according to the classification.

There is enormous dispersion and diversity in the coding according to the TNM classification.

IV.4.1. Criterion T – tumour size

There are 1,057 patients (50.3%) for whom data on tumour size is available, with no tumour formation found in 8 patients. The highest relative proportion is among patients with T3, who account for 55.3% of those for whom data is available, followed by patients with T4, who account for 25.2%, patients with T2 – 14.9%, and the lowest proportion of patients with established tumour size are those in T1, who account for 3.9%.

Table 15. Distribution of patients by tumour size (T)

T – tumour size	Number	Relative share	Valid relative share (%)	Cumulative proportion
T0	8	0.4	0.8	0.8
T1	41	1.9	3.9	4.6
T2	157	7.5	14.9	19.5
T3	585	27.8	55.3	74.8
T4	266	12.6	25.2	100.0
Total with data for T	1057	50.3	100.0	
No data for T	1046	49.7		
Total	2103	100.0		

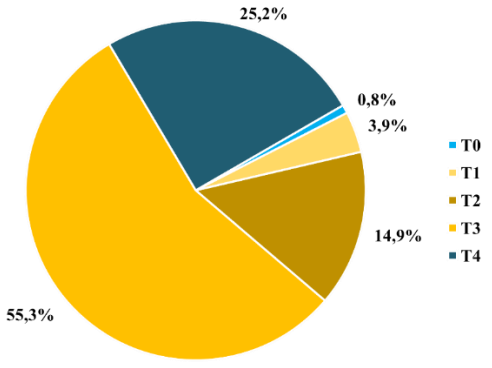


Figure 14. Distribution of patients by tumour size (T) (n = 1057)

Combining the distribution by T and gender of patients yields the following results:

– patients with T_0 are distributed equally between the two genders;

– 56.1% of patients with T1 are men and 43.9% are women;

– 61.1% of patients with T2 are men and 38.9% are women;

– 63.2% of patients with T3 are men and 36.8% are women;

– 60.5% of patients with T4 are men and 39.5% are women.

Male patients are distributed by T as follows:

– 0.6% with T_0 ;

– 3.5% with T1;

– 14.7% with T2;

– 56.6% with T3;

– 24.6% with T4.

Female patients are distributed by T as follows:

– 1.0% with T_0 ;

– 4.5% with T1;

– 15.1% with T2;

– 53.3% with T3;

– 26.1% with T4.

The average age is lowest among patients with T4 (65.60 years) and highest among patients with To (69.13 years). In all categories, the T-coefficient of variation has low values.

Table 16 shows the relationship between absolute frequencies (number of patients) according to diagnosis at admission and diagnosed tumour size.

Table 16. Relationship between tumour size (T) and patient age

T – tumour size	Number	Mean	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation (
T0	8	69.13	2.900	65	75	4.2
T1	41	66.73	10.630	46	86	15.9
T2	157	67.11	9.578	30	86	14.3
T3	585	68.26	9.753	28	92	14.3
T4	266	65.60	10.285	29	94	15.7
Total	1057	67.37	9.916	28	94	14.7

Table 17 presents the absolute frequencies (number of patients) according to the leading diagnosis and the diagnosed tumour size. This analysis also reveals a similar trend – all final diagnoses in the "Top 10" have an **ICD-C** code, with the top 3 being **C20** *Malignant neoplasm of* the rectum; **C18.7** *Malignant neoplasm of the sigmoid colon* and **C18.2** *Malignant neoplasm of the ascending colon.* In addition, the number of patients with these diagnoses is increasing, and staging shows a deterioration in the T3 and T4 parameters.

Table 17. Relationships between tumour size (T) and diagnosis at admission – "Top ten"

ICD code	T – tumour size					(n)
	T0	T	T2	T3	T4	Total
C20	4	8	35	127	41	215
C18.7	0	5	18	73	20	116
K56.6	1	2	6	45	17	71
C18.2	0	5	8	43	10	66
K56.0	1	1	3	29	21	55
K62.5	0	2	8	22	16	48
C16.2	0	5	11	17	12	45
C18.0	0	0	3	26	11	40
C16.0	0	0	8	20	11	39
C18.4	0	0	3	26	7	36
Total	8	41	157	585	266	1057

Of the total number of patients staged according to TNM, 1057 had histological confirmation, 1028

Table 18. Tumour size (T) and leading diagnosis – "Top ten"

ICD code	T – tumour size					(n)
	T	T1	T2	T3	T4	Total
C20	6	11	52	166	69	304
C18.7	0	6	21	107	29	163
C18.2	0	6	7	48	12	73
C18.0	1	0	4	42	17	64
C18.4	0	0	4	42	9	55
C16.3	0	4	9	19	17	49
C16.0	0	0	6	22	13	41
C16.8	0	0	2	12	20	34
C18.5	0	0	1	24	6	31
C18.3	0	1	4	13	11	29
Total	8	41	157	585	266	1057

V.4.2. Criterion N – lymph node involvement

In 1057 (50.3% of all patients) there is information on staging according to criterion N – lymph node involvement.

Among these patients, those with Nx (31.9%) have the highest relative share, followed by those with N1 (29.8%) and N0 (21.9%). The N3 category includes 2.5% (26 patients).

Table 19. Distribution of patients according to lymph node involvement (N)

N – lymph node involvement	Number	Relative share (%)	Valid relative share (%)	Cumulative share (%)
Nx	337	16	31.9	31.9
N0	231	11	21.9	53.7
N1	315	15	29.8	83.5
N2	148	7.0	14.0	97.5
N3	26	1.2	2.5	100.0
Total with data for N	1057	50.3	100.0	
No data for N	1046	49.7		
Total	2103	100		

Combining the distribution by N and gender of patients, the following results are obtained:

– 62.9% of patients with Nx are men and 37.1% are women;
– 65.8% of patients with N0 are men and 34.2% are women;
– 62.9% of patients with N1 are men and 37.1% are women;
– 51.4% of patients with N2 are men, and 48.6% are women;
– 61.5% of patients with N3 are men, and 38.5% are women.

Distribution of men N:

– 32.4% with Nx;
– 23.2% with N0;
– 30.3% with N1;
– 11.6% with N2;
– 2.4% with N3.

Distribution of women by N:

– 31.0% with Nx;
– 19.6% with N0;
– 29.0% with N1;
– 17.9% with N2;
– 2.5% with N3.

The average age was lowest in patients with N2 (66.22 years) and N3 (66.38 years) and highest in those with N0 (68.85 years). The dispersion in terms of age was low.

Table 20. Lymph node involvement (N) and age correlations

N – lymph node involvement	Number	Mean	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation (%)
Nx	337	67.27	9.864	30	94	14.7
No	231	68.85	8.899	38	88	12.9
N1	315	67.01	10.154	28	92	15.2
N2	148	66.22	10.738	33	88	16.2
N3	26	66.38	10.621	44	88	16
Total	**1057**	**67.37**	**9,916**	**28**	**94**	**14.7**

Table 21 presents the relationships between absolute frequencies (number of patients), admission diagnosis and staging according to lymph node involvement (N). The highest proportion is found in the group with unclear lymph node involvement – Nx. Patients with Nx and N0 account for 52.79%, or more than half, with unclear preoperative status in terms of lymph node involvement.

