



Wait times to diagnosis and treatment in patients with colorectal cancer in Hungary



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ABSTRACT

Background: Mortality from colorectal cancer (CRC) in Hungary is the highest in Europe. It was the aim of the present study to determine the wait times from first presentation to diagnosis, in a sample of Hungarian patients with CRC, as well as to assess the stages of CRC at diagnosis.

Methods: A retrospective study based on data from 212 patients with CRC in Baranya county was carried out. Data extraction was performed from 26 GP practices and from the database of the University of Pécs Clinical Center. Total Diagnostic Interval (TDI) was determined as the number of days from the first patient-physician consultation with symptoms until the pathologically confirmed date of diagnosis. Total Treatment Interval (TTI) was calculated until the first day of any form of treatment. Statistical analyses, descriptive analysis and analysis of variance, were performed.

Results: A minority (36.8%) of the diagnosed CRC cases were early stage cancers (Stages I-II), while the majority (59.9%) of the cases were diagnosed as advanced stage (Stages III-IV) cancers. The median TDI was 41 days, and the median TTI was 67 days. There was a wide range between minimum and maximum waiting times regarding both diagnosis and initiation of therapy (369–371 days).

Conclusions: Wait times to diagnosis and treatment of CRC in Hungary are similar to Western countries however the ratio of advanced cancers at diagnosis is higher. The cause of late diagnosis may be due to patient delay, indicating the need for implementation of primary and secondary prevention.

1. Background

Colorectal cancer is the second most common cancer and cause of cancer-related death in Hungary [1,2]. Among 32 countries in Europe, where causes of death were assessed, Hungary is leading in CRC-related mortality [3].

The development of CRC takes time: a premalignant lesion requires 10–15 years to transform into a malignant disease [4]. This interval allows for timely detection and successful treatment of the illness [4]. The determining predictive factor for CRC survival has been shown to be the stage of the disease at diagnosis [1,5–7]. Detection of localized stage cancer leads to 5-year survival in 90% of the cases, while metastatic (stage IV) cancer has a dismal 5-year survival rate of only 14% [8].

Delays in setting up the correct diagnosis of CRC are partly due to

patient-related delays and partly to healthcare-related delays. Patients may remain asymptomatic for many months [9] or they may consider their symptoms belonging to a minor comorbidity, which result in patient-related delays [10–12]. The symptoms patients most often present with include bowel-specific symptoms, such as rectal bleeding, abdominal pain and change in bowel habit as well as general symptoms, like loss of weight or appetite and fatigue [8,13,14].

Other barriers in the diagnosis of CRC are healthcare-related. According to a study by Lyratzopoulos et al., one third of patients with CRC have three or more consultations with a GP before they are referred to a specialist, compared with only 17.9% for all cancers [15]. Insufficient diagnostic capacity, including lack of imaging techniques and trained endoscopic professionals add to wait times within health care.

The wait times from onset of symptoms to diagnosis and treatment

Abbreviations: CRC, colorectal cancer; TDI, total diagnostic interval; TTI, total treatment interval; GP, general physician

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have been widely studied in the Western world [16–20]. Some countries have implemented guidelines regarding diagnostic and treatment wait times. The recommended longest interval between referral and diagnosis of CRC is 14 days, with initiation of treatment within an additional 14 days in Denmark [21]. The UK guideline states that cancer patients should have treatment initiated within 2 months of referral by their GPs [22].

Screening of the asymptomatic population for CRC has been shown to reduce mortality in CRC and has proven to be a valuable method for preventing CRC-related deaths therefore CRC screening strategies have been adopted in a number of countries [23–26]. Model screening programs have been conducted with small samples of the Hungarian population since the year 2000 [4] but debate surrounding the adoption of the one- or two-step screening procedures have hindered the implementation of regular screening [3]. To date there is no regular, national screening program for CRC in Hungary.

The dismal morbidity and mortality figures of the Hungarian population regarding CRC have prompted the need for investigations of the underlying causes. Patients suffering from CRC in Hungary are more prone to die as a result of their illness than in any other European country [3].

