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Cost, Cost-effectiveness and Survival Impact Assessment for A Better Management of Colorectal Cancer Patients: A Single Centre Comprehensive Analysis

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ABSTRACT

Background & Aims: The world healthcare systems are currently challenged by the accumulating burden of colorectal cancer (CRC), and cancer registries represent an important segment for prevention and developing management plans, being useful in providing data regarding incidence, mortality, survival, exposure to carcinogens, lifestyle. Retrospective data from CRC patients in Romania was used to assess survival impact, costs, and cost-effectiveness considering three crucial aspects: pharmacology, chemo-/radio-therapy, and hospitalization for care and management of these patients.
Methods: 423 CRC patients from the Institutional Cancer Registry of the Prof. Dr. Ion Chiricuta Institute of Oncology in Cluj-Napoca, Romania were included in the cost analysis. For the assessment of cost efficiency of the primary treatment strategy, we collected data regarding direct medical costs associated with surgery, radiotherapy and medication, as well as the afferent day or continuous hospitalization, for each patient. For the cost-effectiveness analysis we used the method of estimation of incremental cost-effectiveness ratio.
Results: No compelling differences regarding survival time were observed in different therapeutic options per CRC stage. Substantial differences in cost effectiveness among therapeutic options in the same stage of several thousand Euros in stages I-III, while for stage IV, the ICER was more than 100,000 Euros per life saved.
Conclusions: Systematic evaluation of costs, cost-effectiveness, and survival impact, helps healthcare systems can make informed decisions to improve the management of colorectal cancer patients, optimizing outcomes while minimizing financial burden.

Key words: colorectal cancer – cost-effectiveness – treatment – survival – management.

Abbreviations: ACER: average cost-effectiveness ratio; CH: surgery; CH+S: surgery+systemic treatment (adjuvant chemo-/radio-therapy); CT: chemotherapy; CRC: colorectal cancer; ICER: incremental cost-effectiveness ratio; IOCN: Institute of Oncology Cluj-Napoca Romania; OS: overall survival; RT: radiotherapy; S: systemic treatment (adjuvant chemo-/radio-therapy); SDI: social development index; €: Euros.

INTRODUCTION

According to the Global Cancer Observatory, colorectal cancer (CRC) is the third most diagnosed cancer while being the second cause of mortality worldwide, with 1,926.425 (9.6% of total cancer cases) new cases and 904 019 (9.3%) deaths in 2022 [1]. Although the 5-year survival for all CRC patients is 65.1%, according to the National Cancer Institute - SEER Program Colorectal Cancer, survival time is steadily determined by stage, as the 5-year survival rate in stage IV CRC is crucially worse, down to 15.1% [2]. The incidence of CRC appears to vary geographically, with higher incidence rates in wealthy countries, while low-income countries registered lower incidence rates [3]. On the other hand, in countries with high social development index (SDI), incidence appears to be stable over the years, while mortality rates are reduced compared to various countries that are classified as middle- and low- SDI, where there is an increase in the age-standardized incidence rates in CRC patients [4]. This trend of increased incidence of lifestyle-related pathologies is a clear indicator of the transformation of developing countries and embracing a more Western lifestyle, which is, among others, defined by an unhealthy diet, sedentarism, smoking, and alcohol consumption [5, 6].

The world healthcare systems are currently challenged by the accumulating burden of CRC, and cancer registries represent an important segment for prevention and developing

management plans, being useful in providing data regarding incidence, mortality, survival, exposure to carcinogens, lifestyle etc. [7]. Considering the three types of sources for survival data – clinical trials, hospital-based follow-up studies, and cancer registries – the methods of survival estimation may differ, as in clinical trials, an assessment of overall/progression-free survival is performed to evaluate the efficiency of various therapeutic approaches, in hospital-based follow-up studies survival analysis is done considering the services and reatments offered by a particular department [8]. In a recent study focused on examining the survival rates of CRC patients in population-based cancer registries, it was observed that the 5-year overall and relative survival rate varied depending on different factors, such as tumor site, age, gender, and geographical region, indicating the need for screening and prevention of CRC programs to ensure the basis for comprehensive clinical research [7].