Table 21. Relationship between lymph node involvement (N) and admission diagnosis – "Top ten"

ICD code	N – lymph node involvement					(n)
	Nx	N	N	N	N3	Total
C20	80	46	51	38	0	215
C18.7	33	34	37	12	0	116
C18.2	24	17	15	9	1	66
K56.0	13	8	19	11	4	55
K62.5	17	9	13	9	0	48
C16.2	9	9	14	7	6	45
C18.0	13	8	13	5	1	40
C16.0	8	7	18	3	3	39
C18.4	11	8	12	5	0	36
C16.3	7	7	7	3	2	26
Total	**337**	**231**	**315**	**148**	**26**	**1057**

Table 22 presents the absolute frequencies (number of patients) according to the leading diagnosis and lymph node involvement (N).

Table 22 Relationship between lymph node involvement (N) and primary diagnosis – "Top ten"

ICD code	N – lymph node involvement					(n)
	Nx	N	N	N	N3	Total
C20	114	64	80	46	0	304
C18.7	50	42	50	20	1	163
C18.2	24	22	15	11	1	73
C18.0	23	10	18	11	2	64
C18.4	17	12	18	8	0	55
C16.3	10	13	13	10	3	49
C16.0	9	4	19	4	5	41
C16.8	13	2	5	9	5	34
C18.5	5	10	12	4	0	31
C18.3	5	6	13	5	0	29
Total	**337**	**231**	**315**	**148**	**26**	**1057**

All final diagnoses in the "Top 10" have an ICD-C code, with the top three being **C20** *Malignant neoplasm of the rectum*; **C18.7** *Malignant neoplasm of the sigmoid colon* and **C18.2** *Malignant neoplasm of the ascending colon*. The distribution of lymph node involvement remains constant. The highest proportion is found in the group with unclear involvement – Nx. Patients with Nx and N0 account for 52.79%. In C20 and C18.7, there is an increase in absolute values. Table 23 shows the absolute frequencies (number of patients) according to histological diagnosis and lymph node involvement (N).

Table 23. Lymph node involvement (N) – and histological diagnosis**"Top ten"**

ICD code	N – lymph node involvement					(n)
	Nx	N	N	N	N3	Total
C20	88	54	65	30	0	237
C18.7	47	40	49	19	1	156
C18.2	24	22	13	9	1	69
C18.0	23	10	17	11	1	62
C18.4	17	11	17	7	0	52
C16.3	10	12	11	7	3	43
C16.0	7	3	18	4	5	37
C18.5	5	10	11	4	0	30
C18.3	4	6	12	5	0	27
C78.6	8	2	9	4	4	27
Total	**327**	**228**	**306**	**142**	**25**	**1028**

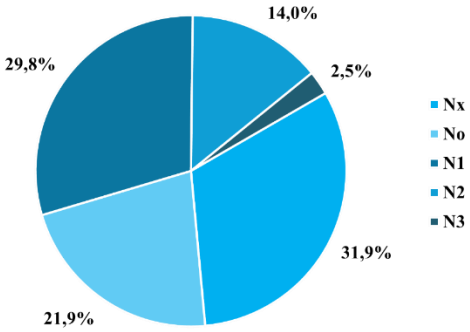


Figure 15. Distribution of patients according to lymph node involvement (n = 1057)

IV.4.3. Criterion M – presence/absence of metastases

Of the total number of registered records (patients) 2103, 1057 (50.3%) have registered data on the presence or absence of metastases. Among this group, the largest relative share (63.6%) are patients without distant metastases. In 11.7% of cases, metastases cannot be determined, and in 24.7% of cases, distant metastases are present.

Table 24. Distribution of patients by presence/absence of metastases (M)

M – presence of distant metastases	Number	Relative share	Valid relative share (%)	Cumulative share (%)
Mx	124	5.9	11.7	11.7
Mo	672	32.0	63.6	75.3
M1	261	12.4	24.7	100.0
Total with data for M	1057	50.3	100.0	
No data for M	1046	49.7		
Total	**2103**	**100.0**		

Combining the distribution by M and gender of patients, the following results are obtained:

– 56.5% of patients with Mx are men and 43.5% are women;

– 63.8% of patients with Mo are men, and 36.2% are women;

– 59.4% of patients with M1 are men, and 40.6% are women

Distribution of male patients by M:

– 10.7% with Mx;

– 65.6% with Mo;

– 23.7% with M1.

Distribution of female patients by M:

– 13.4% with Mx;

– 60.3% with Mo;

– 26.3% with M1.

The average age of patients with M1 is the lowest (66.51 years), but patients with Mx are only a few months older (66.80 years). The highest average age is among patients with Mo – 70.00 years. At the same time, a low degree of dispersion in terms of age is observed in all three categories.

Table 25. Relationship between the presence/absence of metastases (M) and patient age

M – presence of distant metastases	Number	Mean	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation (%)
Mx	124	66.80	9.652	40	87	14.4
Mo	672	67.81	9.787	28	92	14.4
M1	261	66.51	10.326	29	94	15.5
Total	**1057**	**67.37**	**9.916**	**28**	**94**	**14.7**

Table 26 shows the absolute frequencies (number of patients) according to the diagnosis at admission and the presence of distant metastases (M).

Table 26. Staging according to criterion M upon admission – "Top ten"

ICD code	Presence/absence of metastases (M)			(n)
	Mx	M	M1	Total
C20	14	165	36	215
C18.7	20	66	30	116
C18.2	10	38	18	66
K56.6	13	35	23	71
K56.0	6	33	16	55
K62.5	3	35	10	48
C16.2	9	25	11	45
C18.0	5	21	14	40
C16.0	9	23	7	39
C18.4	4	20	12	36
Total	**124**	**672**	**261**	**1057**

Table 27 shows the absolute frequencies (number of patients) according to the leading diagnosis and the presence/absence of metastases (M).

A similar trend is observed with the other analysed parameters – all final diagnoses in the "Top 10" have an **ICD-C** code, and the top 3 are again **C20** *Malignant neoplasm of the rectum*; **C18.7** *Malignant neoplasm of the sigmoid colon* and **C18.2** *Malignant neoplasm of the ascending colon*. The results are identical when comparing the absolute frequencies (number of patients) according to the histological diagnosis and the presence/absence of distant metastases.

Table 27. Relationship between presence/absence of metastases (M) and primary diagnosis

ICD code	Presence/absence of metastases (M)			(n)
	Mx	M	M1	Total
C20	25	223	56	304
C18.7	23	102	38	163
C18.2	12	46	15	73
C18.0	6	36	22	64
C18.4	6	32	17	55
C16.3	5	35	9	49
C16.0	10	23	8	41
C16.8	5	12	17	34
C18.5	5	16	10	31
C18.3	2	15	12	29
Total	**124**	**672**	**261**	**1057**

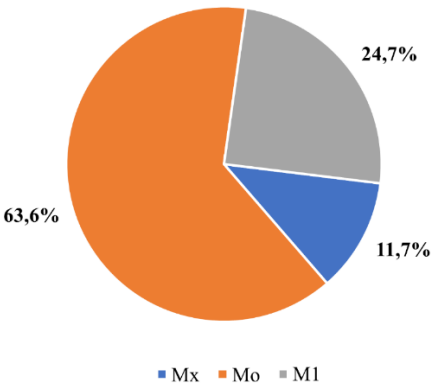


Figure 16. Distribution of patients by presence of distant metastases, n = 1057

IV.5. STAGING ACCORDING TO THE G CLASSIFICATION

The G classification determines how aggressive the carcinoma is – what is the nature of tumour growth and its differentiation and invasiveness. It is as follows:

Gx – the degree of differentiation of the tumour cells cannot be determined.