Although many studies have been conducted in Western countries, data regarding wait times from Central-European countries is extremely limited. Therefore, it was the aim of the current investigation to determine the diagnostic and treatment wait times (TDI and TTI) in a sample of patients presenting with CRC symptoms in Baranya county, Hungary. Our study's goal was to give an overview about the practice and process leading to diagnosis and treatment of CRC by assessing the most common symptoms of patients, referral urgency, the stages of the disease at diagnosis and the wait times to diagnosis and treatment within our healthcare system.

2. Methods

2.1. Study design

A retrospective study was designed and conducted to gather data from GP practices within a 5-year interval (2012.01.01.–2016.12.31.). All GP practices registered in Baranya county in the Southwestern Region of Hungary, were mailed invitations explaining the objectives of the study. From these, 26 independent GP practices were recruited to collect data regarding their patients with colorectal cancer from their databases. Participation in the study was voluntary. Three documents were mailed to the participants: one explaining the procedure, one containing an agreement form and one with a Microsoft Excel Table for the requested data.

2.2. Ethics

The authors obtained approval from the local Ethical Committee (Ethical Approval Number: 6744) to conduct the retrospective investigation.

2.3. Databases

A total of 390 cases were identified as patients with colorectal cancer. Patients younger than 18 years old and those considered as recurrent cases were excluded from the study. After exclusion of patients with incomplete data, there were 212 patients with complete, valid data remaining. All patients were included, who had a diagnosis of some form of invasive colorectal cancer (International Classification of Diseases) within the given time period, meaning diagnoses set 5 years prior to or during the given time period. Additional information (clinical records) was gathered from the University of Pécs Clinical Center's Database, the MedSol by the study investigators.

2.4. Data extraction and analysis

Data extracted from the GPs' and the Clinical Center's database included (1.) demographic characteristics, (2.) symptoms at first visit to the doctor, (3.) urgency of referral, (4.) the speciality of the first doctor to encounter the patient, (5.) the stage of the tumor at diagnosis, (6.) the date of diagnosis and (7.) the date of therapy. The initial date or initial consultation was defined as the day on which a patient had a medical appointment with at least one clinical manifestation of CRC or CRC-related symptom (8.). The first doctor to encounter the patient and to initiate the process of examinations or to refer the patient to an examination (e.g., lab test, ultrasound, colonoscopy) was considered the initial consultant and was either the patient's GP, the physician at the Emergency Room or any doctor from another speciality. Referral was considered urgent if the initial consultation was at the Emergency Room or if the consulting GP or other specialist judged the case of the patient was urgent. This decision was based on the clinical assessment of the individual patient and not on a certain guideline. All other cases were considered as non-urgent referrals. The staging of the tumor was based on the histology, CT scan and formal Oncoteam opinion, in accordance with the 8th European Society for Medical Oncology guidelines regarding lower gastrointestinal cancers. Review of the accurate staging of the tumors was performed by a clinical Oncologist. The date of the diagnosis was the day when the cancer was pathologically confirmed. The treatment date was considered the first day of any form of treatment of the tumor, meaning surgical or oncological (chemo-, radiotherapy) treatment with the intention of reducing the size of the tumor. Checking and calculation of the data were performed by two independent investigators to ensure accuracy of data.

2.5. Statistical analysis

Statistical analysis was undertaken using IBM SPSS Statistics for Windows version 24. We performed descriptive analysis (Frequency and Crosstab) and analysis of variance. Statistical significance was assessed by Wilcoxon and Kruskal-Wallis tests. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient and clinical characteristics

Data from 212 patients with invasive colorectal cancer from Baranya county were evaluated. Gender distribution was 56.1% male and 43.9% female. Most of the patients were between 61–70 years of age when they were diagnosed with CRC. 53.3% of the patients had colon cancer and 42.5% rectal cancer.

A minority (36.8%) of the diagnosed CRC cases were stage I-II cancers, while the majority (59.9%) of the cases were diagnosed as advanced stage (Stages III-IV) cancers. A substantial share (22.6%) of the patients had distant organ metastases at the time of diagnosis (Table 1).

Urgency of referral to diagnostic procedures by the first physician to examine the patient was assessed. The number of urgent (46.2%) versus non-urgent (52.4%) referrals was split almost equally (Table 1).