Moreover, existing data indicates that incidence increases with age, the majority of cases (80%) being diagnosed in patients 55 years and older [1]. Considering global trends regarding demographic aging as well as population growth, an expansion of the number of new CRC cases is expected in the next decades [9]. It is believed that one in 24 persons (one in 29 women and one in 19 men) are at risk of developing CRC, while the chances of dying of CRC are highest in Eastern and Central Europe (one in 36 females, one in 20 males, and one in 28 for both sexes combined). Since 90% of new cases and 92% of CRC related deaths affect people over the age of 50, it is clear that colorectal cancer has become a public health issue, with a serious socioeconomic burden [10]. The financial burden is also experienced at a more generalized level, since the care for an oncological patient involves high costs for hospitalization, treatment, medical procedures and personnel, which grow proportionally with the complexity of the case which, is in direct relation with the advanced stages in which CRC is usually diagnosed [11]. A recent study shows that in 2018 the costs for managing CRC at European level added up to a staggering 19 billion Euros (€), which translates into an enormous economic burden for the health system, the patients and their families [12].

Environmental and lifestyle risk factors for developing CRC are age, gender, smoking, alcohol consumption, diabetes, obesity, consumption of processed and red meats, and a sedentary life lackng phisical activity [13]. Along with the lifestyle risk factors, there are also various genetic factors that increase the predisposition of an individual of developing CRC during their lifetime [14]. It is estimated that one third of CRC appears as a consequence of familial clustering, although only about 5-16% of CRC cases are correlated with germline pathogenic mutations in genes associated with predisposition to CRC [15-17]. Prevalence of genetic predisposition appears to be higher in younger patients, reports indicating a prevalence of 16-33% of germline mutations in CRC patients aged 50 and less [18, 19].

Treatment options in the management of CRC include surgery, chemo- and radio-therapy, immunotherapy, stoma construction, as well as targeted compounds [20]. The technical progress and improvements achieved in the last decades led to considerable enhancements in the detection and treatment of CRC, reflected in a better survival and lower mortality rates of these patients [21]. Still, the use of modern technologies and new high-priced therapeutic compounds entails substantial costs associated with CRC management, constraining policymakers to ensure adequate care for these patients considering, at the same time, an effective use of the limited healthcare budget [22].

In this context, the present study used retrospective data from CRC patients in Romania as means to assess survival impact, costs, and cost-effectiveness considering three crucial aspects: pharmacology, chemo-/radio-therapy, and hospitalization for care and management of these patients.

METHODS

Study Population

The present study was approved by the institutional Ethics Committee of Iuliu Hatieganu University of Medicine and Pharmacy (UMPh), no. 102/20.06.2018 and of IOCN no. 5615/13.06.2018. A total of 492 patients diagnosed between January 1, 2016, and December 31, 2018, with invasive CRC were identified in the institutional cancer registry of the Prof. Dr. Ion Chiricuta Institute of Oncology Cluj-Napoca (IOCN) Romania. The registry records demographic data (date of diagnosis, gender, age, residence at diagnosis, date of death), data regarding the primary tumor (site, morphology, grade, stage) as well as treatment data, as shown in Table I. We considered all cases with ICD-O-3 topography code from 18.0 to 20.9. For the cost analysis, we excluded 56 cases diagnosed in IOCN but did not receive any treatment within

Table I. Demographic and clinico-pathological characteristics of CRC patients included in the study

Characteristics		CRC cohort (n=423), n (%)
Age	Mean - 62.8 years Median – 64 years	
Gender	Male	271 (64.1)
	Female	152 (35.9)
Geographical region	Rural	171 (40.4)
	Urban	252 (59.6)
Stage	I	28 (6.6)
	II	88 (20.8)
	III	234 (55.3)
	IV	73 (17.3)
Grade	1	95 (21.7)
	2	251 (59.3)
	3	27 (6.4)
	4	2 (0.5)
	X	51 (12.1)
Histology	Adenocarcinoma, FAI	284 (67.1)
	Adenocarcinoma, tubular	47 (11.1)
	Adenocarcinoma, tubulovilous	43 (10.2)
	Adenocarcinoma, mucinous	22 (5.2)
	Adenocarcinoma, intestinal type	16 (3.8)
	Carcinoma, signet ring cell	3 (0.7)
	Adenocarcinoma, mixed subtypes	2 (0.5)
	Malignant neoplasm	2 (0.5)
	Adenocarcinoma, colloid	1 (0.2)
	Adenocarcinoma, papillary	1 (0.2)
	Carcinoma, cribiform	1 (0.2)
	Carcinoma, undifferentiated	1 (0.2)