G1 – well-differentiated tumour.

G2 – moderately differentiated.

G3 – poorly differentiated or undifferentiated tumour – highly aggressive and very malignant.

Only 96 patients (4.56% of all 2,103 patients) have data available for staging according to the G classification.

Of these, those falling into category G2 predominate with 79.17%, followed by G3 with 13.54%.

Table 28. Staging according to the G classification

G classification	Number	Relative share (%)	Valid relative share (%)	Cumulative share (
Gx	-	-	-	0.0
G1	1	0.05	1.04	1.04
G2	76	3.61	79.17	80.21
G2-3	5	0.24	5.21	85.42
G3	13	0.62	13.54	98.96
G4	1	0.05	1.04	100.00
Total with data for G	96	4.56	100.00	
No data for G	2007	95.44		
Total	**2103**	**100.00**		

Combining the distribution by G and gender of patients, we obtain:

– 1 patient in category G1 is female;

– 65.8% of patients in G2 are men and 34.2% are women;

– 60.0% of patients in G2-3 are men and 40.0% are women;

– 69.2% of patients in G3 are men and 30.8% are women;

– 1 patient in G4 is male.

Distribution of men according to the G classification:

– 79.4% in G2;

– 4.8% in G2-3;

– 14.3% in G3;

– 1.6% in G4.

Distribution of women according to G classification:

– 3.0% in G1;

– 78.8% in G2;

– 6.1% in G2-3;

– 12.1% in G3.

The average age of patients with G2 is 64.07 years, and that of patients with G3 is 63.69 years, with low variation in all categories.

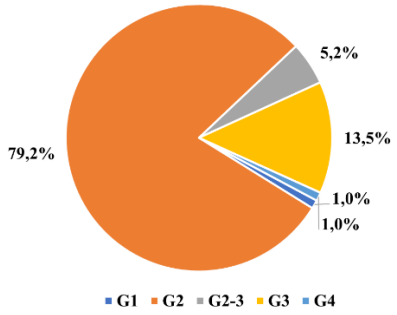


Figure 17. Distribution of patients by G classification, n = 96

IV.6. UNIVERSAL STAGING SYSTEM FROM STAGE I TO STAGE IV

The universal staging system consists of 6 groups, designated by Roman numerals. Each stage is assigned a corresponding TNM classification.

Stage 0 – T_{is} N_0 M_0
Stage IA – T_1 N_0 M_0
Stage IB – T_2 N_0 M_0
Stage II – T_3 N_0 M_0
Stage II – $T_4N_0M_0$ or $T_{1\text{-}4}N_{1\text{-}3}M_0$
Stage IV – $T_{1\text{-}4}N_{1\text{-}3}M_1$

The analysed medical records include staging data for 1,057 patients, or 50.3% of the total 2,103. The available stages are distributed as follows:
Stage III – 35.9%,
Stage II – 25.4%
Stage IV – 24.5%.
Only 6 patients are in Stage 0, and 3.0% are in Stage IA.

The results are presented in Table 29.

Table 29. Distribution of patients by stages 0-IV

Stage	Number	Relative share (%)	Valid relative share (%)	Cumulative share (%)
Stage 0	6	0.3	0.6	0.6
Stage IA	32	1.5	3.0	3.6
Stage IB	113	5.4	10.7	14.3
Stage II	268	12.7	25.4	39.6
Stage III	379	18.0	35.9	75.5
Stage IV	259	12.3	24.5	100.0
Total with staging data	1057	50.3	100.0	
No staging data	1046	49.7		
Total	**2103**	**100.0**		

Combining the distribution by stage and gender of patients, the following results are obtained:

– 66.7% of patients in stage 0 are men and 33.3% are women;
– 62.5% of patients in stage IA are men and 37.5% are women;
– 66.4% of patients in stage IB are men and 33.6% are women;
– 64.9% of patients in stage II are men and 35.1% are women;
– 60.2% of patients in stage III are men and 39.8% are women;
– 59.1% of patients in stage IV are men and 40.9% are women.

Distribution of male patients by stage:
– 0.6% in stage 0;
– 3.1% in stage IA;
– 11.5% in stage IB;
– 26.6% in stage II;
– 34.9% in stage III;
– 23.4% in stage IV.

Distribution of female patients by stage:
– 0.5% in stage 0;
– 3.0% in stage IA
– 9.4% in stage IB;
– 23.3% in stage II;
– 37.5% in stage III;
– 26.3% in stage IV.

Patients in stage IV have the lowest average age – 66.38 years, but those in stage IA are very close to them – 66.41 years. Patients in stage II have the highest average age – 69.47 years. There is a low degree of variation in age across the different stages.

Table 30. Stages and age of patients

Stages	Number	Average	Standard deviation (SD)	Minimum	Maximum	Coefficient of variation
Stage 0	6	68.50	1.871	65	70	2.7
Stage IA	32	66.41	10.485	46	81	15.8
Stage IB	113	66.99	10.111	30	86	15.1
Stage II	268	69.47	8.789	40	88	12.7
Stage III	379	66.73	10.192	28	92	15.3
Stage IV	259	66.38	10.308	29	94	15.5
Total	**1057**	**67.37**	**9.916**	**28**	**94**	**14.7**

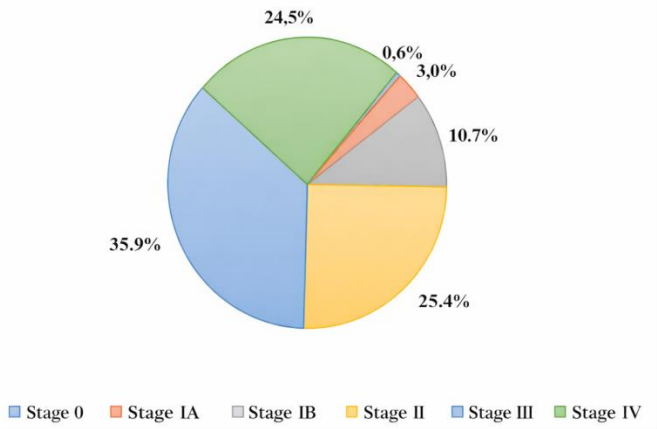


Figure 18. Distribution of patients from stage 0 to stage IV, n = 1057

IV.7. ECOG STAGING

In order to understand whether a patient is fit for therapy, standardised criteria have been introduced in real clinical practice to measure how the disease affects the patient's daily ability to care for themselves, their daily activity and their physical abilities (walking, self-care, work, etc.). This is also a way for doctors to track changes in the patient's activity level as a result of treatment.

The ECOG Performance Status Scale was developed by the Eastern Cooperative Oncology Group (ECOG) and published in 1982.

The ECOG scale for patient behaviour includes 5 levels:

0 – Fully active, able to maintain all pre-illness indicators without restrictions;

1– Limited in strenuous physical activities, but ambulatory and able to perform light activities, such as light, non-strenuous work at home or in the office;

2– Ambulatory and capable of all self-care, but unable to perform work activities for more than approximately 50% of working hours;

3– Capable only of limited self-care. Activities are limited to bed or chair for more than 50% of waking hours;

4– Completely inactive, unable to perform independent care, completely confined to bed or chair.

5– Death.