The proportion of referrals made by GPs, ER physicians and other specialists was also evaluated. The majority (59.9%) of the patients visited their GPs with their symptoms and were referred by their GPs to further examinations. Almost a fourth of the patients suffered urgent symptoms, such as acute bowel obstruction, and were examined and referred first by an ER physician. A smaller percentage (16.5%) was examined and referred initially by another specialist, who was treating the patient for a disease other than CRC (Table 1).

Table 1
Patient and clinical characteristics.

	Number of cases (%)	
Gender		
Men	119 (56.1)	
Women	93 (43.9)	
Age (years)		
28–50	13 (6.1)	
51–60	49 (23.1)	
61–70	75 (35.4)	
71–80	53 (25.0)	
80+	22 (10.4)	
Tumour location		
Colon	113 (53.3)	
Rectum	91 (42.9)	
Unknown	8 (3.8)	
Tumour stage		
I	15 (7.1)	} }78 (36.8)
II	63 (29.7)	
III	79 (37.3)	} }127 (59.9)
IV	48 (22.6)	
Unknown	7 (3.3)	
Referral urgency		
Urgent	98 (46.2)	
Non-urgent	111 (52.4)	
Unknown	3 (1.4)	
Initial examination and referral		
GP	127 (59.9)	
Physician at the ER	49 (23.1)	
(Other)Specialist	35 (16.5)	
Unknown	1 (0.5)	

3.2. Symptoms

The symptoms indicative of CRC that patients presented with at the first consultation (GP, ER physician, other specialist) were assessed. Some patients had two or more symptoms at this initial visit. 30.7% of the patients suffered from abdominal or rectal pain and over a quarter (26.9%) of the patients had blood in their stool. Almost every fifth patient complained of weakness/fatigue (19.3%), weight loss (18.4%) or diarrhea (18.4%). A smaller share of the patients had noticed a change in their bowel habits (11.8%) or „felt full” in their abdomen (9%). Only 4% of the patients were asymptomatic at the first patient-doctor consultation (Table 2).

3.3. Total diagnostic interval (TDI) and total treatment interval (TTI)

Based on data extracted from the GPs' and the Clinical Center's databases, we calculated the number of days from the date the patient first presented with his/her symptoms at a physician's office or clinic

Table 2
Symptoms at onset of CRC.

Symptoms	Number of cases (%) [*]
Abdominal/rectal pain	65 (30.7)
Blood in stool	57 (26.9)
Weakness/Fatigue	41 (19.3)
Weight loss	39 (18.4)
Diarrhea	39 (18.4)
Change in bowel habits	25 (11.8)
“Feeling full” in abdominal area	19 (9.0)
Constipation	11 (5.2)
Asymptomatic	9 (4.2)
Pain indicative of metastases (e.g. back pain, headache)	3 (1.4)
Nausea, vomiting	3 (1.4)
Other symptoms	22 (10.4)

* Percentages do not add up to 100 because many patients experienced multiple symptoms at onset.

Table 3
Time-to diagnosis (TDI) and time-to treatment (TTI).

TDI	Days
Minimum	2
Maximum	371
Range	369
Mean	53.68
Std. Deviation	52.43
Median	41
TDI	Number of cases (%)
TDI ≤ Median	106 (50.7)
TDI > 60 days	61 (29.2)
TDI > 90 days	32 (15.3)
TDI > 120 days	17 (8.1)
TTI	Days
Minimum	1
Maximum	372
Range	371
Mean	78.81
Std. Deviation	61.94
Median	67
TTI	Number of cases (%)
TTI ≤ Median	97 (50.8)
TTI > 60 days	108 (56.5)
TTI > 90 days	62 (32.5)
TTI > 120 days	33 (17.3)

until the date the CRC was pathologically confirmed (TDI). The number of days that elapsed between the first presentation with symptoms to the first day of therapy, which included any form of treatment (surgical or oncological), was considered the total treatment interval (TTI). TDI and TTI were determined (Table 3).

The median wait time to diagnosis (TDI) was 41 days, and the median wait time to commencement of treatment (TTI) was 67 days. There was a wide range between minimum and maximum waiting times regarding both diagnosis and initiation of therapy. A third of the patients had to wait more than 60 days, while 15.3% of the patients waited more than 90 days for a pathologically confirmed diagnosis. Regarding initiation of treatment, 32.5% of the patients waited more than 90 days for treatment, and almost fifth of the patients had a TTI of over 120 days (Table 3).