IOCN. Additionally, we have excluded 13 cases with missing data regarding stage. Hence, 423 patients were included in the cost analysis. To analyze the cost efficiency of the primary treatment strategy, we collected data regarding direct medical costs associated with surgery, radiotherapy and medication, as well as the afferent day or continuous hospitalization, for each patient, from the information system of IOCN.

Cost-effectiveness Analysis

To perform a cost-effectiveness analysis, we used the method of estimation of incremental cost-effectiveness ratio (ICER) by Bang et al. 2012 [23]. Survival time was considered the measure of the effectiveness of the treatments compared. In the present study, ICER was calculated as the ratio of the difference in costs (C) to the difference in effectiveness (E) between different competing treatment strategies, similar to the method used by Onisim et al. (2019) [24]. Given the asymmetry generated in cost distribution, as a means to estimate the ICER value, we used the mean and median of costs and effectiveness using the following formula for ICER:

$$\mathrm{ICER}_{\mathrm{median}}=\frac{median\ (C_{T1})-median(C_{T2})}{median(E_{T1})-median\ (E_{T2})}$$

$$\mathrm{ICER}_{\mathrm{mean}}=\frac{mean\ (C_{T1})-mean(C_{T2})}{mean(E_{T1})-mean\ (E_{T2})}$$

The cost-effectiveness plane was used to explain ICER values. An estimation of average cost-effectiveness ratio (ACER) was performed asses the cost per year of survival per treatment type. The formula used for ACER was the following:

$$\mathrm{ACER}_{\mathrm{T1}}=\frac{median\ (C)}{median(E)}$$

$$\mathrm{ACER}_{\mathrm{T2}}=\frac{mean\ (C)}{mean(E)}$$

Statistical Methods

For the survival analysis we considered the overall survival time of patients and was defined as the time between diagnosis and death or last follow-up (31 august 2022) and we used the Kaplan-Meier survivor estimate. We assessed the significance of the difference in survival between patients using the Log-rank test. Statistical analysis was performed with STATA Statistical Software: Release 15.1 (College Station, TX: StataCorp LLC). The clinical characteristics are summarized using descriptive statistics. Association between two categorical variables was assessed using Pearson's chi-square test. P=0.05 was used for all two-sided statistical tests, and a test result was considered significant when p≤0.05.

RESULTS

Descriptive Statistics

Table I summarizes demographic and clinico-pathological characteristics of the 423 CRC patients in the study cohort. The cohort included individuals with a mean age of 62.8 years. Most of these patients were males (64.1%) and came from an urban geographical area (59.6%). Colorectal cancer patients were diagnosed with stages I-IV, while more than half were stage III (55.3) at the time of diagnosis. Regarding tumor grade, most of the patients (59.3%) had grade 2 No. of patients (%), moderately differentiated CRC tumor cells tissues. In terms of histology, adenocarcinoma FAI was the most common histological type (67.1%).

One initial analysis was to observe if there are any correlations between the stage at diagnosis and geographical region of residence in CRC patients (Table II). Pearson chi2 p = 0.232, indicating no correlation between stage at diagnosis and residence status in our cohort of CRC patients.

Table II. Distribution of patients diagnosed in stages I-IV considering the geographical region of residence (rural/urban).

Stage	Rural, n (%)	Urban, n (%)
I	7 (4)	21 (8.3)
II	41 (24)	47 (18.6)
III	95 (55.6)	139 (55.2)
IV	28 (16.4)	45 (17.9)

Cost-efficiency for Each Treatment Approach in CRC Stages I-IV

The treatment approach for each patient was considered according to stage, established protocols and particular factors (Table III). In stage I, surgery (CH) was the treatment of choice, but in some cases, systemic treatment (S) was added (adjuvant chemotherapy and/or radiation therapy). We performed a cost-efficiency analysis between surgery alone and surgery plus systemic therapy. There are no significant differences regarding the frequency of each treatment within each age group (Pearson chi2 p = 0.261).