1068 patients (50.8% of all) are classified with ECOG status, with the majority (77.3%) falling into the "symptomatic" category. The "normal" category accounted for 7.6%. "Disabling tumour manifestations" accounted for 12.9%, and the "severely disabled" category according to ECOG status accounted for 1.8%. Four patients (0.4%) were registered as severely ill (100% bedridden) (Table 31, Figure 19).

Table 31. Distribution of patients by ECOG status

ECOG status	Number	Relative share	Valid relative share (%)	Cumulative share
Standard	81	3.9	7.6	7.6
With symptoms present	826	39.3	77.3	84.9
With disabling tumour manifestations	138	6.6	12.9	97.8
Severe disability	19	0.9	1.8	99.6
Seriously ill (100% bedridden)	4	0.2	0.4	100.0
Total with ECOG status	1068	50.8	100.0	
Without ECOG status	1035	49.2		
Total	**2103**	**100.0**		

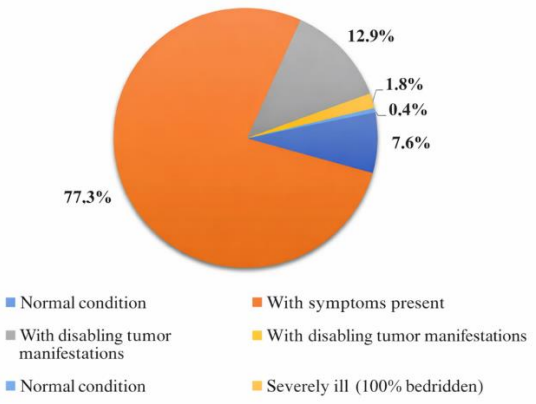


Figure 19. Distribution of patients by ECOG status, n = 1068

V. DISCUSSION OF RESULTS AND CONCLUSIONS FROM THE DISSERTATION

Data from the National Statistical Institute (NSI) show that in 2022 a total of 16,301 Bulgarians died of cancer.

National and international epidemiological data show persistent geographical differences in morbidity and outcomes, with higher rates of stomach cancer and colorectal carcinoma observed in Eastern Europe and East Asia. These differences highlight the need for regionally adapted screening programmes and treatment protocols. The future of surgical oncology in the gastrointestinal tract is increasingly defined by multidisciplinary collaboration, molecular profiling of tumours, and the integration of digital navigation and planning tools. These factors encourage the use of precision medicine and personalisation of surgical treatment according to the individual characteristics of each patient.

The most significant result of the dissertation research is the analysis of surgical approaches to the treatment of malignant diseases of the gastrointestinal tract, with a focus on clinical and epidemiological aspects in a specific region – North-Eastern Bulgaria.

This is the first time in Bulgaria that an epidemiological study of this scale and duration has been conducted using a uniform protocol and retrospective observational design, based on electronic medical records prepared for the needs of the health insurance system.

In ***the Introduction***, we outlined a series of reasons that motivated us to work on this topic, but the most important one was that we found no evidence of such studies having been conducted in Bulgaria.

We conducted literature searches in various directions.

In the first part of the literature review, "Analysis of the Health Problem," we examined epidemiology, aetiology, pathogenesis, pathoanatomy, clinical picture, diagnosis, instrumental examinations, staging, surgical treatment, non-surgical treatment, postoperative complications, follow-up, prognosis, palliative treatment and other aspects of carcinomas of the gastrointestinal tract – oesophageal cancer, stomach cancer, small intestine cancer, colon cancer, pancreatic cancer, gallbladder and bile duct cancer, liver cancer. The analyses of the health problem "Malignant diseases of the gastrointestinal tract" are based on 171 scientific publications.

In the second part of the literature review, we present a systematic review of scientific publications on the topic of "Surgical interventions and perioperative strategies in malignant diseases of the gastrointestinal tract." in accordance with the recommendations of the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [175-177].

Compared to the analysis of abstracts, the analysis of full texts reveals significant dissociation and heterogeneity of results, with the proportion of unspecified interventions increasing and accounting for an extremely high share.

Three main themes dominate the analysed literature: the transition to minimally invasive surgery, the critical importance of precise lymphadenectomy and pathological assessment, and the growing focus on optimising perioperative management.

Minimally invasive surgery: Data consistently support the advantages of minimally invasive approaches in reducing short-term morbidity. However, this short-term benefit has not yet translated into a statistically significant survival advantage. Severe postoperative complications are an independent risk factor for reduced survival. The choice of approach should be individualized to minimize postoperative stress. *Lymphadenectomy and pathological assessment*: The accuracy of surgical staging remains fundamental. Studies in pancreatic cancer emphasise the need for adequate lymph node dissection and detailed assessment for occult metastases. The extent of lymph node dissection should be tailored to the histology.

Perioperative management: There is growing evidence supporting the use of specific perioperative interventions as part of enhanced recovery protocols (ERAS). Studies demonstrate how targeted actions can directly influence postoperative recovery and the incidence of complications. There has been a shift in focus from purely surgical technique to the patient's overall journey through the perioperative period.

Available Bulgarian publications show that minimally invasive and robot-assisted surgeries performed in Bulgaria demonstrate the typical benefits of MIS: reduced bleeding, faster recovery, shorter hospital stay, and good lymphatic drainage in some cases. This supports the hypothesis that most of the benefits described in the world literature are also applicable to the Bulgarian population.

Publications with Bulgarian sources mainly describe implementation, early/short-term results and validation of instruments/scales, but at the same time, the lack of large RCTs, meta-analyses and long-term data means that the scientific level of evidence remains limited.

To evaluate the results, we applied the PICOS criteria system – Population, Intervention, Comparison, Outcomes, and Study design. The modified version of PICOS also includes study design, limiting the likelihood of inappropriate scientific publications being included in the analysis. Over a period of 25 years, 796 scientific publications were found. Only scientific publications containing at least one of the keywords – *oesophageal cancer, stomach cancer, pancreatic cancer, liver cancer, colon cancer, rectal cancer, colorectal cancer* – were analysed. A second mandatory condition was the presence of the keyword *surgical treatment and/or radical surgical treatment of..., palliative surgical treatment of..., lymph node dissection, intraoperative complications, postoperative complications, individualised approach*.

None of the scientific articles contain the abbreviation PICO or PICOS, and none of the abstracts mention the application of this methodology in surgical oncology practice.

The category "**I – intervention**" is highly fragmented and heterogeneously coded: the most common single value is "Surgery – unspecified" (6.3%; n = 19), with the predominant share falling into the "Other" group (82.2%). *There is a lack of standardised definitions and high variability in the description of interventions.* Preliminary grouping into clinically meaningful categories (e.g. radical resection; minimally invasive/robot-assisted; palliative; combined procedures; perioperative strategies) before performing associative tests proves practically impossible!

In the "**Type of surgery**" distribution, there is a high proportion of missing/unspecified information (44.6%; n = 135). Among the values listed, radical surgery dominates (39.3%; n = 119) dominates among the values listed, followed by palliative surgery (8.6%; n = 26). The proportion of unspecified cases limits interpretation and does not allow reliable conclusions to be drawn about the distribution of surgical outcomes, especially when comparing tumour groups.

The "**Outcomes**" category is fragmented – the results are not presented with the primary, secondary and surrogate endpoints customary in oncological practice, or they are not applied as required in surgical practice!