GP-TDI and GP-TTI were calculated if the first physician to encounter the patient was a GP, and S-TDI and S-TTI, if the first referring physician was an ER physician or any other specialist (Table 4).

When TDI and TTI were calculated based on the specialty of the doctor giving the first referral, we found, that patients referred by their GP-s waited longer for diagnosis and treatment (GP-TDI, GP-TTI), than patients first examined by an ER physician or another specialist (S-TDI, S-TTI). The median GP-TDI was 52 days compared with 19 days for S-TDI. GP-TTI was more than twice as long (86 days) compared to S-TTI, where the lagtime to treatment was only 38 days (Table 4).

4. Discussion

With effective screening methods, CRC is one of the few cancers which can be prevented [27]. Randomized clinical trials proved that if people with average-risk were screened, it led to decreased incidence and mortality from CRC [24,28,29]. Studies have also shown that the determining prognostic factor for CRC is the stage of the tumor at the time of detection [5–7]. Since the morbidity and mortality rates from CRC in Hungary are extremely high, we sought to investigate possible underlying causes. We found that the majority (59.9%) of the patients were diagnosed with advanced stage cancers. In comparison, a study conducted in Spain reported only 42.5% diagnosed with advanced CRC

Table 4

Time to Diagnosis (TDI) and Time to treatment (TTI), if primary contact physician was a GP (GP-TDI, GP-TTI) or if primary contact was an ER or other specialist (S-TDI, S-TTI).

TDI	GP-TDI (days)	S-TDI (days)
Minimum	9	2
Maximum	371	154
Range	362	152
Mean	66.81	32.88
Std. Deviation	57.39	35.26
Median	52.00	19.00
Wilcoxon test	<i>P-value 0.000</i>	
TTI	GP-TTI (days)	S-TTI (days)
Minimum	16	1
Maximum	372	176
Range	356	175
Mean	99.58	45.88
Std. Deviation	64.89	39.47
Median	86.00	38.00
Wilcoxon test	<i>P-value 0.000</i>	

[17]. A lower percentage of 49% with advanced stage CRC was found in a study from the U.S., and an even lower share (17.2%) of Stage III-IV cancers were detected in an investigation in the UK [16,19].

CRC tends to remain asymptomatic for a long time until the cancer has progressed into a more advanced stage [27]. Even when patients do develop symptoms, they often fail to realize alarming signs, such as rectal bleeding, which they attribute to hemorrhoids [10–12]. Approximately a third of the patients in our study presented with abdominal/rectal pain and/or blood in their stool. Our results are similar to data from other countries [17,18,30]. Interestingly, change in bowel habits was reported as one of the most common (16–51.9%) symptoms in a few studies, but it was only present in 11.8% of the Hungarian cases [4,17,30]. Although it is possible that our patients did not experience change in bowel habits often, we question whether the general population in Hungary is adequately educated about noticing symptoms such as change in bowel habits. Since most of the patients consulted their physicians due to pain or weakness (a consequence of progressing anaemia), it is possible that patients had other symptoms previously which they had for some time neglected or not noticed at all.

The majority (59.89%) of the patients in our study consulted their GPs initially with their symptoms, however, this proportion was much smaller compared with studies from other countries, where the first examination and referral of the patient was almost always made by a GP [17,18]. Interestingly, the number of emergency admissions (23.1%) did not differ from emergency admissions in some Western European studies [16,17], which indicates that a higher proportion of patients in Hungary are diagnosed with CRC with referrals from specialists other than GPs or physicians in the ER.