In stage II patients, surgery followed by adjuvant chemotherapy (CT) was the most frequent treatment. We decided to analyze the cost-efficiency of chemotherapy and surgery compared to surgery + radiation therapy (RT). There are no significant differences regarding the frequency of each treatment within each age group (Pearson chi2 p = 0.627).

In stage III patients, the most frequent choice was neoadjuvant chemotherapy along with radiation therapy, followed by surgery with lymphadenectomy (neoCT RT +CH). Yet, in certain cases, surgery was performed first (CHfirst + CT + RT). We analyzed the cost efficiency of these 2 treatment approaches. There are no significant differences regarding the frequency of each treatment within each age group (Pearson chi2 p = 0.403).

In stage IV patients, systemic therapy is the accepted choice, but there are cases when surgery could add benefits in terms of survival. In our assessment, we observed that there are no significant differences regarding the frequency of each treatment within each age group (Pearson chi2 p = 0.696).

Survival Statistics

At the end of the follow-up period, we recorded 221 (52.3% of patients) deaths, while 202 (47.7%) patients were still alive (Table IV). Overall, the median survival time was 47.6 months (95%CI: 44.76 – 49.81).

The analysis regarding overall survival (OS) considering stage and treatment of choice revealed that worse survival

Table III. Statistics regarding treatment strategies in CRC patients stages I-IV

Stage	Treatment	Age group (years)			Total/ stage
		≤59, n (%)	60-69, n (%)	≥70, n (%)	
Stage I	CH	0 (0)	5 (41.7)	5 (50)	10 (35.7)
	CH+S	4 (66.7)	4 (33.3)	2 (20)	10 (35.7)
	S	2 (33.3)	3 (25)	3 (30)	8 (28.6)
Stage II	CH+CT+/-RT	21 (70)	23 (79.3)	20 (69)	64 (72.7)
	CH +RT (nonCT)	9 (30)	6 (20.7)	9 (31)	24 (27.3)
Stage III	CHfirst + CT + RT	23 (30.3)	22 (23.9)	22 (33.3)	67 (28.6)
	neoCT RT +CH	53 (69.7)	70 (76.1)	44 (66.7)	167 (71.4)
Stage IV	CH+/- CT+RT	14 (45.2)	10 (34.5)	5 (38.5)	29 (39.7)
	CT+/-RT - nonCH	17 (54.8)	19 (65.5)	8 (61.5)	44 (60.3)

CH: surgery; CH+S: surgery+systemic treatment (adjuvant chemo-/radio-therapy); S: systemic treatment (adjuvant chemo-/radio-therapy); CT: chemotherapy; nonCT: surgery with no chemotherapy; CHfirst: chemotherapy before surgery; neoCT RT+CH: neoadjuvant chemo-/radio-therapy before surgery; CH+/- -with/without surgery; nonCH: no surgery.

Table IV. Survival statistics by in CRC patients by stage up to August 2022

Stage	No. of patients alive, n (%)	No. of deaths, n (%)	Total
I	22 (78.5)	6 (21.5)	28
II	45 (51.1)	43 (48.9)	88
III	129 (55.1)	105 (44.9)	234
IV	6 (8.2)	67 (91.8)	73
Total	202 (47.7)	221 (52.3)	423

time is encountered in patients diagnosed with stage IV, with no significant differences determined by treatment of choice. Mean and median survival time was 24.02 and 17.6 months in CH+- CT+RT, while in CT+/-RT - nonCH, it was 24.13 and 17.88, respectively. As expected, survival time decreases with stage, with median survival time being 52.5 months in stage I patients who underwent only surgery and 55.5 in CRC patients who were treated with surgery and some form of systemic treatment. 49.88 and 46.82 months were the median survival time in stage II patients who underwent CT and nonCT treatments. Interesting observations were made in stage III, where median survival time in CHfirst was 45.17 months. In comparison, in neoadjuvant chemo-/radio-therapy before surgery it was 52.6 months, more than in stage II patients and stage I patients treated exclusively surgical.