Surgically determined composite endpoints, different time horizons and definitions of complications were used, which makes direct comparison based on the original statistical categories unreliable. We consider it mandatory to apply a pre-defined grouping of endpoints – survival – OS and/or DFS and/or PFS; perioperative: mortality, morbidity, complications; functional/quality of life; resource/economic).

V.1. LIMITATIONS, INCOMPLETENESS, OMISSIONS AND SHORTCOMINGS OF THE SYSTEMATIC REVIEW

Lack of high-quality data: Most of the included studies are retrospective in design. There is a lack of long-term data from large randomised controlled trials for many of the interventions studied, which limits the strength of the conclusions.

Heterogeneity of practices: There is considerable heterogeneity in surgical techniques and perioperative protocols. For example, the heterogeneity in anastomosis techniques in MIE, as seen in the study by Straatman et al. [184], where a high incidence of insufficiency is noted, makes direct comparison of results between centres extremely difficult and highlights the need for standardisation.

Focus on patient-oriented outcomes: While oncological outcomes (survival, recurrence) have been well studied, less attention has been paid to long-term patient-reported outcomes (PROs). Future studies should focus more on quality of life, functional recovery, and social reintegration [204].

Validation of new technologies: The development of innovative intraoperative navigation technologies and predictive biomarkers is a promising area. However, prospective studies are needed to validate their clinical benefit and effectiveness in personalising surgical treatment.

ECOG status is practically impossible to analyse for change in this set: it is missing/not specified in 92.1% of publications (n = 279).

TNM staging data are inconsistently reported – data are missing in 52.1% of publications. There is a serious difficulty in conducting stage-adjusted comparisons and interpreting the results.

Data on the incidence and mortality of gastrointestinal cancer in Bulgaria at national level are collected by various institutions such as the National Statistical Institute, the National Centre for Public Health and Analyses, the National Cancer Registry and the National Health Insurance Fund. Scientific medical societies also actively participate in data collection and analysis.

The National Cancer Registry (NCR) was established in 1952 and is one of the oldest in Europe. It was closed at the end of 2023, and its management activities were transferred to the NCPHA in 2016. The latest publicly available and official information is from 2017.

According to data from the European Cancer Information System (ECIS), Bulgaria has seen an improvement in the five-year relative survival rate for almost all gastrointestinal carcinomas.

The results of the analysis of the available data on the epidemiology of gastrointestinal cancer in Bulgaria are contradictory and raise a number of questions regarding the reliability of the data, the methodology for its collection and which institutions should be responsible for this.

We analysed a set of data according to 15 criteria:

1. **Demographic data** – gender and age; 2. **Clinical pathway (CP) upon admission**; 3. **CP upon discharge**, with determination of the degree of match; 4. **Disease code upon admission** according to the International Classification of Diseases (ICD); 5. **ICD code at discharge**, with determination of the degree of correspondence; 6. **Deceased – relative share**; 7. **Comorbidities – ICD code**, number of comorbidities per patient; 8. **Histological diagnosis**; 9. **Admission type** – planned or emergency; 10. **Bed days** – by gender, age, ICD; 11. **Admission diagnosis** – ICD code; 12. **Leading diagnosis** – ICD code; 13. **Match between admission and leading diagnosis**; 14. **Staging according to TNM classification**; 15. **Staging according to ECOG.**

All the advantages and disadvantages of retrospective designs that we analysed in the general overview section of the dissertation were also evident in our study.

Esophageal cancer is an aggressive malignant disease with a poor prognosis, despite significant advances in multimodal therapy. Its clinical significance stems from its late symptoms and tendency to metastasise early, which often leads to diagnosis at an advanced stage. The treatment of ES is complex and requires a coordinated multidisciplinary approach that integrates the efforts of gastroenterologists, surgeons, medical oncologists, radiotherapists, pathologists and imaging specialists, in accordance with current clinical guidelines from leading organisations such as the European Society for Medical Oncology (ESMO) and the National Comprehensive Cancer Network (NCCN), USA. The prognosis of oesophageal cancer depends on the stage at diagnosis, the histological type and the response to the multimodal treatment applied. Achieving "clean" surgical margins is the strongest independent prognostic factor for long-term survival. The absence of residual tumour is the main goal of surgery. The number of metastatic lymph nodes (pN) is a key predictor of recurrence and survival. Patients without affected lymph nodes have a significantly better prognosis. Response to neoadjuvant therapy: Achieving a pathological complete response (pCR), in which no residual tumour is found in the resected material, is associated with significantly better survival.

The prognosis for gastric cancer is generally poor, mainly due to late diagnosis. Several factors have a strong influence on survival: 1. Pathological stage (TNM): TNM stage is the most dominant prognostic factor. 2. R-status: Achieving R0 resection (microscopically negative margins) is essential for cure. 3. Lymph node involvement: A large number of positive lymph nodes (N3a/N3b) is associated with a significantly worse prognosis. 4. Histological and molecular subtype: Diffuse histology and the genomically stable (GS) molecular subtype usually carry a poorer prognosis, while the MSI subtype has a relatively favourable prognosis. 5. Peritoneal involvement: Positive peritoneal cytology (CY1) or macroscopic peritoneal metastases are powerful independent indicators of a very poor prognosis, with median survival measured in months. The goals of follow-up after treatment are early detection of recurrence and treatment of long-term consequences of surgery. Regular clinical examinations are necessary, combined with serial CT scans, endoscopic surveillance, and monitoring of tumour markers.

The prognosis for small bowel cancer is highly variable and is determined primarily by the histology of the tumour and the stage at diagnosis. Understanding prognostic factors is of strategic importance for risk stratification, patient counselling and the development of appropriate follow-up regimens. Key negative prognostic factors: The presence of lymph node involvement (stage III) and distant metastases (stage IV) are the strongest negative predictors of survival; poorly differentiated histology (high grade) is associated with poorer outcomes. The prognosis for NEC and EATL is particularly poor; Positive resection margins (R1 resection) are a significant negative prognostic factor; Duodenal localisation is independently associated with poorer overall survival in adenocarcinoma; Poor ECOG performance status (≥ 2) is an independent factor for poorer survival; Specific molecular characteristics, such as p53 mutation in SBA, may be associated with poor prognosis. The approximate 5-year overall survival (OS) rates for SBA by stage, based on broader registries, are as follows: I – 57-66%; II – 43-50%; III – 31-42%; IV – 5-19%.

Malignant tumours of the colon, rectum and anal canal, although anatomically adjacent, represent different disease entities with unique epidemiological, aetiological, molecular and clinical characteristics. It is crucial to apply sub-localisation-specific approaches to diagnosis, staging (MRI for rectal CRM, size-based staging for anal carcinoma) and treatment (TME for rectal, definitive chemoradiotherapy for

anal, consideration of the side in mCRC). Future research directions include personalising adjuvant therapy by monitoring minimal residual disease (MRD) through circulating tumour DNA (ctDNA) and continuing to refine organ preservation strategies in rectal cancer.

Pancreatic cancer remains one of the deadliest malignant diseases, characterised by challenging epidemiology, late diagnosis and complex molecular biology. Despite these difficulties, modern multimodal therapeutic paradigms integrating surgery, systemic chemotherapy and, increasingly, targeted and immunotherapies offer hope for improved outcomes. It is essential for modern clinical practice that the treatment of these patients be carried out by multidisciplinary teams in high-tech centres where expertise in all aspects of care can be provided. Future research should focus on developing reliable strategies for early screening in high-risk individuals and identifying new molecular targets to improve therapeutic efficacy and change the trajectory of this devastating disease.