Healthcare-related waiting times, meaning wait times from symptom onset to diagnosis and treatment have been evaluated in many countries of the Western world [16–20]. The shortest time to diagnosis intervals were reported from Canadian, U.S. and Danish studies, ranging from less than one month to 64 days [20,21,31]. Time to treatment intervals were also relatively short according to these reports, between 28–76 days [20,21,31]. Longer TDI-s and TTI-s were found in studies conducted in Spain and the U.K. Median TDI was 91–111 days depending on the place of primary referral in the Spanish study and median provider delay was 119 days in an investigation from the UK [16,17]. The wait times in the Hungarian sample were comparable to wait times recorded in Canada and the US. Median TDI was 42 days and median TTI was 67 days, indicating that at least half of the patients were diagnosed within 1.5 months of symptom onset and commenced therapy within 2.5 months' time. In accordance with previous investigations, TDI and TTI referred by GP-s was significantly

longer than when patients first consulted a specialist with their symptoms [17]. The ranges between maximum and minimum waiting times was very wide (369 days for TDI and 371 days for TTI), which shows that a fourth (23.1%) of the patients needed to wait over 3 months for diagnosis and 49.8% for treatment. In contrast, ranges between diagnostic wait times in investigations from Canada, the U.S., and Spain were narrower, 264, 230 and 223 days, respectively [17,20,31]. Our results imply that although waiting times are fairly short for a large proportion of patients, there are no regular referral pathways within healthcare for Hungarian patients to go through, which leads to great individual differences in health-care related wait times. The factors underlying these differences are unclear but may partly be due to organizational challenges within the Hungarian healthcare system. When patients experience possible symptoms of CRC in Hungary, they turn to GPs working in primary care, who refer them to further examinations (e.g. lab tests) or other specialists (e.g. gastroenterologists), if necessary. GPs can only refer non-urgently to these specialists, urgent referral can only be given to the ER, however exceptions exist, where –on personal request– GPs can directly ask their gastroenterologist colleagues for an earlier appointment. Health coverage is universal and services are accessible to all Hungarian citizens, however private clinics are also available and popular due to shorter wait-times. Since the ranges of wait times were half as wide when patients were referred by ER physicians or other specialists, the data suggests that GPs have unreliable referral pathways within the Hungarian healthcare system. It must be added that the role of patient-related delays in the prolongation of TDI and TTI are also contributing factors.

4.1. Limitations

Several weaknesses of our investigation should be noted. First, the sample size was relatively small and not representative of the Hungarian population. The second limitation was that recorded data at the GP's offices were more prone to inaccuracies than data recorded in the clinical database, therefore collection of reliable information was more difficult. Finally, patients were diagnosed and treated in a university-based clinic, where patients could have been at an advantage regarding wait times than patients diagnosed and treated in other, smaller, more rural settings. The characteristics of the population and health care system are probably heterogeneous across the country. Therefore, different waiting times may be found if a large-scale study was conducted.

5. Conclusions

To our knowledge, our study is the first to evaluate wait times associated with CRC in a Central- Eastern European country. We found that patients' wait times to diagnosis and commencement of treatment in our study were acceptable and comparable with those reported in Western countries. The proportion of patients with advanced stage cancer at diagnosis however, was one of the highest, indicating that patient-related rather than health-care related delays may be to blame for late diagnosis. Lack of nationwide patient education – regarding the prevention of CRC and awareness of CRC-related symptoms – may lead to prolonged patient-related delays. A national colorectal screening program, which could detect CRC at an early stage is also lacking. The observed large differences between individual waiting-times suggest that inequalities exist between access to diagnostic and therapeutic procedures. Absence of predictable patient pathways within the Hungarian healthcare system may be underlying causes. Our investigation also showed that the urgency of symptoms patients presented with at their initial visit and consequently the urgency of referral by their physicians were not indicative of the stage of their tumors. Further studies are needed to confirm the implications of our study's results. Based on our findings, patient- education programs regarding CRC and the implementation of a national screening program appear to

be vital tools if CRC morbidity and mortality rates in Hungary are to be improved.

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Availability of data and materials

The data involved in the current study are available upon request. Anyone who is interested in the information should contact the corresponding author.

Authors' contributions

Concept and design: EP, CsB, ACs; Collection of data: EP, DF, SzB; Data analysis and interpretation: EP, DF, CsB, SzB; Manuscript drafting: EP, CsB, ACs; Final approval of manuscript: EP, CsB, ACs. All authors have read and approved the manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was carried out according to the Good Clinical Practice guidelines of the Helsinki declaration. The study was approved by the local ethics committee (University of Pécs Clinical Center Regional and Institutional Research Ethical Committee, decision: 2017/6744)

Conflicting interests

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