Considering the results of the Log-rank test, the difference in survival times between stages I, II, III, and IV is statistically significant ($p<0.001$), with patients diagnosed with stages IV having the worst survival time (Fig. 1).

The analysis regarding costs is detailed in Table VI. We observed differences in median costs regarding stage and type of treatment followed by CRC patients. In stage I, cost values in CH vs. CH+S/S were 1180.77€ vs. 2249.19€; in stage II cost values in CH+CT+/-RT vs. CH +RT (nonCT) were 1437.43€ vs. 2599.41€; in stage III cost values in CHfirst + CT + RT vs. neoCT RT +CH were 1387.19€ vs. 2747.37€; in stage IV the cost values in CH+- CT+RT vs. CT+/-RT - nonCH were 1474.55€ vs. 5574.3€. The results indicated that incremental cost increased with stage, being 1068.42€ in stage I, 1161.97€ in stage II, 1360.18€ in stage III, and an extensive increase of 4099.74€ in stage IV. Expressed in years of survival, the effectiveness is 0.25 years in stage I, 0.26 years in stage II, 0.62 years in stage III, and 0.02 years in stage IV.

These results were used in the cost-effectiveness analysis of treatment in different stages of CRC. Therefore, we assessed the cost values with the effectiveness of each treatment type/stage measured in survival time (years). The median and mean ICER values were calculated, and in stage I, the values obtained

Table V. Survival time statistics by stage and the type of primary treatment

Stage		Cases	Mean (months)	95% CI	Median (months)	95% CI
Stage I	CH	10	43.86	24.52 – 63.19	52.52	8.23 – 68.08
	CH+S/S	18	49.81	39.41 – 60.20	55.55	46.64 – 63.44
Stage II	CH+CT+/-RT	64	46.83	41.77 – 51.90	49.88	46.62 – 56.85
	CH +RT (nonCT)	24	44.82	34.98 – 54.66	46.82	32.27 – 60.34
Stage III	CHfirst + CT + RT	67	41.47	36.41 – 46.52	45.17	41.74 – 52.86
	neoCT RT +CH	167	47.96	44.46 – 51.45	52.60	48.94 – 55.73
Stage IV	CH+- CT+RT	29	24.02	16.16 – 31.89	17.60	11.99 – 26.37
	CT+/-RT - nonCH	44	24.13	17.80 – 30.47	17.88	11.48 – 24.79

For abbreviations see Table III.

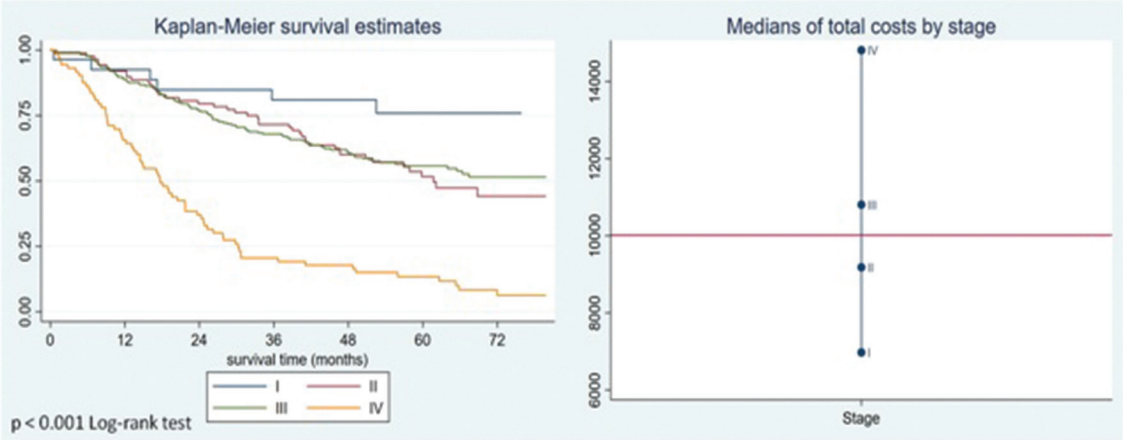

Fig. 1. (A) Survival time distribution between the four (I-IV) stages CRC tumors; (B) Median costs (EUR) by CRC tumor stage.