Gallbladder and bile duct cancers are aggressive malignancies with increasing incidence, particularly for intrahepatic cholangiocarcinoma. Epidemiological trends, different risk profiles, and the unique molecular biology of these tumours underpin the current paradigm of multimodal treatment. Although surgery remains the only curative treatment, the integration of immunotherapy and targeted agents based on molecular profiling is transforming therapeutic approaches and offering new opportunities for patients with advanced disease.

Despite significant advances, several major challenges remain in the treatment of liver cancer. According to key sources such as EASL guidelines and publications, "unmet needs" include: Better tools for surveillance and early diagnosis; Effective adjuvant therapies; Predictive biomarkers; Precision oncology; Biomarker-based clinical trials; Combination and multimodal approaches. The investigation of new combinations of systemic therapies, as well as the integration of systemic treatments with locoregional approaches (e.g., neoadjuvant therapy), has the potential to improve outcomes at all stages of the disease.

Literature data on morbidity and mortality from malignant neoplasms of the GI tract in Bulgaria show contradictory and opposing trends, which seems illogical. Usually, when such deviations in demographic statistics are observed, it is necessary to find an explanation for the reasons that led to these trends. Our country is one of two countries in the EU, along with Cyprus, where cancer mortality increased between 2011 and 2021 (from 229 to 242 cases per 100,000 people), while existing data from the National Centre for Public Health and Analyses (NCPHA) for the period 1980-2024 show a downward trend in the incidence of all types of cancer – from 30,338 newly diagnosed cases in 2019 to 25,225 cases in 2024. NCZHA data also reveal that the incidence of malignant neoplasms of the digestive organs will decrease in 2023 and 2024. In terms of gender distribution, oesophageal cancer shows the most pronounced predominance of men among all gastrointestinal malignant diseases, with a ratio of 4.3:1. This ratio is more than twice as high as that for stomach cancer (1.7:1) identical to that of small intestine cancer and three times higher than colorectal carcinoma (1.34:1), suggesting a significant role for male-specific risk factors such as smoking and alcohol consumption.

The results of our research confirm some of the data in the literature. Malignant diseases of the gastrointestinal tract are more common in males. The average age of patients is 67.66 years. The youngest patient is 24 years old, and the oldest is 94 years old. The 66-75 age group has the highest relative share. *Malignant neoplasm of the rectum* is the diagnosis with which the largest share of patients were admitted during the period – 15.22%. Next in line are those admitted with a diagnosis *of malignant*

neoplasm of the sigmoid colon. Perioperative mortality in patients with malignant neoplasms of the gastrointestinal tract is 8.1%, which is approximately the same as in the available literature. Over 62% of patients are over 66 years of age, with 91.87% of patients having at least one concomitant disease, the main one being *hypertensive heart without (congestive) heart failure*, which occurs in 22.62% of patients with comorbidities. There is significant comorbidity in the analysed group of patients. 50% of patients have arterial hypertension, and 16.9% have type II diabetes mellitus. The high comorbidity of Bulgarian patients is striking when compared to different cohorts of studies from different geographical areas (East – China, Japan, and West – USA, Western Europe), which is the most likely reason for Bulgaria's leading position in Europe in terms of demographic indicators of morbidity and mortality.

Patients with verified histological diagnoses at discharge numbered 2,055 (97.72%). Only 48 (2.28%) patients did not have a verified histological diagnosis or rather lacked data. 64.6% of admissions were planned, and 34.4% were urgent to varying degrees, most often with an urgency of up to 6 hours or 27.5%. The admission of nearly one-third of patients on an emergency basis is a sign of poor organisation of the Bulgarian healthcare system in terms of delayed diagnosis and manifestation of complications of the malignant process such as bleeding, obstruction, etc. The average number of bed days is 11. The minimum stay is 1 bed day (0.2%), and the longest is 70 bed days (0.05%). There is almost no difference in the average number of bed days depending on the patient's gender. One in four patients (23.40%) has a primary diagnosis of C20. The length of hospital stay is confirmed depending on the type of surgery – open conventional surgery versus minimally invasive or robotic surgery.

Among patients for whom tumour size data is available, the highest relative proportion is that of T3 patients, who account for 55.3% of those for whom data is available, followed by T4 patients, who account for 25.2%, patients with T2 – 14.9%, and the lowest proportion of patients with established tumour size are those in T1, who account for 3.9%. Of the total number of registered records (patients) 2103, 1057 (50.3%) have registered data on the presence or absence of metastases. Among this group, the largest relative share (63.6%) are patients without distant metastases. In 11.7% of cases, these cannot be determined, and in 24.7% of cases, distant metastases are present. In terms of the differentiation of malignant tumours, those falling into category G2 predominate with 79.17%, followed by G3 with 13.54%.

Patients with malignant diseases of the GI tract are diagnosed late, the clinical manifestations of the diseases are not actively sought and remain unrecognised for a long period of time, and there are no national screening programmes, all of which provide answers to the questions about late diagnosis, advanced disease and the lack of alternatives and a good prognosis for patients.

1068 patients (50.8% of all) were classified with ECOG status, with the majority (77.3%) falling into the "symptomatic" category. The "normal" category accounted for 7.6%. Those with "disabling tumour manifestations" accounted for 12.9%, and the "severely disabled" category according to ECOG status accounted for 1.8%. Four patients (0.4%) were registered as severely ill (100% bedridden)**.**

This dissertation is the first attempt in Bulgaria and the first on such a scale to analyse surgical oncological pathology through a retrospective observational study of electronic medical records using the Health Technology Assessment (HTA) tool.

Health technology assessment is a structured form of analysis based on evidence and scientific research that generates information about clinical and cost-effective health technologies. In healthcare, technology is understood to mean any intervention that can be used for: improving health, prevention, diagnosis or treatment of a specific disease, rehabilitation programmes, long-term medical care, etc. [217].

Surgery and invasive diagnostic procedures are an integral part of health technologies and are subject to assessment according to established standards. The main elements of HTA are presented in Figure 21. HTA includes four main areas, the most important of which from a clinical point of view is the assessment of clinical effectiveness.

Clinical effectiveness describes the ability of a health technology to achieve a clinically significant impact on the patient's health status. The assessment of clinical effectiveness is carried out in two areas: 1) Measurement of results or effects and effectiveness, and 2) Comparative analyses using established methods of comparison or meta-analyses [216].

We analysed contemporary surgical approaches to malignant diseases of the gastrointestinal tract, focusing on clinical and epidemiological aspects in a specific region – North-Eastern Bulgaria.

The retrospective observational design we chose is a research method for documenting clinical, economic and/or medico-social and medico-biological outcomes in real medical practice.

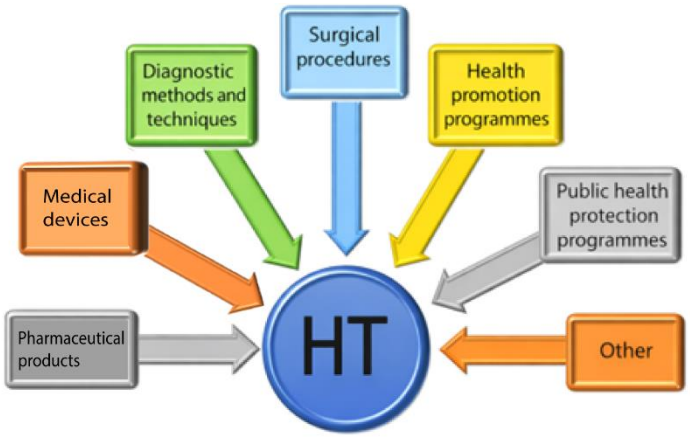


Figure 20. Types of health technologies

Figure 21. Elements of HTA

V.1.1. Advantages and disadvantages of observational studies

Retrospective observational studies analyse treatments and outcomes that have already occurred. First, observational retrospective studies are less expensive and take less time than randomised controlled clinical trials because researchers do not have to recruit patients for the study. Second, retrospective databases allow researchers to analyse information collected over a long period of time at relatively low cost. Thirdly, observational studies can provide a more realistic picture of treatment problems for a larger patient population and the actual cooperation of patients during treatment. Fourthly, sensitivity analyses can be performed easily by changing the baseline data (baseline visit and data). The inclusion and exclusion criteria (age, gender, underlying disease, comorbidities, ongoing treatment, treatment restrictions, clinical condition, severity, duration, etc.) of the patients in the study, which are tested as baseline data at the initial visit or used as baseline data, can be modified, changed, expanded or reduced to see whether the results are sensitive or not to the different limits of these criteria [215].

The most important limitations in the use of data from observational studies are that the information collected over the years may be incomplete, inaccurate or even incorrect. Most retrospective databases are collected and used primarily for the purposes of paying for treatment and health services rendered, rather than for evaluating outcomes from the patients' perspective. If the patient is in an insurance system that pays per patient

served, the doctor may only indicate one diagnosis because adding others does not change the amount he will receive. If reimbursement is related to the severity of the disease and the number of diagnoses, even minor diagnoses may be entered. Bias errors are also very common, whereby patients with certain characteristics are more likely to be prescribed one procedure or medication over another.

A major drawback is the presence of significant differences in the baseline data in the patient groups at the outset, which may lead to inaccurate study results due to these differences. There is no randomisation, and therefore errors are often found in the selection of patients, as well as in the choice of treatment and therapeutic regimen. The main reasons for errors in retrospective studies may be: incorrectly determined disease severity, resistance to standard therapy, unfamiliarity with new treatment methods, lack of therapeutic algorithms, concomitant diseases, drug interactions, and others [216].

Based on the studies conducted, their analysis and synthesis, specific conclusions and recommendations can be formulated aimed at improving the quality, reliability and comparability of studies in the field of surgical oncology.

1. Encouraging prospective designs. As already mentioned, the observed dominance of retrospective studies limits the level of evidence. In order to establish clear causal links between interventions and clinical outcomes, it is essential to encourage more prospective cohort studies and, where ethically and practically possible, randomised controlled trials.

2. Standardised reporting of surgical approaches. The identified heterogeneity in the description of interventions necessitates the creation and adoption of consensus reporting protocols. Guidelines similar to CONSORT for randomised trials would ensure the completeness, consistency and comparability of data on surgical techniques. Without such a standard, surgical oncology risks remaining in methodological stagnation, generating a huge volume of data with a low degree of synthesis and limited clinical utility.

3. Standardisation of definitions. It is necessary to reach a consensus on the definitions of key concepts such as "radical," "curative," and "palliative" surgery. Clear and universally accepted definitions will avoid ambiguity and allow for the correct comparison of results from different centres.

4. Development of consensus classifications. To overcome the problem of data fragmentation, it is advisable to develop consensus taxonomies (classifications) of surgical interventions. This will allow for their adequate grouping in statistical analyses and facilitate the conduct of high-quality meta-analyses. In the absence of such standards, the accumulation of publications with heterogeneous and incomplete reporting limits the possibility of reliable secondary synthesis and hinders the translation of scientific data into clinical recommendations. Therefore, the introduction of structured reporting frameworks would increase the comparability, reproducibility, and clinical interpretability of future studies.

V.1.2. Key conclusions

1. Contemporary literature in surgical oncology is distinctly current (≈ 64.7% of publications are from the 2020s), but the predominance of retrospective designs remains pronounced, which limits the levels of evidence and increases the risk of systematic biases typical of observational studies.

2. There is a geographical concentration of publications in Asia (mainly Japan and China), which should be taken into account when extrapolating the results to other populations, given potential epidemiological, clinical and organisational differences.

Main conclusion. There are serious gaps in the prevention of malignant diseases. Indirectly, it can be argued that there is a delay in diagnosis and late seeking of specialised medical care.

VI. CONTRIBUTIONS

VI.1. ORIGINAL CONTRIBUTIONS OF A SCIENTIFIC-THEORETICAL AND METHODOLOGICAL NATURE

1. For the first time in Bulgaria, surgical oncological pathology is analysed through the *Health Technology Assessment* toolkit by means of a retrospective observational study of electronic medical records from real clinical practice.
2. For the first time in scientific literature, a systematic review of scientific publications on the PRISMA standard for the assessment of surgical oncology practice in diseases of the gastrointestinal tract has been conducted.
3. For the first time in international surgical research practice on oncological gastrointestinal diseases, a study is conducted to assess clinical effectiveness based on the PICOS tool.
4. For the first time in Bulgaria, a narrative observational study of contemporary surgical approaches to the treatment of malignant diseases of the gastrointestinal tract at international and national level has been conducted based on an analysis of scientific publications by Bulgarian authors.
5. For the first time in Bulgaria, an epidemiological study of malignant diseases of the digestive tract was conducted based on a systematic analysis of data from the European Cancer Information System (ECIS) and the International Agency for Research on Cancer of the World Health Organization (IARC/GLOBOCAN).
6. For the first time in Bulgaria, a loco-regional longitudinal retrospective study of malignant diseases of the gastrointestinal tract was conducted, covering one of the six administrative regions of Bulgaria.
7. An original author's protocol with an original design for a retrospective study has been developed and a unique research tool has been introduced to conduct a systematic review of scientific publications for the evaluation of surgical interventions.
8. An original author's version of the PICOS tool designed to evaluate oncological gastrointestinal diseases has been developed. In addition to the standard 5 elements – P – population, I – intervention, C – comparator, O – outcome, S – study design, the modified tool contains Tumor type, TNM classification, ECOG performance status, and Type of surgery radical/palliative. This modified version of PICOS (which can be referred to as a'Modo Angelov) represents an original contribution of international significance. Without the addition of these elements to PICOS, it would be impossible to assess the clinical effectiveness of surgical interventions.

VI.2. CONTRIBUTIONS OF A SCIENTIFIC AND APPLIED NATURE

1. The study enriches the knowledge of medical professionals on the practical application of retrospective studies of electronic medical records, both for the purposes of the health insurance system and for fundamental medical science and practice.
2. The scale of the data processed and the results obtained are generalisable and extrapolatable on a national and international scale.
3. The study reveals three main future directions:

– transition to minimally invasive surgery;
– the critical importance of precise lymphadenectomy and pathological assessment; and
– the growing focus on optimising perioperative management.

4. National and international epidemiological data show persistent geographical differences in morbidity and outcomes, with higher rates of gastric and colorectal cancer observed in Eastern Europe and East Asia. These differences highlight the need for regionally adapted screening programmes and treatment protocols.

5. The future of surgical oncology in the gastrointestinal tract is increasingly defined by multidisciplinary collaboration, molecular profiling of tumours, and the integration of digital navigation and planning tools. These factors encourage the use of precision medicine and personalisation of surgical treatment according to the individual characteristics of each patient.