were 4,231.37 € and 4,652.45 € per year of survival; in stage II 4,556.76 € and 30,543.43 €; in stage III 2,196.78 € and 5,440.11 €; stage IV 17,5703.29 € and 547,334 €. In addition, considering treatment type, we calculated the ACER for each treatment type/stage. Calculated based on medians ACER was lower in stage I CH (269.79 €/year of survival), in stage I CH+S/S was 485.87 €, with similar values in stage II CH +RT (nonCT) and stage III CHfirst + CT + RT (368.42 € and 368.53 €) and in stage II CH+CT+/-RT and stage III neoCT RT +CH (625.36 € and 626.78 €), and higher values in stage IV CH+- CT+RT (1005.38 €) and CT+/-RT - nonCH (3741.14 €).

DISCUSSION

Various studies and other data suggest improvement in the overall survival of CRC patients in the last two decades [2, 25]. On the other hand, the countries which are part of the Belt and Road Initiative, which include countries with different SDI (although the majority are considered low- and middle-SDI) across Europe (including Romania), Middle East, Africa, and Asia, account for about 80% of new CRC cases and more than 83% of cancer-related deaths worldwide [26, 27]. In a recent study published by Gorasso et al. [28] regarding costs associated with colorectal cancer in Belgium, the researchers revealed that average incremental costs for colon and rectal cancer were 4,030 €, respectively 6,309 €. In addition, their results indicated that costs for CRC exceeded the amount of 300 million € in 2018, being the third most costly cancer site after lung and breast [28]. A similar study performed in the United States indicated CRC as the second most costly cancer site after breast, with total national costs of $21 billion in 2015 [29]. Data regarding costs of cancer in Europe and OECD/WHO countries is available in various studies that appraised costs [30, 31] and although broad estimates regarding health status in Romania can be found in one of them, it is clear that enhanced estimates of these costs can be obtained via accessing regional or institutional cancer registries to assess costs related to CRC management in Romania. Surgical

Table VI. Cost analysis statistics by stage and the type of primary treatment in Euros (€)

Stage	Stage I		Stage II		Stage III		Stage IV	
	CH	CH+S/S	CH+CT+/-RT	CH +RT (nonCT)	CHfirst + CT + RT	neoCT RT + CH	CH+- CT+RT	CT+/-RT - nonCH
Median cost	1180.77	2249.19	1437.43	2599.41	1387.19	2747.37	1474.55	5574.30
Incremental cost	1068.42		1161.97		1360.18		4099.74	
Median survival time (years)	4.38	4.63	3.90	4.16	3.76	4.38	1.47	1.49
Effectivness	0.25		0.26		0.62		0.02	
ICER (median)	4231.37		4556.76		2196.78		175703.29	
ACER (median)	269.79	485.87	368.42	625.36	368.53	626.78	1005.38	3741.14
Mean cost	1054.67	3361.51	1480.84	6596.86	4461.36	7403.56	9021.39	24337.33
Incremental cost	2306.84		5116.02		2942.19		15315.94	
Mean survival time (years)	3.66	4.15	3.90	3.74	3.46	4.00	2.00	2.01
Effectivness	0.50		-0.17		0.54		0.01	
ICER (mean)	4652.45		-30543.43		5440.11		547334.00	
ACER (mean)	288.56	809.84	379.46	1766.23	1290.97	1852.43	4506.94	12103.11

ACER: average cost-effectiveness ratio; ICER: ICER: incremental cost-effectiveness ratio. For the rest of abbreviations, see Table III.

resection is applied as the first strategy for cure in stage I, II, and III CRC (this strategy is also applied for patients with resectable distant metastases) when neoadjuvant therapy is not considered in the treatment approach [32-34]. As a means to reduce or overcome recurrence and improve the outcomes of CRC patients, adjuvant postoperative chemotherapy is usually applied in stage III patients and selected stage II patients. In stage IV CRC treatment usually is first-line chemotherapy [35, 36]. Assessing the cost, cost-effectiveness, and survival impact of management strategies is crucial for optimizing care for colorectal cancer patients considering expenses directly related to treatment such as surgery, chemotherapy, radiation therapy, and hospitalization; expenses indirectly related to treatment, such as loss of productivity due to illness, transportation costs for medical appointments, and care giving expenses; consideration of costs over the patient's lifetime, including surveillance, management of treatment-related complications, and supportive care. In addition, we aimed to evaluate the impact of different treatment modalities on patient survival considering overall survival rates as long-term follow-up is essential to assess the durability of treatment effects and late complications.