6. Innovative surgical techniques and their added benefits are presented in depth.

7. The lack of precise tumour staging in the scientific literature is demonstrated as a fundamental methodological shortcoming not only at the national but also at the international level.

VI.2. CONTRIBUTIONS OF A CONFIRMATORY NATURE

1. Based on a systematic review of 171 scientific publications, it has been confirmed that:

– esophageal cancer is an aggressive malignant disease with a poor prognosis despite significant advances in multimodal therapy;

– the prognosis for stomach cancer continues to be poor, mainly due to late diagnosis;

– the prognosis for small intestine cancer is highly variable and is determined primarily by the histology of the tumour and the stage at diagnosis;

– malignant tumours of the colon, rectum and anal canal, although anatomically adjacent, represent different disease entities with unique epidemiological, aetiological, molecular and clinical characteristics;

– Malignant tumours of the colon continue to have the highest incidence among tumours of the gastrointestinal tract.

– Pancreatic cancer remains one of the most deadly malignant diseases, characterised by challenging epidemiology, late diagnosis and complex molecular biology despite advances in pharmacological therapies.

– Gallbladder and bile duct cancers are aggressive malignant diseases with increasing incidence, especially intrahepatic cholangiocarcinoma.

– Despite significant advances, the treatment of liver cancer remains a serious challenge.

VII. RECOMMENDATIONS

1. The predominance of retrospective studies limits the level of evidence. In order to establish clear causal relationships between interventions and clinical outcomes, it is essential to encourage prospective cohort studies and randomised controlled trials.

2. There is a need to create and adopt consensus reporting protocols. Without universally accepted standards, surgical oncology risks remaining in methodological stagnation, generating a huge volume of data with a low level of evidence.

3. To overcome the problem of data fragmentation, it is advisable to develop consensus taxonomies (classifications) of surgical interventions. The introduction of structured reporting frameworks would increase the comparability, reproducibility and clinical interpretability of future studies.

VIII. SCIENTIFIC PUBLICATIONS RELATED TO THE DISSERTATION

VIII.1. PUBLICATIONS PUBLISHED IN SCIENTIFIC JOURNALS, REFEREED AND INDEXED IN WORLD-RENOWNED DATABASES WITH SCIENTIFIC INFORMATION

1. K. Angelov in 2015 European Society of Coloproctology (ESCP) collaborating group. Patients with Crohn's disease have longer post-operative in-hospital stay than patients with colon cancer but no difference in complications' rate. World J Gastrointest Surg 2019; 11(5): 261-270 [PMID: 31171957 DOI: 10.4240/wjgs.v11.i5.261]

2. K. Angelov in 2015 European Society of Coloproctology Collaborating Group, Predictors for Anastomotic Leak, Postoperative Complications, and Mortality After Right Colectomy for Cancer: Results From an International Snapshot Audit, Diseases Of The Colon & Rectum Volume 63: 5 (2020), DOI (link to publisher): 10.1097/DCR.0000000000001590

3. M Sokolov, B Petrov, S Maslyankov, K Angelov, M P Atanasova, D Tzoneva, P Gribnev, Technical considerations depending on the level of vascular ligation in laparoscopic rectal resection, Surgical endoscopy, 2022 Mar;36(3):1961-1969

4. K. Angelov in 2015 European Society of Coloproctology Collaborating Group; Development of a Clinical Prediction Model for Anastomotic Leakage in Colorectal Surgery, JAMA Netw Open. 2025 Oct 1;8(10):e2538267. Doi: 10.1001/jamanetworkopen.2025.38267.

5. Angelov K, Nachev N, Yordanov E, Stoyanova S, Rangelov A, Hayat N, Sharkov A, Zlatarov A, Dyulgerov T. News in the management of colorectal cancer – a systematic review. (2025). Nursing, 57(4) 64-70. ISSN 1310-7496

6. Angelov K, Nachev N, Yordanov E, Stoyanova S, Khayat N, Sharkov A, Zlatarov A, Dyulgerov T. Diagnostic and therapeutic approaches in the treatment of gastric cancer – a scoping review. (2026) Acta Medica Bulgarica, 53 (1), pp 232-238. https://doi.org/10.2478/AMB-2026-0035

7. Angelov K, Nachev N, Yordanov E, Rangelov A, Hristov E, Khayat N, Sharkov A, Zlatarov A, Dyulgerov T. Let's not forget that there is a pancreas in the abdomen – a literature review on pancreatic cancer. (2026) Acta Medica Bulgarica, 53 (1), pp 223-231. https://doi.org/10.2478/AMB-2026-0034

8. Angelov K, Nachev N, Yordanov E, Stoyanova S, Rangelov A, Khayat N, Sharkov A, Zlatarov A, Dyulgerov T. A narrative review study summarising and interpreting the existing literature on the diagnosis and treatment of small bowel tumours. (2026) Acta Medica Bulgarica, 53 (1), pp 216-222. https://doi.org/10.2478/AMB-2026-0033

9. Angelov K, Stoyanova S, Yordanov E, Parvova I, Khayat N, Sharkov A, Zlatarov A, Dyulgerov T. Novelties in locoregional, systemic and multimodal treatment of primary malignant liver tumours. (2026) Acta Medica Bulgarica, 53 (1), pp 206-215. https://doi.org/10.2478/AMB-2026-0032

10. Angelov K, Stoyanova S, Yordanov E, Parvova I, Khayat N, Sharkov A, Zlatarov A, Dyulgerov T. Integration of genomic features, immunotherapy and targeted agents in the treatment of gallbladder and bile duct cancer – a review. (2026) Acta Medica Bulgarica, 53 (1), pp 200-205. https://doi.org/10.2478/AMB-2026-0031

11. Kostadin Angelov, Nikolay Nachev, Emanuil Yordanov, Nabil Hayat, Arkadi Sharkov, Alexander Zlatarov, Tihomir Dyulgerov, Etiopathogenetic, clinical-diagnostic and therapeutic approaches to oesophageal cancer - "State of the art", (2026). Nursing, 58(1) 33-37. ISSN 1310-7496

VIII.2. PUBLICATIONS PUBLISHED IN NON-REFEREED JOURNALS WITH SCIENTIFIC REVIEW OR PUBLISHED IN EDITED COLLECTIVE VOLUMES

12. Tsvetelina Paycheva, Kostadin Angelov, Vasil Pavlov and Svilen Maslyankov, Multimodal approach for metastatic colorectal cancer A clinical model. Case report, International Journal of Surgery and Medicine, 2019, International Journal of Surgery and Medicine (2019) 5(4):218-222

13. Angelov, K. Innovative surgical techniques for malignant diseases of the gastrointestinal tract. Contemporary Medicine (ISSN 1311- 9982), 2025; LIX(1-2):12-24

14. Angelov, K. Epidemiology of gastrointestinal oncological diseases in Bulgaria. Yearbook of Hospital Pharmacy (ISSN print: 2367-8763, ISSN online: 2603-3852), 2026;12(1):@-@ doi: 10.14748/ahp.v12i1.104.. (accepted for publication)

15. Angelov, K. Modern strategies and new health technologies in the surgical treatment of oncological diseases of the gastrointestinal tract. Yearbook of Hospital Pharmacy (ISSN print: 2367-8763, ISSN online: 2603-3852), 2026;12(1):@-@ doi: 10.14748/ahp.v12i1.104. (accepted for publication)