In this concern, the present study aimed to use retrospective data in the institutional cancer registry of the IOCN is a regional oncology institute in Romania that provides services for patients in the North-Western region of Romania while highlighting the need for the development of a comprehensive and well-organized national cancer registry in Romania. Therefore, we estimated the outcomes of CRC patients diagnosed and treated in IOCN in different stages. We evaluated two to three therapeutic approaches for each CRC stage in this concern. Most of the patients were diagnosed in stage III (55.3%). We also observed that there are no significant differences regarding the frequency of each treatment within each age group. When we assessed survival time, we observed that in patients diagnosed is stage I, the most efficient treatment strategy appeared to be surgery coupled with systemic treatment and or systemic treatment (CH+S/S), with a median survival time of 55.55 months. As expected, in stage II, median survival was superior in patients who underwent chemotherapy – 49.88 months; in stage III, patients who followed neoadjuvant therapy before surgery had a median survival time of 52.6 months, more than patients diagnosed in stage II, while in stage IV survival time drops dramatically to about 17 months survival in both groups of treatment strategy (Table V).

In this study we addressed the subject of cost-effectiveness of different therapeutic strategies applied in Romania in CRC stages I-IV. We observed that the costs were higher in stage IV CRC, with the most expensive therapeutic option in this stage being CT+/-RT - nonCH (5,574.3 €). This might be due to the fact that patients with advanced disease who are not eligible for surgery might need longer periods of time for hospitalization and palliative chemotherapy [37]. After CT+/-RT - nonCH, the second most costly therapeutic option was neoCT RT +CH in stage III (2,747.37 €). Similarly, high costs associated with this group might be attributed to more aggressive surgical procedures that are followed by many days of hospitalization, as well as higher rates of post-surgical complications [24]. Comparing the cost assessments with the above analysis regarding survival, it is obvious that higher costs do not guarantee improved survival in stage IV CRC patients. Considering these aspects, we calculated the ICER, which indicates differences among therapeutic options in the same stage and obtained a median value of 4,231.37 € for stage I, 4,556.76 € for stage II, 2,196.78 € for stage III, and 17,5703.29 € for stage IV per life saved. The cost analysis was further enhanced by estimating the ACER. Considering median and mean values, surgical resection alone (stage I) is the most cost-effective option (269.79 € and 288.56 €/year of survival). In contrast, the least cost-effective therapeutic option was CT+/-RT - nonCH (stage IV) – 3,741.14 €, respectively 12,103.11 €/year of survival. We also observed differences in ACER in stage II and III different treatment approaches that indicate that therapeutic strategies involving adjuvant chemo-/radio-therapy before and after surgical resection (CT and neoCT RT +CH) are less cost-effective than those in which no chemo-/radio-therapy is applied before surgery (CH +RT (nonCT) and CHfirst + CT + RT).

CONCLUSIONS

In this regional study we observed that no compelling differences regarding survival time were observed in different therapeutic options per CRC stage. On the other hand, there are substantial differences in cost effectiveness among therapeutic options in the same stage of several thousand Euros in stages I-III, while for stage IV, the ICER was more than 100,000 € per life saved. By systematically evaluating costs, cost-effectiveness, and survival impact, healthcare systems can make informed decisions to improve the management of colorectal cancer patients, optimizing outcomes while minimizing financial burden.

Conflicts of interest: None to declare

Author' contributions: A.I.G., C.B, and P.A.A.-C. conceived the study. C.A.C., E.O.M, T.A.P. designed the methodology. I.A.G. collected and analysed the data. A.I.G., C.B. and C.A.C drafted the manuscript. C.B. and I.B.N revised the manuscript. I.C.V, I.B.N., and P.A.A.-C. supervised the study. All authors have read and agreed to the published version of the manuscript.

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